concordance for dichorionic twins (Davis, Phelps, and Bracha 1995); though this work has not yet been replicated in ASD twins, in principle it opens the door to non-genetic interpretations of any concordance figures that have generally been assumed to be indicators of heritable genetics. The authors of this study interpreted their findings as consistent with data on viral infection as a contributor to schizophrenia risk (a possibility also entertained in ASDs (Patterson 2012; Teixeira and Barichello 2012; Atladottir et al. 2012, 2012; Hornig et al. 1999), but one could also consider the possibility of differences in the dichorionic cases in the integrity of the placental barrier.

All of this calls into question the idea that genetics can be presumed to be the 'cause' of autism simply based upon heritability calculations, and upgrades the importance of looking not only at the environment and environmentally vulnerable physiology, but also at acquired mutations. There is certainly progress being made through genetic research to the identification of networks of genes and mechanisms on which genes converge (Voineagu et al. 2011), but environmental mechanisms converge on these mechanisms too (Stamou et al. 2012), and the mechanisms are what drive the impacts.

Genotoxicity

One route through which environmental impacts may influence an organism's status is by changing genes through mutation – that is, by genotoxicity. This has been proposed as a mechanism for the generation of 'de novo' mutations (found in children but not their parents) being found in ASDs (Kinney et al. 2010) and increasingly in other settings as well, making mutations something that needs to be accounted for rather than simply assuming tey are associated with normal, stable variation. Reviews and published scientific papers on genotoxicity and EMF report that both ELF-EMF and RFR exposures can be considered genotoxic – i.e., damaging to DNA – under certain conditions of exposure, including under conditions of intermittent and/or chronic ELF and RFR exposure that are of low-intensity and below current world safety standards (Ruediger 2009; Ivancsits et al. 2005; Diem et al. 2005; Blank and Goodman 2011; Phillips, Singh, and Lai 2009; REFLEX 31 May 2004; Sage and Carpenter 2009; Lai and Singh 2004). Types of genetic damage reported have included DNA fragmentation and single- and double-strand DNA breaks, micronucleation and chromosome aberrations, all of which indicate genetic instability. Genotoxic impacts of EMF/RFR are further reviewed in the BioInitiative Working Group 2007 contribution by Lai as well as in Section 6 of the present Bioinitiative Report {Lai, 2007; Lai, 2012).

The European research program REFLEX (Risk Evaluation of Potential Environmental Hazards From Low-Energy Electromagnetic Field Exposure Using Sensitive in vitro Methods – a 5FP EU project) documented many changes in normal biological functioning in tests on DNA at exposure levels below existing public safety standards(REFLEX 31 May 2004). Some of the key findings included:

- Gene mutations, cell proliferation and apoptosis which are caused by or result in altered gene and protein expression profiles. The convergence of these events is required for the development of all chronic diseases.
- Genotoxic effects and a modified expression of numerous genes and proteins after EMF exposure could be demonstrated with great certainty.
- Genotoxic effects produced by RF-EMF in fibroblasts, HL- 60 cells, granulosa cells of rats and neural progenitor cells derived from mouse embryonic stem cells.
- Response of cells to RF exposure between SAR levels of 0.3 and 2 W/Kg with a significant increase in single- and double-strand DNA breaks and in micronuclei frequency.
- A clear demonstration of increase in intracellular generation of free radicals in HL-60 cells accompanying RF-EMF exposure.
- The observation that the induced DNA damage was not based on thermal effects, which raises concerns about the thermal-based environmental safety limits for ELF-EMF exposure.

These impacts could be contributors to a role for genetics in ASDs that does not derive from only inheritance but also from environmental and epigenetic influences. Moreover, in the light of the great heterogeneity of genetic findings in ASD alongside the documented impacts of EMF/RFR upon many other levels of pathophysiology than simply genetics, it becomes worth reflecting whether genetics might not be the primary problem but instead, in many cases at least, just one of many levels of collateral damage from environmental impacts. Whatever genetic variants a person carries may bias their system toward specific vulnerability, or may contribute more generically by increasing entropy and molecular disorder; in either capacity they may aggravate the situation but may not be part of the main cause.

Contributors to Genotoxicity

Oxidative stress and free radical damage to DNA

Oxidative stress and excessive free radical production are very well known to be potentially genotoxic. They can be a consequence of myriad environmental factors, including but by no means limited to EMF/RFR. The DNA damage that can result could very well be one cause of 'de novo' mutations. Although there is not a consensus at this time about the rates or causes of *de novo* mutations in ASDs, and using present methods of detection are only found in a small percentage of individuals with ASDs, given the potential contribution of environmentally triggered oxidative stress and free radical damage that we know is present in at least large numbers of people with ASDs, a serious investigation of the potential contribution of EMF and RFR to de novo mutations in ASD seems warranted, given the large increase in exposure to these phenomena accompanying the massively increased non-ionizing radiation exposures in daily life due to

electrification and the global saturation of RFR from wireless technologies (BioInitiative 2012 Report, Section 24, Public Health Implications, Sage and Carpenter, 2012).

Challenge to DNA repair mechanisms

Reduced DNA repair may contribute to increased risk of cancers, but it may also contribute to a variety of other diseases and disturbances of growth and development. When the rate of damage to DNA exceeds the rate at which DNA can be repaired, there is the possibility of retaining mutations and initiating pathology. Failure to trigger DNA damage repair mechanisms, or incomplete or failed repair, may be a consequence of a variety of commonplace stressors, including EMF/RFR exposure. A decrease in DNA repair efficiency has been reported to result from exposure to low-intensity RFR in human stem cells, and other cells. Mobile phone frequency GSM exposure at the frequency of 915 MHz consistently inhibited DNA repair foci in lymphocytes (Markova et al. 2005; Belyaev et al. 2005; Belyaev, Markova, and Malmgren 2009). Belyaev, Markova and colleagues (2005) and Markova et al. (2009) reported that very low-intensity microwave radiation from mobile phones inhibits DNA repair processes in human stem cells. A significant reduction in 53BP1 ((tumor suppressor p53 binding protein 1) foci was found in cells exposed to microwave radiofrequency radiation within one hour of exposure. Fibroblast cells were impacted in this fashion but adapted over time, whereas stem cells were similarly affected (inhibited 53BP1 foci) but did not adapt to microwave radiation during chronic exposure (Markova et al. 2005; Belyaev et al. 2005). Additional challenges to DNA repair mechanisms include not only toxicants and other damaging inputs but also nutritional insufficiencies of substances important to the proper functioning of DNA repair mechanisms, including Vitamin D, essential fatty acids, and minerals such as selenium and molybdenum (Christophersen and Haug 2011). The high possibility that various such contributors may combine supports an 'allostatic load' model of environmental injury and genotoxicity. Also note the overlap between nutritional risk factors for oxidative stress and for impaired DNA repair mechanisms. This supports a vicious circle model where the more oxidative damage to the genome, the less the cells will be prepared to deal with it successfully. It can also work the other way around – nutrients can attenuate the degree of damage; instances of this will be discussed in the Melatonin section below.

Chromatin condensation

Chromatin condensation is another hallmark of damage from EMF and RFR. Orderly chromatin condensation is a normal part of cell division, but it can also be provoked pathologically. The work of Markova, Belyaev and others has repeatedly shown that RFR exposure can cause chromatin condensation. Belyaev (1997) reported that super-low intensity RFR resulted in changes in genes, and chromatin condensation of DNA at intensities comparable to exposures from cell towers (typically at RFR levels of 0.1 to 1.0 uW/cm2) (Belyaev, Alipov, and Harms-Ringdahl 1997). Significant microwave-induced

changes in chromatin conformation were observed when rat thymocytes were analyzed in-between 30-60 min after exposure to MW (Belyaev and Kravchenko 1994). This effect nearly disappeared if the cells were incubated more than 80 min between exposure and analysis.

In recent studies, human lymphocytes from peripheral blood of healthy and hypersensitive to EMF persons were exposed to non-thermal microwave radiation NT MW) from the GSM mobile phones (Belyaev et al. 2005; Markova et al. 2005). NT MW induced changes in chromatin conformation similar to those induced by heat shock, which remained up to 24 h after exposure. The same group has reported that contrary to human fibroblast cells, which were able to adapt during chronic exposure to GSM/UMTS low intensity RFR exposure, human stem cells did not adapt (Belyaev, Markova, and Malmgren 2009).

Researchers have recently identified large numbers of "spontaneous genetic glitches," or de novo mutations, more likely to be transmitted by fathers than by mothers to their children (Neale et al. 2012; O'Roak et al. 2012; Sanders et al. 2012). These glitches are widely distributed across the genome, with their location rather than their size conferring risk. The Eichler team at the University of Washington found that 39% of the 126 most severe or disruptive mutations map to a network associated with chromatin remodeling that has already been ranked as significant amongst autism candidate genes (O'Roak et al. 2012). Whether the prominence of chromatin-related gene mutations can be related in any meaningful way to the impacts of EMF/RFR on chromatin condensation is not possible to say at this point in time and this apparent parallel between ASDs and EMF/RFR may be a pure coincidence, though an intriguing one worth looking into further, including regarding how these mutations and the chromatin-remodeling impacts of EMF/RFR exposure may interact.

Gonadal and germline impacts

De novo mutations have been shown to be more of a problem related to paternal age (O'Roak et al. 2012; Paul, Nagano, and Robaire 2011; Iossifov et al. 2012; Cantor et al. 2007; Alter et al. 2011), and this may be related to the impact of environmental factors such as EMF/RFR on the stem cell genome, particularly in sperm which have no DNA repair capacity. Vulnerability of testes and ova, and of sperm and egg cells, relates to the tissue milieu in which damage to the germline can take place, as well as on the greater vulnerability of stem cells. Several international laboratories have replicated studies showing adverse effects on sperm quality, motility and pathology in men who use and particularly those who wear a cell phone, PDA or pager on their belt or in a pocket (Agarwal et al. 2008; Agarwal et al. 2009; Wdowiak, Wdowiak, and Wiktor 2007; De Iuliis et al. 2009; Fejes et al. 2005; Aitken et al. 2005) Kumar, 2012). Other studies conclude that usage of cell phones, exposure to cell phone radiation, or storage of a

mobile phone close to the testes of human males affect sperm counts, motility, viability and structure (Aitken et al. 2004; Agarwal et al. 2007; Erogul et al. 2006). Animal studies have demonstrated oxidative and DNA damage, pathological changes in the testes of animals, decreased sperm mobility and viability, and other measures of deleterious damage to the male germ line (Dasdag et al. 1999; Yan et al. 2007; Otitoloju et al. 2010; Salama et al. 2009) Behari et al. 2006; Kumar et al. 2012). Of note, altered fatty acids consistent with oxidative stress have been found in sperm cells in male infertility (Zalata et al. 1998; Zalata, Hafez, and Comhaire 1995).

There are fewer animal studies that have studied effects of cell phone radiation on female fertility parameters. Panagopoulous et al. 2012 report decreased ovarian development and size of ovaries, and premature cell death of ovarian follicles and nurse cells in *Drosophila melanogaster* (Panagopoulos 2012). Gul et al (2009) report rats exposed to stand-by level RFR (phones on but not transmitting calls) caused decrease in the number of ovarian follicles in pups born to these exposed dams (Gul, Celebi, and Ugras 2009). Magras and Xenos (1997) reported irreversible infertility in mice after five (5) generations of exposure to RFR at cell phone tower exposure levels of less than one microwatt per centimeter squared (μW/cm2) (Magras and Xenos 1997).

Implications of genotoxicity

The issue of genotoxicity puts the contribution of genetic variation into a different light – as something that needs to be accounted for, not necessarily assumed as the starting point. In this regard it has been speculated that the apparent higher rates of autism in Silicon Valley, discussed in the past as related to 'geek genes' (Silberman 2001), might be conditioned by higher levels of exposure to EMF/RFR. The relationship between the greater vulnerability of male sperm than of female eggs to adverse effects of EMF/RFR exposure and the marked (4:1) predominance of paternal origin of de novo point mutations (4:1 bias), also deserves further careful attention (O'Roak et al. 2012).

5. Implications of Damage

We have reviewed parallels between ASD and EMF/RFR in molecular, cellular and tissue damage, including cellular stress (oxidative stress, the heat shock response and protein misfolding), injury of membranes, aberrant calcium signaling, and compromise of junctions and barriers. The genotoxicity of EMF/RFR was reviewed in relation to issues of environmental contributions to autism and of the phenomenon of de novo mutations. The compromise of the tissue substrate appears to have many commonalities in ASDs and in EMF/RFR exposures. Also notable was the possibility of attenuating some of the damage through increasing antioxidant status.

These commonalities come to mind in considering the implications of a recent study documenting arrest of symptomatology in a mouse model of Rett syndrome through a

bone marrow transplant of wild-type microglia (Derecki et al. 2012; Derecki, Cronk, and Kipnis 2012). The introduction of these competent microglia cells did not directly target the neuronal defect associated with the MECP2 gene mutation; instead the benefits of the transplant were diminished through inhibition of phagocytosis. Phagocytosis involves removing debris. This suggests that while research has focused on how specific molecular defects, particularly in the synapse, may contribute to Rett pathophysiology, there may also be an important contribution from cellular debris, misfolded proteins and other disordered cellular structure and function. Such disorder could be accumulating in cells under the conditions of pathophysiological disarray reviewed above. This has potentially broad implications for other genetic disorders, as well as for conditions like ASDs which are for the most part idiopathic. Based on this study as well as on the levels of damage just reviewed, problems in cells that are pertinent to ASDs most likely go beyond any specific defect introduced by a mutation. Additionally it is conceivable that many of the mutations may be not part of normal background variation but instead collateral damage from the same environmental factors that are also driving the damage to the pathophysiology. It is also encouraging that at least some of the damage and dysfunction was reversible by a generic cellular mechanism (phagocytosis), and this could have broad significance for idiopathic ASDs as well, along with other conditions involving related pathophysiological challenges.

B. Degradation of System Integrity

In the setting of molecular, cellular and tissue damage, one would predict that the organization and efficiency of a variety of organelles, organs and systems would also be degraded. EMF/RFR exposures yield a stressful situation of chronically interrupted homeostasis. Here we will review disturbances from EMF/RFR in systems (including include oxidative and bioenergetics metabolism, immune function and electrophysiological oscillations) that include molecular and cellular components subject to the kinds of damage discussed in the previous section. We will review disturbances that have been associated with EMF/RFR, and consider the parallel disturbances that have been documented in ASDs.

1. Mitochondrial dysfunction

Mitochondria are broadly vulnerable, in part because the integrity of their membranes is vital to their optimal functioning – including channels and electrical gradients, and their membranes can be damaged by free radicals which can be generated in myriad ways. Moreover, just about every step in their metabolic pathway can be targeted by environmental agents, including toxicants and drugs, as well as mutations (Wallace and Starkov 2000). This supports an allostatic load model for conditions in which mitochondrial dysfunction is an issue, which includes ASDs as well as myriad other chronic conditions.

Mitochondria are commonly discussed in terms of the biochemical pathways and cascades of events by which they metabolize glucose and generate energy. But in parallel with this level of function there also appears to be a dimension of electromagnetic radiation that is part of the activity of these organelles. For example, electromagnetic radiation can be propagated through the mitochondrial reticulum, which along with the mitochondria has a higher refractive index than the surrounding cell and can serve to propagate electromagnetic radiation within the network (Thar and Kuhl 2004). It is also the case that *"The physiological domain is characterized by small-amplitude oscillations in mitochondrial membrane potential (delta psi(m)) showing correlated behavior over a wide range of frequencies…. Under metabolic stress, when the balance between ROS [reactive oxygen species, or free radicals] generation and ROS scavenging [as by antioxidants] is perturbed, the mitochondrial network throughout the cell locks to one main low-frequency, high-amplitude oscillatory mode. This behavior has major pathological implications because the energy dissipation and cellular redox changes that occur during delta psi(m) depolarization result in suppression of electrical excitability and Ca2+ handling…"* (Aon, Cortassa, and O'Rourke 2008). These electromagnetic aspects of mitochondrial physiology and pathophysiology could very well be impacted by EMF/RFR.

There are also a variety of types of mitochondrial damage that have been documented in at least some of the studies that have examined the impacts of EMF/RFR upon mitochondria. These include reduced or absent mitochondrial cristae (Khaki et al. 2006; Lahijani, Tehrani, and Sabouri 2009; Esmekaya et al. 2011), mitochondrial DNA damage (Xu et al. 2010), swelling and crystallization (Lahijani, Tehrani, and Sabouri 2009), alterations and decreases in various lipids suggesting an increase in their use in cellular energetics (Chernysheva 1987), damage to mitochondrial DNA (Xu et al. 2010), and altered mobility and lipid peroxidation after exposures (Wang et al. 2002). Also noted has been enhancement of brain mitochondrial function in Alzheimer's transgenic mice and normal mice (Dragicevic et al. 2011). The existent of positive as well as negative effects gives an indication of the high context dependence of exposure impacts, including physical factors such as frequency, duration, and tissue characteristics; these are

intensively reviewed in Belyaev's contribution to BioInitiative 2012 in Section 15 (Belyaev 2012).

The idea that mitochondrial dysfunction might be common in ASDs met with a fair bit of consternation, and many professionals have preferred to limit their consideration to mitochondrial disorders with proven genetic mutations. However the concept of mitochondrial dysfunction is better established in other areas of medicine, with thousands of papers and hundreds of reviews carrying "mitochondrial dysfunction" in their titles. By now there is a large amount of evidence for biochemical and other abnormalities in a large portion of children with autism that are consistent with mitochondrial dysfunction (Giulivi et al. 2010; Palmieri et al. 2010; Pastural et al. 2009). Recently published postmortem brain tissue studies that have added a new dimension of evidence for mitochondrial abnormalities in ASDs will be reviewed in the section on alteration of brain cells below.

Some have called the mitochondrial issues most commonly seen in ASDs 'secondary mitochondrial dysfunction' (Zecavati and Spence 2009; Rossignol and Frye 2011) to indicate that it results from environment insults and/or other pathophysiological dysfunction rather than directly from genetics (Hadjixenofontos et al. 2012); the already discussed potential for EMF/RFR to damage channels, membranes and mitochondria themselves could contribute in a number of ways to degrading mitochondrial function without a basis in genetic mutation, as could toxicant exposures and immune challenges. In a meta-analysis of studies of children with ASD and mitochondrial disorder, the spectrum of severity varied, and 79% of the cases were identified by laboratory not associated with genetic abnormalities (Rossignol and Frye 2011). "*Substantial percentages of autistic patients display peripheral markers of mitochondrial energy metabolism dysfunction, such as (a) elevated lactate, pyruvate, and alanine levels in blood, urine and/or cerebrospinal fluid, (b) serum carnitine deficiency, and/or (c) enhanced oxidative stress……In some patients, these abnormalities have been successfully explained by the presence of specific mutations or rearrangements in their mitochondrial or nuclear DNA. However, in the majority of cases, abnormal energy metabolism cannot be immediately linked to specific genetic or genomic defects."* (Palmieri and Persico 2010)

2. Melatonin dysregulation

Melatonin, mitochondria, glutathione, oxidative stress

Melatonin is well-known for its role in regulation of circadian rhythms, but it also plays important metabolic and regulatory roles in relation to cellular protection, mitochondrial malfunction and glutathione synthesis. (Leon et al. 2005; Luchetti et al. 2010; Limon-Pacheco and Gonsebatt 2010) *"It is known that melatonin scavenges oxygen and*

nitrogen-based reactants generated in mitochondria. This limits the loss of the intramitochondrial glutathione and lowers mitochondrial protein damage, improving electron transport chain (ETC) activity and reducing mtDNA damage. Melatonin also increases the activity of the complex I and complex IV of the ETC, thereby improving mitochondrial respiration and increasing ATP synthesis under normal and stressful conditions." (Leon et al. 2005) It also helps prevent the breakdown of the mitochondrial membrane potential, decrease electron leakage, and thereby reduce the formation of superoxide anions. (Hardeland 2005) Pharmacological doses of melatonin not only scavenge reactive oxygen and nitrogen species, but enhance levels of glutathione and the expression and activities of some glutathione-related enzymes. (Limon-Pacheco and Gonsebatt 2010; Gupta, Gupta, and Kohli 2003)

Melatonin can attenuate or prevent some EMF/RFR effects

Melatonin may have a protective effect in the setting of some EMF/RFR exposures, apparently in relation to these functions just described. EMF/RFR can impact melatonin; one example is exposure to 900-MHz microwave radiation promoted oxidation, which reduced levels of melatonin and increased creatine kinase and caspase-3 in exposed as compared to sham exposed rats (Kesari, Kumar, and Behari 2011).

Further types of adverse impacts can be seen in the next set of examples, but what is interesting is that melatonin can attenuate or prevent them. In an experiment exposing rats to MW from a GSM900 mobile phone with and without melatonin treatment to study renal impacts (Oktem et al. 2005), the untreated exposed rats showed increases of lipid peroxidation markers as reduction of the activities of superoxide dismutase, catalase and glutathione peroxidase indicating decrement in antioxidant status. However these negative effects were inhibited in the exposed rats treated with melatonin. Melatonin also inhibited the emergence of preneoplastic liver lesions in rats exposed to EMFs (Imaida et al. 2000). The development of DNA strand breaks was observed in RFR exposed rats; this DNA damage was blocked by melatonin (Lai and Singh 1997). Exposure of cultured cortical neurons to EMF led to an increase in 8-hydroxyguanine in neuronal mitochondria, a common biomarker of DNA oxidative damage, along with a reduction in the copy number of mitochondrial DNA and the levels of mitochondrial RNA transcripts; but these effects could all be prevented by pretreatment with melatonin (Xu et al. 2010). In a study of skin lesion induced by exposure to cell phone radiation, the skin changes in the irradiated group (which included thicker stratum corneum, epidermal atrophy, papillamatosis, basil cell proliferation, increased epidermal granular cell layer and capillary proliferation, impaired collagen tissue distribution and separation of collagen bundles in dermis) were prevented (except for hypergranulosis) by melatonin treatment (Ozguner et al. 2004). Melatonin as well as caffeic acid phenyethyl ester (an antioxidant) both protected against retinal oxidative stress in rates exposed long-term to mobile phone irradiation (Ozguner, Bardak, and Comlekci 2006). Nitric oxide (NO) was increased in

nasal and sinus mucosa in rats after EMF exposure, with this NO possibly acting as a defense mechanism suggesting tissue damage; but this was prevented by pretreatment with melatonin (Yariktas et al. 2005). Melatonin treatment significantly prevented the increase in the MDA (malondyaldehyde, a marker of lipid peroxidation) content and XO (xanthine oxidase) activity in rat brain tissue after 40 days of exposure, but it was unable to prevent the decrease of CAT activity and increase of carbonyl group contents (Sokolovic et al. 2008).

Of note, the melatonin production of infants in isolettes in neonatal intensive care units appears to be impacted by the high ELF-EMF environment, in that when infants were removed from those exposures they showed an increase in melatonin levels (Bellieni, Tei, et al. 2012). There is an increased prevalence of ASDs in children who were born prematurely (Indredavik et al. 2010; Indredavik et al. 2008; Johnson et al. 2011; Johnson et al. 2010; Johnson and Marlow 2011; Lampi et al. 2012; Limperopoulos 2009, 2010; Limperopoulos et al. 2008; Matson, Matson, and Beighley 2011; Pinto-Martin et al. 2011). There are many potential prematurity-associated factors that could contribute to increased risk for ASDs, but electromagnetic exposure might be one of them worthy of further consideration, as it could be modified; conversely, such exposures in vulnerable infants are likely to have much broader impacts beyond reducing melatonin synthesis.

Melatonin and autism

Based on the commonality of both sleep disorders and low melatonin levels, Bourgeron (2007) proposed that synaptic and clock genes are important in ASDs, and that future studies should investigate the circadian modulation of synaptic function (Bourgeron 2007). A number of melatonin-related genetic variants have been identified as associated with ASDs. Polymorphisms, deletions and polymorphisms in the ASMT gene, which encodes the last enzyme of melatonin synthesis, have been found (Pagan et al. 2011; Jonsson et al. 2010; Melke et al. 2008), and variations have been found as well for melatonin receptor genes (Chaste et al. 2010; Pagan et al. 2011; Jonsson et al. 2010). CYP1A2 polymorphisms have been found in slow melatonin metabolisers, in whom melatonin levels are aberrant and initial response to melatonin for sleep disappeared in a few weeks (Braam et al. 2012).

Regarding melatonin status in people with ASDs, a recent meta-analysis summarized the current findings as indicating that *"1) Physiological levels of melatonin and/or melatonin derivatives are commonly below average in ASD and correlate with autistic behavior, 2) Abnormalities in melatonin-related genes may be a cause of low melatonin levels in ASD, and 3) … treatment with melatonin significantly improves sleep duration and sleep onset latency in ASD."* (Rossignol and Frye 2011) The meta-analysis also showed that polymorphisms in melatonin-related genes in ASD could contribute to lower melatonin

concentrations or an altered response to melatonin, but only in a small percentage of individuals, since pertinent genes were found in only a small minority of those screened.

Autism AND Melatonin AND Glutathione

Whereas PubMed searches for "autism AND melatonin" and "autism AND glutathione" each coincidentally yielded 72 citations, and "melatonin AND glutathione" yielded 803 citations, the search for "autism AND melatonin AND glutathione" yielded zero citations. This is interesting given the strong connection of melatonin and glutathione metabolically, as discussed above, alongside of the strongly established interest in both glutathione and melatonin in ASD research and increasingly in clinical practice. Hopefully one contribution of an investigation of EMF/RFR links to ASDs will be to help bring attention to this relationship, which may help identify potential environmental and physiological causes for low melatonin in those without pertinent mutations. Of pertinence, tryptophan hydroxylase (TPH2) – the rate limiting enzyme in the synthesis of serotonin, from which melatonin is derived – is extremely vulnerable to oxidation, and tends to misfold when its cysteine residues are oxidized, with the enzyme being converted to a redox-cycling quinoprotein (Kuhn and Arthur 1999; Kuhn and Geddes 1999; Kuhn et al. 2011; Kuhn and Arthur 1997).

3. Disturbed immune function

There is by now a broad appreciation of the presence of immune disturbances in ASDs, to the point where there is an emerging discussion of ASDs as neuroimmune disorders (Bilbo, Jones, and Parker 2012; Persico, Van de Water, and Pardo 2012). Research identifying immune features in ASDs spans from genetics where risk genes have been identified to epigenetics where altered expression of immune genes is being reported as prominent in ASD epigenetics (Kong et al. 2012; Waly et al. 2012; Lintas, Sacco, and Persico 2012), and also includes prenatal infectious and immune disturbances as risk factors for autism as well as other neurodevelopmental and neuropsychiatric diseases as well as other conditions such as asthma (Patterson 2011; Smith et al. 2007; Fox, Amaral, and Van de Water 2012). Immune disturbances in infants and children with ASD are heterogeneous, with some but not all manifesting autoimmunity (Soumiya, Fukumitsu, and Furukawa 2011; Martin et al. 2008). Anecdotally, recurrent infection is common while on the other hand some get sick less often than their peers. It is common for people with autism to have family members with immune or autoimmune diseases (Croen et al. 2005). The immune system is turning out to have an important role in brain development (Bilbo and Schwarz 2012; Schwarz and Bilbo 2012; Boksa 2010). As mentioned, glial activation associated with brain immune response has been identified in a growing number of studies. Whether or not EMF/RFR contributes to these features of ASDs causally, based on the evidence below regarding immune impacts of EMF/RFR exposure (which is also reviewed much more thoroughly by Johansson in Section 8 of the present

Bioinitiative Report) (Blank 2012), it is certainly plausible that such exposures could serve as aggravating factors.

Low-intensity exposures

It is clear that the body's immune defense system responds to very low-intensity exposures. Chronic exposure to factors that increase allergic and inflammatory responses on a continuing basis is likely to be harmful to health, since the resultant chronic inflammatory responses can lead to cellular, tissue and organ damage over time. We are increasingly appreciating the extent to which many chronic diseases are related to chronic immune system dysfunction. Disturbance of the immune system by very low-intensity electromagnetic field exposure is discussed as a potential underlying cause for cellular damage and impaired healing (tissue repair), which could lead to disease and physiological impairment (Johansson 2009; Johannson 2007).

Both human and animal studies report that exposures to EMF and RFR at environmental levels associated with new technologies can be associated with large immunohistological changes in mast cells as well as other measures of immune dysfunction and dysregulation. Mast cells not only can degranulate and release irritating chemicals leading to allergic symptoms; they are also widely distributed in the body, including in the brain and the heart, which might relate to some of the symptoms commonly reported in relation to EMF/RFR exposure (such as headache, painful light sensitivity, and cardiac rhythm and palpitation problems).

Consequences of immune challenges during pregnancy

As mentioned, infection in pregnancy can also increase the risk of autism and other neurodevelopmental and neuropsychiatric disorders via maternal immune activation (MIA). Viral, bacterial and parasitic infections during pregnancy are thought to contribute to at least 30% of cases of schizophrenia (Brown and Derkits 2010). The connection of maternal infection to autism is supported epidemiologically, including in a Kaiser study where risk was associated with psoriasis and with asthma and allergy in the second trimester (Croen et al. 2005), and in a large study of autism cases in the Danish Medical registry (Atladottir et al. 2010) with infection at any point in pregnancy yielding an adjusted hazard ration of 1.14 (CI: 0.96-1.34) and when infection occurred during second trimester the odds ratio was 2.98 (CI: 1.29-7.15). In animal models, while there is much variation in study design, mediators of the immune impact appear to include oxidative stress, interleukin-6 and increased placental cytokines (Smith et al. 2007; Patterson 2009; Boksa 2010). Garbett et al. (2012) commented on several mouse models of the effects of MIA on the fetal brain that *"The overall gene expression changes suggest that the response to MIA is a neuroprotective attempt by the developing brain to counteract environmental stress, but at a cost of disrupting typical neuronal differentiation and axonal growth."* (Garbett et al. 2012). Maternal fetal brain-reactive

autoantibodies have also been identified in some cases (Braunschweig et al. 2012; Braunschweig and Van de Water 2012; Fox, Amaral, and Van de Water 2012; Goines et al. 2011; Wills et al. 2009; Wills et al. 2011; Zimmerman et al. 2007).

Although we have evidence of immune impacts of EMF/RFR, the impact of repeated or chronic exposure to EMF and RFR during pregnancy is poorly studied; could this trigger similar immune responses (cytokine production) and stress protein responses, which in turn would have effects on the fetus? Although this has been poorly studied, we do have data that very low cell phone radiation exposures during both human and mouse pregnancies have resulted in altered fetal brain development leading to memory, learning, and attention problems and behavioral problems (Aldad et al. 2012).

Potential immune contributions to reactivity and variability in ASDs

Immune changes in ASDs appear to be associated with behavioral change (Shi et al. 2003; Ashwood et al. 2008; Ashwood et al. 2011; Breece et al. 2012; Heuer et al. 2008), but the mechanisms are complex and to date poorly understood (Careaga and Ashwood 2012) and likely will need to be elucidated through systems biology methods that capture multisystem influences on the interactions across behavior, brain and immune regulation (Broderick and Craddock 2012), including electrophysiology.

Two of the particularly difficult parts of ASDs are the intense reactivity and the variability in assorted symptoms such as tantrums and other difficult behaviors. Children with ASDs who also have gastrointestinal symptoms and marked fluctuation of behavioral symptoms have been shown to exhibit distinct innate immune abnormalities and transcriptional profiles of peripheral blood monocytes (Jyonouchi et al. 2011). It is worth considering EMF/RFR exposures could be operating through related mechanisms so as to add to allostatic loading in ways that exacerbate behavior. In Johansson 2006 and 2007 a foundation is provided for understanding how chronic EMF/RFR exposure can compromise immune function and sensitize a person to even small exposures in the future (Johannson 2007; Johansson et al. 2006). Johansson discusses alterations of immune function at environmental levels resulting in loss of memory and concentration, skin redness and inflammation, eczema, headache, and fatigue. Mast cells that degranulate under EMF and RFR exposures and substances secreted by them (histamine, heparin and serotonin) may contribute to features of this sensitivity to electromagnetic fields (Johansson et al. 2006). Theoharides and colleagues have argued that environmental and stress related triggers might activate mast cells, causing inflammatory compromise and leading to gut-blood-brain barrier compromise, seizures and other ASD symptoms (Theoharides et al. 2012, 2010), and that this cascade of immune response and its consequences might also be triggered in the absence of infection by mitochondrial fragments that can be released from cells in response to stimulation by IgE/anti-IgE or by the proinflammatory peptide substance P (Zhang, Asadi, et al. 2012).

Seitz et al. (2005) reviewed an extensive literature on electromagnetic hypersensitivity conditions reported to include sleep quality, dizziness, headache, skin rashes, memory and concentration impairments related to EMF and RFR (Seitz, 2005). Some of these symptoms are common in ASDs, whether or not they are due to EMF/RFR exposure, and the experience of discomfort may be hard to document due to difficulties with self-reporting in many people with ASDs.

Johansson (2007, 2009) also reports that benchmark indicators of immune system allergic and inflammatory reactions occur under exposure conditions of low-intensity non-ionizing radiation (immune cell alterations, mast cell degranulation histamine-positive mast cells in biopsies and immunoreactive dendritic immune cells) (Johannson 2007; Johansson 2009). In facial skin samples of electro- hypersensitive persons, the most common finding is a profound increase in mast cells as monitored by various mast cell markers, such as histamine, chymase and tryptase (Johansson et al. 2001). In ASDs, infant and childhood rashes, eczema and psoriasis are common, and they are common in family members as well (Bakkaloglu et al. 2008).

4. Alteration of and damage to cells in the brain

Brain cells have a variety of ways of reacting to environmental stressors, such as shape changes, metabolic alterations, upregulation or downregulation of neurotransmitters and receptors, other altered functionality, structural damage, production of un-metabolizable misfolded proteins and other cellular debris, and apoptosis; these range along a spectrum from adaptation to damage and cell death. These types of alterations can be looked at in animals under controlled conditions, but in human beings direct cellular examination can only be done on surgical biopsy tissue – which is hardly ever available in people with ASDs – or after death, at which point there has been a whole lifetime of exposures that are generally impossible to tease apart if there were even motivation to do so. This complicates the comparison of brain cell and tissue-related pathophysiology between what is seen in ASDs and what is associated with EMF/RFR exposures.

Brain cells

Impact of EMF/RFR on cells in the brain has been documented by some of the studies that have examined brain tissue after exposure, although the interpretation of inconsistencies across studies is complicated by sometimes major differences in impact attributable to differences in frequencies and duration of exposure, as well as to differences in resonance properties of tissues and other poorly understood constraints on cellular response. These studies and methodological considerations have been reviewed in depth in Belyaev, 2012 in section 15 of the 2012 BioInitiatve Report (Belyaev 2012), as well as by Salford et al. (2012) in Section 10 (Salford, Nittby, and Persson 2012). A few examples of observations after exposure have included dark neurons (an indicator of neuronal damage), as well as alteration of neuronal firing rate (Bolshakov and Alekseev

1992), and upregulation of genes related to cell death pathways in both neurons and astrocytes (Zhao, Zou, and Knapp 2007). Astrocytic changes included increased GFAP and increased glial reactivity (Chan et al. 1999; Ammari et al. 2008; Ammari et al. 2010; Brillaud, Piotrowski, and de Seze 2007), as well as astrocyte-pertinent protein expression changes detected by Fragopoulou et al, 2012 as mentioned above. Also observed has been a marked protein downregulation of the nerve growth factor glial maturation factor beta (GMF) which is considered as an intracellular signal transduction regulator in astrocytes, which could have significant impact on neuronal-glial interactions as well as brain cell differentiation and tumor development. Diminution of Purkinje cell number and density has also been observed, (Ragbetli et al. 2010) including in two studies of the impacts of perinatal exposure (Albert, 1981; Albert, 1981). Promotion of pro-inflammatory responses in EMF-stimulated microglial cells has also been documented (Yang et al. 2010).

Neuropathology findings in ASDs have been varied and have been interpreted according to various frameworks ranging from a regionalized approach oriented to identifying potential brain relationships to ASD's behavioral features (Amaral, Schumann, and Nordahl 2008) to identifying receptor, neurotransmitter and interneuron abnormalities that could account for an increased excitation/inhibition ratio (Levitt 2009; Geschwind 2007; Anney 2010; Casanova 2006; Rubenstein 2003). Studies have documented a range of abnormalities in neurons, including altered cellular packing in the limbic system, reduced dendritic arborization, and reductions in limbic GABAergic systems. Over the past decade a shift has occurred from presuming that all pertinent brain changes occurred prior to birth, to an acknowledgement that ongoing cellular processes appear to be occurring not only after birth but well into adulthood (Bauman and Kemper 2005). One of the reasons for this shift was the observation that head size (as well as brain weight and size) was on average larger in children with autism, and the head sizes of children who became diagnosed with autism increased in percentile after birth (Herbert 2005).

Neuroinflammation, glial activation and excitotoxicity

Although much attention has been paid in ASD brain literature to specific regions manifesting differences in size and activity in comparison to those without ASDs, there are other observations that are not strictly regional in nature, such as more widely distributed scaling differences (e.g. larger brains, wider brains, increased white matter volume, along with altered functional connectivity and coherence to be discussed below). Recently more studies have appeared identifying pathophysiological abnormalities such as neuroinflammation, mitochondrial dysfunction and glutathione depletion in brain tissue. Neuroinflammation was first identified in a study of postmortem samples from eleven individuals aged 5-44 who had died carrying an ASD diagnosis, in which activated astrocytes and microglial cells as well as abnormal cytokines and chemokines were found. Other research has identified further astrocyte abnormalities include, altered

expression of astrocyte markers GFAP abnormalities including elevation, antibodies, and altered signaling (Laurence 2005; Singh 1997; Fatemi et al. 2008). Increased microglia activation and density as well as increased myeloid dendritic cell frequencies have also been documented. (Vargas et al. 2005; Breece et al. 2012; Tetreault et al. 2012), as has abnormal microglial-neuronal interactions (Morgan et al. 2012). Recently through use of the PET ligand PK11105 microglial activation was found to be significantly higher in multiple brain regions in young adults with ASDs (Suzuki et al. 2013). Genes associated with glial activation have been documented as upregulated. Garbett et al measured increased transcript levels of many immune genes, as well as changes in transcripts related to cell communication, differentiation, cell cycle regulation and chaperone systems (Garbett et al. 2008). Voineaugu and colleagues performed transcriptomic analysis of autistic brain and found a neuronal module of co-expressed genes which was enriched with genetically associated variants, and an immune-glial module showing no such enrichment for autism GWAS signals (Voineagu et al. 2011).

Neuroinflammation also does not appear to be strictly localized in a function-specific fashion, and it may contribute both to more broadly distributed and more focal features for tissue-based reasons. It may be that brain regions with particular prominence in ASDs may have distinctive cellular characteristics – e.g. the amygdala (Baron-Cohen et al. 2000; Dziobek et al. 2010; Hall et al. 2010; Mercadante et al. 2008; Nordahl et al. 2012; Otsuka et al. 1999; Schulkin 2007; Schumann and Amaral 2006; Schumann et al. 2009; Truitt et al. 2007; Zirlinger and Anderson 2003), which may have a larger or more reactive population of astrocytes (Johnson, Breedlove, and Jordan 2010) or the basal ganglia which may have greater sensitivity to even subtle hypoxia or perfusion abnormalities. In this case it may be the histology of these areas that makes them vulnerable to environmental irritants, and this may contribute to how environmental factors such as EMF/RFR might trigger or aggravate some of ASD's features. More widely distributed brain tissue pathology be part of what leads to differences in ASDs in brain connectivity. However these types of tissue-function relationships have been poorly investigated. The contribution of tissue differences is one of the physical considerations covered by Belyaev (2012) in Section 15 of the 2012 BioInitiative Report (Belyaev, 2012).

Various signs of mitochondrial dysfunction and oxidative stress have also been identified in the brain. Findings include downregulation of expression of mitochondrial electron transport genes (Anitha, Nakamura, Thanseem, Matsuzaki, et al. 2012) or deficit of mitochondrial electron transport chain complexes (Chauhan et al. 2011), brain region specific glutathione redox imbalance (Chauhan, Audhya, and Chauhan 2012), and evidence of oxidative damage and inflammation associated with low glutathione redox status (Rose, Melnyk, Pavliv, et al. 2012). Oxidative stress markers were measured as increased in cerebellum (Sajdel-Sulkowska, Xu, and Koibuchi 2009).

Additional support for the presence of tissue pathophysiology-based changes in brains of people with ASDs comes from the various studies documenting reduction in Purkinje cell numbers (Whitney et al. 2009; Whitney et al. 2008; Bauman and Kemper 2005; Shi et al. 2009; Blatt and Fatemi 2011; Fatemi et al. 2002; Fatemi et al. 2012), possibly due to oxidative stress and an increased excitation/inhibition ratio that could potentially be acquired (Fatemi et al. 2012). Also of note are changes in the glutamatergic and GABAergic systems, which when imbalanced can disturb the excitation/inhibition ratio and contribute to seizure disorders; reductions in GABA receptors as well as in GAD 65 and 67 proteins that catalyse the conversion of glutamate into GABA have been measured. (Yip, Soghomonian, and Blatt 2007, 2008, 2009) A consensus statement on the cerebellum in ASDs stated that, *"Points of consensus include presence of abnormal cerebellar anatomy, abnormal neurotransmitter systems, oxidative stress, cerebellar motor and cognitive deficits, and neuroinflammation in subjects with autism."* (Fatemi et al. 2012)

Some indirect corroboration for these findings has come from neuroimaging, where the initial hypothesis regarding the tissue basis of the larger size of brains in so many people with autism – that it was due to a higher density of neurons and more tightly packed axons – came under question with the emergence of contradictory findings, well reviewed a few years ago by Dager and colleagues (Dager et al. 2008). These include reduced rather than increased density of NAA (n-acetylaspartate, a marker of neuronal integrity and density that is produced in the mitochondria), reduced rather than increased fractional anisotropy suggesting less tightly packed axonal bundles (Bode et al. 2011; Cascio et al. 2012; Mak-Fan et al. 2012; Travers et al. 2012; Walker et al. 2012; Wolff et al. 2012); Sundaram, 2008) and greater rather than lower diffusivity, all of which may be more consistent with lower density of tissue and tissue metabolites and more fluid, which could be consistent with neuroinflammation and/or oxidative stress. The early postnatal development of such lower fractional anisotropy and increased diffusivity was measured in the process of occurring recently, in the first large prospective longitudinal imaging study of infants, who trended from 6 months to 2 years in the direction of these findings becoming more pronounced – but still with substantial overlap with those infants who did not develop autism (Wolff et al. 2012). This trend was consistent with prior studies showing increase in head size after birth, and added some information about what was happening in the brain to drive this size increase, although due to its methods it could only indirectly address the possibilty that emergence during the first few years of life of tissue pathophysiology disturbances such as neuroinflammation might be contributing to these trends (Herbert 2012).

There is also substantial variability across many different types of brain findings. Of interest is that a number of functional brain imaging and electrophysiology studies have identified greater heterogeneity in response to stimuli between individuals in the ASD

group than individuals in the neurotypical control group (Muller et al. 2003; Dinstein et al. 2012). This may make more sense from the point of view of non-linear response – i.e. a disproportionality between output and input (as well as state and context sensitivity), in a pathophysiologically perturbed brain system. Nonlinearity has also been a significant methodological issue in EMF/RFR research because linear methods of study design and data analysis have often been insensitive to effects, whereas nonlinear methods have been argued to show greater sensitivity (Carrubba and Marino 2008; Marino, Wolcott, Chervenak, Jourd'heuil, Nilsen, Frilot, et al. 2001; Marino and Frilot 2003; Carrubba et al. 2006; Carrubba et al. 2012; Marino, Nilsen, and Frilot 2003; Marino, Wolcott, et al. 2001, 2001; Carrubba et al. 2007; Marino et al. 2000; Bachmann, 2005).

The presence of various types of tissue pathophysiology both in findings in postmortem tissue from individuals with ASDs and in documented impacts of EMF/RFR exposure are intriguing and suggest overlap in processes involved. But it is not really possible to infer any specific agent of injury from cellular responses since for the most part these are not specific but rather are stress or repair responses generic to a variety of triggers. It is important to entertain how environmental agents could contribute to brain changes in ASDs, and how these changes may develop over progress over time after the earliest periods in brain development. EMF/RFR exposures could be preconceptional, prenatal or postnatal – or all of the above; it is conceivable that this could be the case in ASDs as well.

Altered development

There is some evidence for altered brain and organism development in relation to EMF/RFR exposure. Aldad et al. 2012 exposed mice in utero to cellular telephone radiation, with resultant aberrant miniature excitatory postsynaptic currents, dose-responsive impaired glutamatergic synaptic transmission onto layer V pyramidal neurons of the prefrontal cortex (Aldad et al. 2012). Lahijani exposed preincubated chicken embryos to 50 Hz EMFs, and made the following morphological observations: *"exencephalic embryos, embryos with asymmetrical faces, crossed beak, shorter upper beak, deformed hind limbs, gastroschesis, anophthalmia, and microphthalmia. H&E and reticulin stainings, TEMS, and SEMs studies indicated EMFs would create hepatocytes with fibrotic bands, severe steatohepatitis, vacuolizations, swollen and extremely electron-dense mitochondria, reduced invisible cristae, crystalized mitochondria with degenerated cristae, myelin-like figures, macrophages engulfing adjacent cells, dentated nuclei, nuclei with irregular envelopes, degenerated hepatocytes, abnormal lipid accumulations, lipid droplets pushing hepatocytes' nuclei to the corner of the cells, abundant cellular infiltrations cellular infiltrations inside sinusoid and around central veins, disrupted reticulin plexus, and release of chromatin into cytosol,, with partially regular water layers,"* and attributed cell damage to elevated free radical induced cell membrane disruptions (Lahijani, Tehrani, and Sabouri 2009).

Although it is of great interest to characterize the changes in development associated with ASDs, it is also difficult to do in human beings because at present diagnosis is not possible until at least 2-3 years after birth. By now there have been a lot of prospective studies of infants at high risk for autism, but the in vivo brain imaging and electrophysiology data from these studies is only starting to be published, and so the for now the main sources of information are still inference backwards from post-mortem or imaging data, and animal models, both of which have clear limitations. Thus it is impossible to seek precise parallels here between what we know about the development of ASDs compared with the impacts of EMF/RFR exposures.

Nevertheless it is of real concern that such exposures have elicited some of the brain tissue changes that have been documented, both in early development and subsequently. Already noted above is the question of whether high exposures of neonates to monitoring equipment may affect the melatonin levels of neonates (Bellieni, Tei, et al. 2012); these exposures also impact heartrate variability . There are no studies yet on infants exposed to baby surveillance monitors or DECT wireless phones. However there are good laboratory testing studies yielding actual measurements of these devices that conclude: "*Maximum incident field exposures at 1m can significantly exceed those of base stations (typically 0.1 - 1 V/m). At very close distances the derived or reference exposure limits are violated" for baby surveillance monitors and DECT phones.* Further, the authors conclude that, based on very strictly controlled laboratory testing of everyday devices like baby monitors and some cordless phones *"(W)orse case peak spatial SAR values are close to the limit for the public or uncontrolled environments, e.g., IEEE802.11b and Bluetooth Class I".*(Kuhn et al. 2012) Even exposure of the fetus to laptop computer wireless emissions through the pregnant mother's use of them may on her lap involve induction of strong intracorporeal electric current densities from the power supply possibly even more than the device itself (Bellieni, Pinto, et al. 2012).

Brain blood flow and metabolism

Cerebral perfusion and metabolism abnormalities have been identified in close to 2 dozen papers studying autistic cohorts. Cerebral perfusion refers to the quantity of blood flow in the brain. Abnormal regulation of cerebral perfusion is found in a range of severe medical conditions including tumors, vascular disease and epilepsy. Cerebral hypoperfusion has also been found in a range of psychiatric disorders (Theberge 2008). Neurocognitive hypotheses and conclusions, as well as localization of perfusion changes, have been heterogeneous across these papers. Hypoperfusion or diminished metabolism has been identified in frontal regions (George, 1992; Gupta, 2009; Degirmenci, 2008; Wilcox, 2002; Galuska, 2002; Ohnishi, 2000; temporal lobes (Boddaert, 2002 ; Burroni, 2008 ; Degirmenci, 2008, Galuska, 2002, George, 1992 ; Hashimoto, 2000, Ohnishi, 2000, Ryu, 1999, Starkstein, 2000, Zilbovicius, 2000), as well as a variety of subcortical regions including basal ganglia (Degirmenci, 2008; Ryu, 1999; Starkstein, 2000),

cerebellum (Ryu, 1999), limbic structures (Ito, 2005, Ohnishi, 2000) and thalamus (Ito, 2005, Ryu, 1999, Starkstein, 2000) – i.e., in a widely distributed set of brain regions. It is interesting to note that even with this regional variation in localization, most of these publications showed that cerebral perfusion was *reduced*; in the only one of those studies reporting some areas of localized hyperfusion, these areas were found in the middle of areas in the frontal pole and temporal lobe that were hypoperfused (McKelvey 1995), Only one study showed no difference in perfusion between autistic and control subjects (Herold 1988). Possibly because virtually all of these studies were oriented toward testing neuropsychological rather than pathophysiological hypotheses, there were no probes or tests reported to unearth the tissue level alterations that might be underlying these reductions in blood flow in these brains.

While a large number of animal studies have documented BBB abnormalities from EMF/RFR exposures, only a few PET studies have been performed evaluating EMF exposure effects upon brain glucose metabolism. Volkow et al. performed PET scans both with and without EMF exposure (50 min of GSM-900 with maximum SAR of 0.901 W/kg), and the participants were blinded to the exposure situation (Volkow et al. 2011). A 7% increase in metabolism in the exposure situation compared to controls was identified regionally on the same side of the head as where the mobile phone was placed, in the right orbitofrontal cortex and in the lower part of the right superior temporal gyrus . The strength of the E-field from the phones correlated positively with the brain activation, which the authors hypothesized was from an increase in brain neuron excitability. . A subsequent smaller study by Kwon et al. demonstrated not increased but decreased brain ^{18}FDG uptake after GSM-900 exposure, this time in the temporoparietal junction (Kwon et al. 2011).

Many possible mechanisms could be involved in the metabolic and perfusion abnormalities identified, ranging from altered neuronal activity that was hypothesized in the Volkow et al. (2011) ^{8}FDG PET study to narrowing of vascular lumen in the setting of reduced perfusion. Underlying tissue pathophysiology-based phenomena could influence the measurable metabolism and perfusion abnormalities, via mechanisms such as excitotoxicity, cell stress response, constriction of capillary lumen by activated astrocytes, volume effects of vascular extravasation, subtle alterations in blood viscosity due to immune or oxidative stress-associated blood chemical changes, with other possibilities as well. Given the types of damage at the cellular level covered in this pathophysiology section so far – including oxidative stress, membrane and barrier function damage and poorly functioning channels, which occur both in ASDs as a consequence of EMF/RFR exposure, and given the heterogeneity of localization of abnormalities in the autism perfusion papers as well as considerations of nonlinearity, it may not be so surprising that the results in the two PET studies of human impacts of EMF exposure were not consistent.

6. Electrophysiology perturbations

At this stage the argument we hit a key pivot point, where we look at how the alterations in molecular, cellular and systems physiological function, which occur in the brain as well as in the body, impact the transduction into the electrical signaling activities of the brain and nervous system. Certainly the cells and tissues whose physiological challenges we have already discussed provide the material substrate for the electrical activity. Although ASD behaviors are influenced by many factors, they must in principle be mediated through nervous system electrophysiology.

If the cells responsible for generating synapses and oscillatory signaling are laboring under cellular and oxidative stress, lipid peroxidation, impaired calcium and other signaling system abnormalities, then mitochondrial metabolism will fall short, all the more so because of the challenges from the immune system which in turn be triggered to a major extent by environment. How well will synapses be generated? How well will immune-activated and thereby distracted glial cells be able to modulate synaptic and network activity? (Tasker et al. 2012; Eroglu and Barres 2010; Bilbo and Schwarz 2009; Fields 2006)

At present we are in the early stages of being able to formulate these questions well enough to address them. We do know that microglial activation can impact excitatory neurotransmission mediated by astrocytes (Pascual et al. 2012). We do know that the cortical innate immune response increases local neuronal excitability and can lead to seizures (Rodgers et al. 2009; Gardoni et al. 2011). We do know that inflammation can play an important role in epilepsy (Vezzani et al. 2011). We know less about lower levels of chronic or acute pathophysiological dysfunction and how they may modulate and alter the brain's electrophysiology.

Seizures and Epilepsy

EEG signals in ASDs are abnormal on a variety of levels. At the most severe level, EEGs show seizure activity. In addition to the association of some severe epilepsy syndromes (e.g. Landau Kleffner, tuberous sclerosis) with autism, the risk of epilepsy is substantially higher in people with ASDs than in the general population, with a large subset of these individuals experiencing seizure onset around puberty, likely in relation to aberrations in the dramatic and brain-impactful hormonal shifts of that phase of life. Although less than 50% of people clearly have seizures or epilepsy, a much larger number have indications of epileptiform activity, and an even larger percent have subclinical features that can be noted by a clinical epileptologist though not necessarily flagged as of clinical concern.

Epileptic seizures can be both caused by and cause oxidative stress and mitochondrial dysfunction. Seizures can cause extravasation of plasma into brain parenchyma (Mihaly

and Bozoky 1984; Librizzi et al. 2012; Marchi et al. 2010; van Vliet et al. 2007; Yan et al. 2005) which can trigger a vicious circle of tissue damage from albumin and greater irritability, as discussed above. Evidence suggests that if a BBB is already disrupted, there will be greater sensitivity to EMF/RFR exposure than if the BBB were intact (Tore et al. 2002; Tore et al. 2001), suggesting that such exposures can further exacerbate vicious circles already underway.

The combination of pathophysiological and electrophysiological vulnerabilities has been explored in relation to the impact of EMF/RFR on people with epilepsy – which, as discussed above, is a lot more common in ASDs than in the general population.. EMF/RFR exposures from mobile phone emissions have been shown to modulate brain excitability and to increase interhemispheric functional coupling (Vecchio et al. 2012; Tombini et al. 2012). In a rat model the combination of picrotoxin and microwave exposure at mobile phone-like intensities led to a progressive increase in neuronal activation and glial reactivity, with regional variability in the fall-off of these responses three days after picrotoxin treatment (Carballo-Quintas et al. 2011), suggesting a potential for interaction between a hyperexcitable brain and EMF/RFR exposure.

One critical issue here is nonlinearity and context and parameter sensitivity of impact. In one study, rat brain slices exposed to EMF/RFR showed reduced synaptic activity and diminution of amplitude of evoked potentials, while whole body exposure to rats led to synaptic facilitation and increased seizure susceptibility in the subsequent analysis of neocortical slices (Varro et al. 2009). Another study unexpectedly identified enhanced rat pup post-seizure mortality after perinatal exposure to a specific frequency and intensity of exposure, and concluded that apparently innocuous exposures during early development might lead to vulnerability to stimuli presented later in development (St-Pierre et al. 2007)

Sleep

Sleep involves a profound change in brain electrophysiological activity, and EEG abnormalities including disrupted sleep architecture figure in sleep challenges in ASD. Sleep symptoms include bedtime resistance, sleep onset delay, sleep duration and night wakings, and sleep architecture can involve significantly less efficient sleep, less total sleep time, prolonged sleep latency, and prolonged REM latency (Buckley et al. 2010; Giannotti et al. 2011), with these sleep problems being worse in children with ASDs who regressed than in those who did not regress into their autism (Giannotti, 2011). EEG abnormalities have also been associated with EMF/RFR exposure, including disrupted sleep architecture as well as changes in sleep spindles and in the coherence and correlation across sleep stages and power bands during sleep (Borbely, 1999; Huber, 2003).

Sleep disturbance symptoms are also common in both situations. Insomnia is commonly reported in people who are chronically exposed to low-level wireless antenna emissions. Mann (1996) reported an 18% reduction in REM sleep, which is key to memory and learning functions in humans. In ASDs sleep difficulties are highly pervasive and disruptive not only to the affected individual but also to their whole family due to the associated problems such as noise and the need for vigilance.

The multileveled interconnections involved in the modulation of sleep exemplify the interconnectedness of the many levels of pathophysiology reviewed here: *"Extracellular ATP associated with neuro- and glio-transmission, acting via purine type 2 receptors, e.g., the P2X7 receptor, has a role in glia release of IL1 and TNF. These substances in turn act on neurons to change their intrinsic membrane properties and sensitivities to neurotransmitters and neuromodulators such as adenosine, glutamate and GABA. These actions change the network input-output properties, i.e., a state shift for the network."* (Clinton et al. 2011) With disturbance simultaneously at so many of these levels, it is not surprising that sleep dysregulation is nearly universal in ASDs, and common in the setting of EMF/RFR exposures.

Quantitative electrophysiology

While clinical reading of EEG studies is done visually, a growing number of studies are examining EEG and MEG data using digital signal processing analysis, and often using data collected in controlled research settings with high density array equipment and carefully designed stimuli paradigms. In these settings a variety of abnormalities have been identified other than epileptic. These include abnormalities in the power spectrum, i.e. the distribution of power over the different frequencies present, with some studies showing impaired or reduced gamma-and activity (Sun et al. 2012; Rojas et al. 2008; Rippon, 2007) and others 8) showing reduction of spectral power across all bands (Tierney et al. 2012) while still others showed increased high-frequency oscillations. (Orekhova et al. 2007) Abnormalities in coherence and synchronization between various parts of the brain have been found (Muller 2008; Muller et al. 2011; Wass 2011), comparable to abnormal functional connectivity measured by fMRI (Just et al. 2004) but measurable using EEG or MEG with higher temporal resolution (Duffy, 2012; Isler, 2010; Murias, 2007; Murias, 2007; Coben, 2008). Several studies have identified reduced complexity and increased randomness in EEGs of people with autism (Lai et al. 2010; Catarino et al. 2011), as well as an increase in power but a reduction in coherence (Isler et al. 2010; Mathewson et al. 2012). Some electrophysiological metrics are emerging as potential discriminators between brain signal from individuals with ASDs and those who are neurotypical, such as a wavelet-chaos-neural network methodology applied to EEG signal (Ahmadlou, Adeli, and Adeli 2010).

EMF/RFR also has impacts at levels of brain function measurable by these techniques. At various frequencies and durations of exposure it has been noted to impact alpha and beta rhythms (Hinrikus et al. 2008), to increase randomness (Marino, Nilsen, and Frilot 2003; Marino and Carrubba 2009), to alter power, to modulate interhemispheric synchronization (Vecchio et al. 2007), to alter electrical activity in brain slices (Tattersall et al. 2001) and to alter the patterns of coordination (spectral power coherence) across the major power bands (Hountala et al. 2008). Bachman et al. (2006) showed statistically significant changes in EEG rhythms and dymanics occurred in between 12% and 20% of healthy volunteers (Bachmann, 2006). In children, exposures to cell phone radiation have resulted in changes in brain oscillatory activity during some memory tasks.

Sensory processing

At the symptomatic level issues with sensory processing are highly prevalent in ASDs. Phenomenology can include hypersensitivity to external stimuli, hyposensitivity to internal sensations and difficulty localizing sensation including pain, and difficulty processing more than one sensory channel at one time. (Robledo, Donnellan, and Strandt-Conroy 2012; Perry et al. 2007; Sacco et al. 2010) There is now electrophysiological evidence of abnormalities at early (brainstem) stages of sensory processing, as well as in later stages of processing that occur in the cortex. Some studies have shown lower and some longer latencies of response to an auditory stimulus. Domains of perception where the performance of people with ASDs is superior to that of neurotypical individuals have been identified. (Marco et al. 2011) *"It is obvious…that sensory processing abnormalities in ASD are distributed rather than localized; sensory abnormalities in ASD obviously span multiple dimensions of latency, adaptation, magnitude and behavior abnormalities, with both enhanced and impaired behavior associated with aberrant cortical responses. Given this diversity in findings, the heterogeneity of ASD, and broad variability seen over and over again in the ASD groups almost irrespective of the study, it is hard to imagine that one single theory could account for all of these observations…. It is therefore probable that several mechanisms and neuronal abnormalities, most likely at multiple levels (from single neurons through to inter-area connections), all contribute to varying degrees to the abnormal sensory processing observed in ASD. It is also likely that no single mechanism is unique to one sensory modality, which is why we see such a widely distributed range of abnormalities across modalities."* (Kenet 2011)

It is also possible that the mechanisms may not simply be neural – they may also be modulated by glial, metabolic, immune, perfusional and other physiological processes and physical properties as well. Yet although there is some consideration of the pathophysiology-sensory function interaction (Kern et al. 2010), it has basically not been fleshed out in studies of ASDs with experimental designs integrating pathophysiological and electrophysiology.

Kenet et al. (2010) demonstrated environmental vulnerability of sensory processing in the brain by the exposure of rat dams to noncoplanar polychlorinated biphenyls (PCBs), during gestation and for three subsequent weeks of nursing (Kenet, 2011). *"Although the hearing sensitivity and brainstem auditory responses of pups were normal, exposure resulted in the abnormal development of the primary auditory cortex (A1). A1 was irregularly shaped and marked by internal nonresponsive zones, its topographic organization was grossly abnormal or reversed in about half of the exposed pups, the balance of neuronal inhibition to excitation for A1 neurons was disturbed, and the critical period plasticity that underlies normal postnatal auditory system development was significantly altered. These findings demonstrate that developmental exposure to this class of environmental contaminant alters cortical development."* (Kenet et al. 2007). This study may be particularly relevant for EMF/RFR exposures, as the noncoplanar PCBs were discussed above as targeting calcium signaling as do EMF/RFR exposures – i.e. they both converge upon a common cellular mechanism (Pessah and Lein 2008; Stamou et al. 2012), justifying exploring the hypothesis that the outcomes one might expect from EMF/RFR could be similar.

Autonomic dysregulation

Although there are a fair number of negative studies regarding the impact of EMF/RFR exposure on the autonomic nervous system, increased HRV and autonomic disturbances have been documented (Andrzejak et al. 2008; Szmigielski et al. 1998; Bortkiewicz et al. 2006; Graham et al. 2000; Saunders and Jefferys 2007). Buchner and Eger (2010), in a study in rural Germany of the health impacts of exposures from a new base station yielding novel exposure to EMF/RFR, saw a significant elevation of the stress hormones adrenaline and noradrenaline during the first six months with a concomitant drop in dopamine, with a failure to restore the prior levels after a year and a half. These impacts were felt by the young, the old and the chronically ill, but not by healthy adults (Buchner and Eger 2011).

Effects on the neonate are also evident. Bellieni et al (2008) found that heart rate variability is adversely affected in infants hospitalized in isolettes or incubators where ELF-EMF levels are in the 0.8 to 0.9 μT range (8 to 9 mG). Infants suffer adverse changes in heart rate variability, similar to adults (Bellieni et al. 2008). This electromagnetic stress may have lifelong developmental impacts, based on a study showing that in utero beta 2 agonist exposure can potentially induce a permanent shift in the balance of sympathetic-to-parasympathetic tone (Witter et al. 2009).

Meanwhile clinical observation and a growing body of literature support a major role for stress in ASDs (Anderson and Colombo 2009; Anderson, Colombo, and Unruh 2012; Daluwatte et al. 2012; Ming et al. 2011), with variability amongst individuals in the severity of the stress response but a tendency to have high tonic sympathetic arousal at

baseline (Hirstein, Iversen, and Ramachandran 2001; Toichi and Kamio 2003; Ming, Julu, et al. 2005; Mathewson et al. 2011; Cheshire 2012; Chang et al. 2012).

The impact of EMF/RFR exposure can also be greatly influenced by the stress system status of the individual being exposed. Tore et al sympathecotomized some of his rats before exposure to GSM, to simulate cell phone exposure (Tore et al. 2002; Tore et al. 2001). Salford et al. (2012) reviewed the results:

> *"Comparing the animals, which had been subjected to ganglionectomy, to the other animals, Töre et al. made an interesting observation: as expected, albumin extravasation was more prominent in the sympathectomised sham-exposed rats as compared to normal exposed rats. This was due to the fact that the sympathectomised rats were in a chronic inflammation-prone state with hyper-development of pro-inflammatory structures, such as the parasympathetic and sensory inputs as well as mast cells, and changes in the structure of the blood vessels. Such an inflammation-prone state has a well-known effect on the BBB leakage. However, when comparing sham-exposed sympathectomised rats to GSM-exposed sympathectomised rats, a remarkable increase in albumin leakage was present in the GSM exposed sympathectomised rats compared to the sham rats.* ***In the GSM-exposed sympathectomised rats, both brain areas and the dura mater showed levels of albumin leakage resembling those observed in positive controls after osmotic shock****.[emphasis added] Indeed, more attention should be paid to this finding, since it implicates that the sensitivity to EMF-induced BBB permeability depends not only on power densities and exposure modulations, but also on the initial state of health of the exposed subject."* (Salford, Nittby, and Persson 2012)

This dramatically greater impact on an autonomically and immunologically vulnerable set of animals raises concerns since the vulnerabilities of these animals bear some resemblance to the pathophysiological challenges of individuals with ASDs.

The interconnection between stress and brain connectivity (or coherence) in ASDs is brought out by Narayanan et al. (2010) n a pilot study testing the impact of the beta blocker propranolol on brain functional connectivity measured using functional MRI (Narayanan et al. 2010). A fairly immediate increase in functional connectivity was noted from propranolol – but not from nadolol which has the same vascular effects but does not cross the BBB. Propranolol decreases the burden of norepinephrine, thereby reducing the impact of stress systems on brain processing, and the authors interpreted these effects as creating an improvement of the brain's signal-to-noise ratio (Hasselmo, 1997), allowing it to utilize and coordinate more remote parts of its networks. This suggests that stressors such as EMF/RFR, by adding non-biologically meaningful noise to the system, might have the opposite effects, degrading coherent integration.

C. De-tuning of the Brain and Organism

1. Electromagnetic signaling, oscillation and synchrony are fundamental, and vulnerable

While electrophysiological activity is an intrinsic property of the nervous system, electromagnetic signaling are vital parts of every cell and of molecular structure.

> *"All life on earth has evolved in a sea of natural low-frequency electromagnetic (EM) fields. They originate in terrestrial and extraterrestrial sources. The ever-growing use of electric power over the last century has sharply modified this natural environment in urban environments. Exposure to power-frequency fields far stronger than the natural environment is now universal in civilized society."* (Adey 1994)

Adey published some of the earliest scientific studies on the "cooperativity" actions of cells in communication. Studies showing us that the flux of calcium in brain tissue and immune cells is sensitive to ELF-modulated radiofrequency fields is actually telling us that some of the most fundamental properties of cells and thus of our existence can be modulated by EMF/RFR.

> *"...in first detection of environmental EM fields in tissues, there appears to be a general consensus that the site of field action is at cell membranes. Strands of protein are strategically located on the surface of cells in tissue, where they act as detectors of electrical and chemical messages arriving at cell surfaces, transducing them and transmitting them to the cell interior. The structural basis for this transductive coupling by these protein strands is well known. Through them, cell membranes perform a triple role, in* ***signal detection, signal amplification, and signal transduction to the cell interior****."* (Adey 1994)

Communication between cells through gap junctions, which is a means of "metabolic cooperation," is also vulnerable to disruption, as discussed earlier.

Oscillation is also a universal phenomenon, and biological systems of the heart, brain and gut are dependent on the cooperative actions of cells that function according to principles of non-linear, coupled biological oscillations for their synchrony, and are dependent on exquisitely timed cues from the environment at vanishingly small levels (Buzsaki 2006; Strogatz 2003). The key to synchronization is the joint actions of cells that co-operate electrically - linking populations of biological oscillators that couple together in large arrays and synchronize spontaneously according to the mathematics described for Josephson junctions (Brian Josephson, the 1993 Nobel prize winner for this concept). This concept has been professionally presented in journal articles and also popularized in a book by Prof. Steven Strogatz, a mathematician at Cornell University who has written

about ‘sync’ as a fundamental organizing principle for biological systems (Strogatz 2001) (Strogatz 2003).

> *“Organisms are biochemically dynamic. They are continuously subjected to time-varying conditions in the form of both extrinsic driving from the environment and intrinsic rhythms generated by specialized cellular clocks within the organism itself. Relevant examples of the latter are the cardiac pacemaker located at the sinoatrial node in mammalian hearts and the circadian clock residing at the suprachiasmatic nuclei in mammalian brains. These rhythm generators are composed of thousands of clock cells that are intrinsically diverse but nevertheless manage to function in a coherent oscillatory state. This is the case, for instance, of the circadian oscillations exhibited by the suprachiasmatic nuclei, the period of which is known to be determined by the mean period of the individual neurons making up the circadian clock. The mechanisms by which this collective behavior arises remain to be understood.”* (Strogatz 2003)

The brain contains a population of oscillators with distributed natural frequencies, which pull one another into synchrony (the circadian pacemaker cells). Strogatz has addressed the unifying mathematics of biological cycles and external factors disrupt these cycles. This also applies to mitochondria:

> *“Organisation of mitochondrial metabolism is a quintessential example of a complex dissipative system which can display dynamic instabilities. Several findings have indicated that the conditions inducing instabilities are within the physiological range and that mild perturbations could elicit oscillations. Different mathematical models have been put forth in order to explain the genesis of oscillations in energy metabolism. One model considers mitochondria as an organised network of oscillators and indicates that communication between mitochondria involves mitochondrial reactive oxygen species (ROS) production acting as synchronisers of the energy status of the whole population of mitochondria. An alternative model proposes that extramitochondrial pH variations could lead to mitochondrial oscillations.”* (Iotti, Borsari, and Bendahan 2010)

The field of bioelectromagnetics has studied exposure to very low levels of electromagnetic frequencies.

These exposures can alter critical properties of chemical reactions. *“In a chemical reaction, the bond breaks and each partner reclaims its electron from the bond, moving away to encounter a new partner. It is now an unattached, highly reactive free radical. Reforming a bond requires a meeting between two radicals with opposite electron spins, the union producing a singlet pair. The lifetime of free radicals is typically short, in the*

range of microseconds to nanoseconds. It is in this brief period that imposed magnetic fields may alter the rate and amount of product of a chemical reaction. Since the effect is only on the kinetics of chemical reactions, they are known as magnetokinetic effects (Steiner and Ulrich, 1989). They occur only in nonthermal states of biomolecular systems, defined as an insensitivity to random thermal interactions during the brief period of their existence (Walleczek, 1994). They are a consequence of a coherent quantum-mechanical step which accompanies free radical formation." (Adey 1994)

Not just chemical reactions but synchronous biological oscillations in cells (pacemaker cells) can be disturbed and disrupted by artificial, exogenous environmental signals, whicn can lead to desynchronization of neural activity that regulates critical functions (including metabolism) in the brain, gut and heart and circadian rhythms governing sleep and hormone cycles (Strogatz, 1987). Buzsaki in his book *Rhythms of the Brain* (2006) says "*rhythms can be altered by a wide variety of agents and that these perturbations must seriously alter brain performance."* (Buzsaki 2006)

Disturbance can get increasingly disruptive as more damage occurs and more systems are thrown out of kilter and out of cooperativity. One can think of the kindling model in which repeated induction of seizures leads to longer and more sever seizures and greater behavioral involvement. The combination of disruptive and stimulatory effects of biologically inappropriate EMF/RFR exposures could contribute to disruption of synchronized oscillation and cooperativity at a myriad of levels but particularly in the brain, and this may contribute to the loss of coherence and complexity in the brain in autism, as well as dysregulation of multiple other bodily systems. Strogatz points out that there are many more ways of being desynchronized than being synchronized (Strogatz, 2003). It has even been suggested that autism itself could be due to brain desynchronization (Welsh, 2005).

2. Behavior as an "emergent property"

Although from a pathophysiological point of view one might hypothesize that a brain with greater indications of oxidative stress along with immune activation and mitochondrial dysfunction might generate different oscillatory activity than a brain in which those pathophysiological features were absent, to date almost no attention has been paid to testing this hypothesis in ASD or neurodevelopmental and neuropsychiatric conditions more generally. From this vantage point it would make sense to propose that the compromised whole body health status of at least many with ASDs would make it harder for them to maintain the resilience of their brain cells and brain activities in the face of potentially disruptive exposures. Yet the investigation of how this might occur remains a largely unexplored frontier. But from the point of view of making sense of the

brain impact of environmental challenges – including but not limited to EMF-RFR – this investigation is crucial.

The pathophysiological perspective that guides this review would suggest a move away from considering the behavioral manifestations of ASDs as core 'traits,' *Instead behaviors may be better understood as 'outputs' or emergent properties – what the brain and body produce – when their physiological attributes are altered* in these fashions for whatever reasons – be they genetic, environmental or many combinations of both (Anderson 2009, 2008; Sieb 2004; Smith and Thelen 2003; Custodio et al. 2007; Herbert 2012). Sleep and consciousness have also been considered 'emergent properties' (Krueger et al. 2008; Krueger and Obal 2003). Brain oscillatory activity is critical for organizing behavior, and it arises from cells and subcellular features that are shaped by the environment and can act differently based on their functional status as well as on account of external sensory or psychosocial stimuli.

In particular, a) brain oscillatory activity is intimately connected with underlying cellular, metabolic and immune status, b) EMF/RFR is capable of perpetrating changes at each of these levels, and c) problems at each of these levels can make other problems worse. And as mentioned earlier, EMF/RFR and various toxicants can co-potentiate damage (Juutilainen and Kumlin 2006; Juutilainen, Kumlin, and Naarala 2006; Verschaeve et al. 2006; Ahlbom et al. 2008; Hoyto et al. 2008; Juutilainen 2008; Luukkonen et al. 2009; Markkanen, Juutilainen, and Naarala 2008), amplifying allostatic load.

Put together, all of this implies that the combination of these EMF/RFR impacts may quite plausibly significantly contribute both to how ASDs happen in individuals and to why there are more reported cases of ASDs than ever before (with studies showing that not all of this increase can be written off as artifact (King and Bearman 2009; Hertz-Picciotto and Delwiche 2009).

The hopeful side of this framing of the problem comes from moving beyond the increasingly anachronistic idea that autism is determined overwhelmingly by genetic code about which we can do little or nothing. An emerging model that explains much more of what we now know frames ASDs as the dynamic, active outcomes of perturbed physiological processes – again, more like a chronic but changeable 'state' than a 'trait.' In the latter model, one is empowered to strongly reduce exposures and to make aggressive constructive environmental changes – particularly in diet and nutrition, given their protective potency discussed above (Herbert and Weintraub 2012). In this way allostatic load can be reduced, physiological damage can be repaired, homeostasis can be restored and resilience and optimal function can be promoted.

III. IMPLICATIONS

A. Summary

In the above review, the case has been made that ASDs involve physiological challenges at multiple levels, and that these challenges are paralleled in the physiological impacts of EMF/RFR exposure. Evidence has also been presented to suggest that the many levels of damage and degradation of physiological and functional integrity are profoundly related to each other. Although autism spectrum disorders (ASDs) are defined by problems with behavior, communication, social interaction and sensory processing, under the surface they also involve a range of disturbances of underlying biology that find striking parallels in the physiological impacts of electromagnetic frequency and radiofrequency exposures (EMF/RFR). At the cellular and molecular level many studies of people with ASDs have identified oxidative stress and evidence of free radical damage, evidence of cellular stress proteins, as well as deficiencies of antioxidants such as glutathione. Elevated intracellular calcium in ASDs can be associated with genetic mutations but more often may be downstream of inflammation or chemical exposures. Cell membrane lipids may be peroxidized, mitochondria may function poorly, and immune system disturbances of various kinds are common. Brain oxidative stress and inflammation as well as measures consistent with blood-brain barrier and brain perfusion compromise have been documented. Changes in brain and autonomic nervous system electrophysiology can be measured and seizures are far more common than in the population at large. Sleep disruption and high levels of stress are close to universal. In parallel, all of these phenomena have also been documented to result from or be modulated by EMF/RFR exposure. Moreover, some people with ASDs have de novo mutations (that their parents do not have), and EMF/RFR exposures could contribute to this due to their potential genotoxicity. EMF/RFR exposure during pregnancy may send spurious signals to developing brain cells during pregnancy, altering brain development during critical periods, and may increase oxidative stress and immune reactivity that can increase risk for later developmental impairments, with further disruption later in development increasing risk, physiological dysregulation and severity of outcome.

All of this does not prove that EMF/RFR exposures cause autism, but it does raise concerns that they could contribute by increasing risk, and by making challenging biological problems and symptoms worse in these vulnerable individuals. Placed alongside the dramatic rise in reported cases of ASDs, that parallels the dramatic rise in deployment of wireless technologies, a strong case can be made for aggressively investigating links between ASDs and EMR/RFR, and minimizing exposures for people with autism as well as families preconceptionally, during pregnancy, and around infants and children at home, at school, and in health care centers and hospitals.

These arguments have implications for how we understand what ASDs 'are' and how they work. These implications call upon us to take the environmental contribution very seriously, which involves on the one hand a sobering appreciation of the vast array of exposures that can contribute to risk via perturbed development and physiological degradation, and on the other hand a sense that there are powerful things we can do to improve the situation.

B. Exposures and their Implications

Several thousand scientific studies over four decades point to serious biological effects and health harm from EMF and RFR as are intensively reviewed in the many detailed sections of this BioInitiative Report. These studies report genotoxicity, single-and double-strand DNA damage, chromatin condensation, loss of DNA repair capacity in human stem cells, reduction in free-radical scavengers (particularly melatonin), abnormal gene transcription, neurotoxicity, carcinogenicity, damage to sperm morphology and function, effects on behavior, and effects on brain development in the fetus of human mothers that use cell phones during pregnancy. Cell phone exposure has been linked to altered fetal brain development and ADHD-like behavior in the offspring of pregnant mice.

1. Exposures have outpaced precautions

There is no question that huge new exposures to EMF/RFRs have occurred over the past few decades. As discussed extensively in other parts of this Bioinitiative 2012 update (Sage, 2012), there is much concern that regulations to date have been based on a very limited sense of the pertinent biology, and particularly that limiting concern to thermal impacts is no longer valid since there is a wealth of evidence by now that non-thermal impacts can be biologically very powerful.

Only in the last two decades have exposures to RFR and wireless technologies become so widespread as to affect virtually every living space, and affect every member of societies around the world. Even as some disease patterns like brain tumors from cell phone use have become 'epidemiologially visible', there are no comprehensive and systematic global health surveillance programs that really keep up to report EMF/RFR health trends (Fragopoulou et al. 2010).

> "*The deployment of new technologies is running ahead of any reasonable estimation of possible health impacts and estimates of probabilities, let alone a solid assessment of risk. However, what has been missing with regard to EMF has been an acknowledgement of the risk that is demonstrated by the scientific studies. There is clear evidence of risk, although the magnitude of the risk is*

uncertain, and the magnitude of doing nothing on the health effects cost to society is similarly uncertain. This situation is very similar to our history of dealing with the hazards of smoking decades ago, where the power of the industry to influence governments and even conflicts of interest within the public health community delayed action for more than a generation, with consequent loss of life and enormous extra health care costs to society." (Sage and Carpenter 2009).

2. The population's exposure has increased

Given the range of physiological impacts described in Part 2, the very rapid global deployment of both old and new forms of emerging wireless technologies in the last two decades needs aggressive evaluation from a public health perspective.

In the United States, the deployment of wireless infrastructure (cell tower sites) to support cell phone use has accelerated greatly in the last decades. The Cellular Telephone Institute of America (CTIA) estimated that in 1997 there were only 36,650 cell sites in the US; but increased rapidly to 131,350 in June 2002; 210,350 in June 2007 and 265,561 in June 2012 (Roche, 2012; Cellular Telephone Industry of America (CTIA) 2012). About 220,500 cell sites existed in 2008 (Reardon, 2007; Cellular Telephone Industry of America (CTIA) 2012; Anonymous, May 2005). These wireless facilities for cellular phone voice and data transmission produce RFR over broad areas in communities and are an involuntary and unavoidable source of radiofrequency radiation exposure. Other new RFR exposures that didn't exist before are from WI-FI access points (hotspots) that radiate 24/7 in cafes, stores, libraries, classrooms, on buses and trains, and from personal WI-FI enabled devices (iPads, tablets, PDAs, etc).

Not surprisingly, the use of cell phones has a parallel growth trend. In the late 1980s and early 1990's, only a few percent of the US population were cell phone users. By 2008, eighty-four percent (84%) of the population of the US owned cell phones [16]. CTIA reports that wireless subscriber connections in the US increased from 49 million in June 1997 to 135 million in June 2002 to 243 million in June 2007 to 322 million in June 2012 (Roche, 2012; Cellular Telephone Industry of America (CTIA), June 2012) This represents more than a 100% penetration rate in the US consumer market, up from just a few percent in the early 1990's. The number of wireless subscribers in June 1997 was 18%; in June 2002 it was 47%; in June 2007 it was 81% and in June 2012 it is 101%.

The annualized use of cell phones in the US was estimated to be 2.23 trillion minutes in 2008 and 2.296 trillion minutes in 2010 (CITA, 2012). There are 6 billion users of cell phones world- wide in 2011 up from 2.2 billion in 2008 and many million more users of cordless phones.

The number of US homes with *only* wireless cell phones has risen from 10.5% in 2007 to 31.6% in June of 2012 (Roche, 2012; Cellular Telephone Industry of America (CTIA),

June 2012). There are no statistics for June 1997 nor for June 2002, since landline (non-wireless) phone use predominated. The shift to wireless communications, more minutes of use, and reliance on cell and cordless phones rather than corded phones is an extremely revealing measure of new EMF and RFR exposures for both adults and children.

3. Infants, children and childbearing families are highly exposed and vulnerable

With regard to children, the spread of cell towers in communities, often placed on pre-school, church day-care, and school campuses, means that young children may have hundreds of thousands of times higher RF exposures in home and school environments than existed even 20-25 years ago. In addition, the nearly universal switch to cordless and cell phones, and away from corded landline phones, means close and repetitive exposures to both EMF and RFR in the home. Wireless laptops and wireless internet in schools, and home offices and for homework mean even more chronic exposures to RFR, a designated IARC 2B Possible Human Carcinogen (International Agency for Research on Cancer of the World Health Organization, May 2011; Baan, 2011) The great utility of handheld devices as communication aids and sources of information and satisfaction for people on the autism spectrum may come with a concerning underbelly.

Exposures prior to conception or during pregnancy and infancy are also important to consider. These exposures can come from faulty wiring, proximity to power lines, or high-frequency transients from a proximate transformer on a utility pole, or internal sources of pulsed RFR in the home (examples include an electronic baby monitor in the crib, a wireless router in the next room, a DECT phone that pulses high emissions of RFR on a continuous basis 24/7, or conversion to all compact fluorescent bulbs that produce significant 'dirty electricity' for occupants due to low-kilohertz frequency fields on electrical wiring and in ambient space. Sick and vulnerable infants in neonatal intensive care units are heavily exposed from being surrounded by equipment, with negative metabolic and autonomic consequences documented and other likely consequences needing further investigation (Bellieni et al. 2008; Bellieni, Tei, et al. 2012).

Wireless phones and laptops exposures produce extremely low frequency pulses from the battery of the wireless device (Sage, 2007; Sage and Carpenter 2009) and the exposures to pulsed radiofrequency microwave radiation when the wireless device is transmitting or receiving calls and emails.

Especially since EMF/RFR exposures are already classified as IARC 2B Possible Human Carcinogens, we should be actively investigating these sources of damage to DNA that could reasonably result in 'de novo mutations' but also be aware that common environmental exposures from EMF and RFR might play a role in the higher rates of concordance for autism (ASD) among twins and siblings.

Researchers also should be aware that common environmental exposures from EMF and RFR might play a role in the higher rates of autism (ASD) among twins and siblings, not solely because of maternal use of wireless devices during pregnancy and paternal sperm exposure to wireless devices peri-conception; but also because such oxidative damage to DNA can occur at levels introduced into the world of the fetus, and young developing infant and child via baby surveillance monitoring devices in the crib and wireless devices in the home. The deployment of technologies poses risks to human fertility and reproduction capacity, to the fetus, to children and adults (Sage and Carpenter 2009).

4. ASD risk and genomic damage to future generations

Barouki and Grandjean (2012) make a persuasive case that public health interventions are critically needed in early childhood development to prevent adult diseases that appear decades later (Barouki et al. 2012). Although they do not include EMF or RFR but only chemicals, they do say that physiological stressors, which EMF and RFR certainly have been established to be, should be reduced during critical development windows. They say: "*The current pandemic of non-communicable diseases and the increased prevalence of important dysfunctions demand an open interrogation of why current interventions appear insufficient. We now know that disease risk can be induced very early in the life course and that it is modifiable by nutrients and environmental chemical exposures (along with drugs. infections, and other types of stresses)".*

Part II of this chapter documents the detailed scientific basis for considering EMF/RFR exposures to be of significance to the ASDs crisis. Public health interventions are warranted now to protect the genetic heritage of humans, as well as the other stocks of genetic material in wildlife and plants in the face of what appears to be on-going impairment of these genomes. The risk of genomic damage for future generations is sufficiently documented to warrant strong preventative action and new public safety limits that observe EMF/RFR levels shown to cause adverse effects.

5. De-tuning the organism

Genetic mutations may lead to cancer and other diseases in the present and future generations, but the exposures that are capable of creating genotoxic impacts also compromise physiological function Even genotoxicity can have not only specific but also non-specific effects due to inefficiencies, misfolded proteins, and cellular debris, as discussed in the section "Implications of Damage" at the end of the first part of Part II, regarding the rescue of a mouse model of Rett syndrome through enabling a probably generic process of microglial phagocytosis, critical to debris removal, rather than through correcting some specific molecular defect of the synapse (Derecki et al. 2012; Derecki, Cronk, and Kipnis 2012).

In the present setting, where the argument about the pertinence of the cascade of physiological and genotoxic compromises to autism includes the degradative impact on oscillatory synchronization, it is also worth considering that oscillation is a property of living and even physical systems much more generally, and not just of brain oscillatory networks (Strogatz 2003). Under certain circumstances, phase transitions occur and synchronization emerges, often rather quickly rather than gradually – more like a state change than a gradual trend. On the other hand, as mentioned, synchronization can be lost, and there are an enormous number of ways for a system to be de-synchronized, which may relate to the heterogeneity amongst people with ASD that so vexes researchers.

In the setting of autism, a baby gestated or developing as a neonate in a milieu with excessively elevated EMF/RFR exposures is bound to have interference with the normal development processes, including the organization of information and experience in the brain. This baby's environment also often nutritional insufficiencies (processed denatured pesticide-laden food low in antioxidants, minerals and essential fatty acids essential to cellular protection). The baby's gestational period may have been complicated by the mother's own health issues such as conditions like obesity and diabetes (Krakowiak, 2012) which converge on inflammation, oxidative stress and other common forms of physiological dysregulation associated with or even just eating nutrient-depleted, pesticide-laden processed food. The exquisite 'tuning up' of the brain and body as it develops will integrate and respond to the environmental inputs it receives, and is particularly sensitive to environmental miscues (whether chemical like endocrine disruptors, EMF/RFR, or other hostile environmental conditions whether hostile or nurturing). To the extent that the baby is burdened with more disorganized or hostile cues than nurturing and organizing cues, that baby may lose resiliency and become more physiologically vulnerable –perhaps approaching a tipping point into decompensation.

From a systems point of view, the phenomenon of 'autistic regression' may occur after an accumulation of multisystem signaling interference leading to a tipping point of loss of some vital systems synchronization and increase in randomization. EMF/RFR exposures could plausibly contribute both to this vulnerability and to the decompensation/desynchronization process – as could other stressors such as infection, toxicity, acute stress. The vulnerability, then, is the 'allostatic load' – the total burden of stressors pressing toward disorganization. The tipping point may come in a variety of ways but upon investigation one is likely to find that unless it is a severe stressor it is not triggered simply by a single source of stress in an otherwise blissfully healthy child, but rather is the "straw that breaks the camel's back' laid atop a prior accumulation of 'allostatic load.'

C. Conclusions and Recommendations

1. Change our deployment of EMF/RFR

The deployment of RFR from wireless technologies has incredible momentum, and it has made many things easier and many other things possible for the first time. On the other hand this momentum can interfere with setting up the technology in a fashion truly respectful of biological tolerances. Other sections in the Bioinitiative 2012 update will address recommendations and guidelines for increasing the safety profile. This will undoubtedly provoke controversy. The problems will not get settled immediately, and transformation to healthier arrangements will take time.

> *"There is no question that global implementation of the safety standards proposed in the Bioinitiative Report, if implemented abruptly and without careful planning, have the potential to not only be very expensive but also disruptive of life and the economy as we know it. Action must be a balance of risk to cost to benefit. The major risk from maintaining the status quo is an increasing number of cancer cases, especially in young people, as well as neurobehavioral problems at increasing frequencies. The benefits of the status quo are expansion and continued development of communication technologies. But we suspect that the true costs of even existing technologies will only become much more apparent with time. Whether the costs of remedial action are worth the societal benefits is a formula that should reward precautionary behavior*." (Sage and Carpenter 2009)

2. Encourage precautions right now based on present knowledge

In the meantime many people have already started taking precautionary measures, and more will wish to do so. Physicians and health care people should raise the visibility of EMF/RFR as a plausible environmental factor in clinical evaluations and treatment protocols. Reducing or removing EMF and wireless RFR stressors from the environment is a reasonable precautionary action given the overall weight of evidence.

- Children with existing neurological problems that include cognitive, learning, attention, memory, or behavioral problems should as much as possible be provided with wired (not wireless) learning, living and sleeping environments,
- Special education classrooms should aim for 'no wireless' conditions to reduce avoidable stressors that may impede social, academic and behavioral progress.
- All children should reasonably be protected from the physiological stressor of significantly elevated EMF/RFR (wireless in classrooms, or home environments).
- School districts that are now considering all-wireless learning environments should be strongly cautioned that wired environments are likely to provide better learning and teaching environments, and prevent possible adverse health consequences for both students and faculty in the long-term.

- Monitoring of the impacts of wireless technology in learning and care environments should be performed with sophisticated measurement and data analysis techniques that are cognizant of the non-linear impacts of EMF/RFR and of data techniques most appropriate for discerning these impacts.
- There is sufficient scientific evidence to warrant the selection of wired internet, wired classrooms and wired learning devices, rather than making an expensive and potentially health-harming commitment to wireless devices that may have to be substituted out later, and
- Wired classrooms should reasonably be provided to all students who opt-out of wireless environments.

Undoubtedly risks and the above recommendations will be dismissed by those poised to benefit from the sale of these new systems. Many people also feel that new possibilities have opened up to themselves and the world through wireless technologies. But the public needs to know that these risks exist, that transition to wireless should not be presumed safe, and that it is very much worth the effort to minimize exposures that still provide the benefits of technology in learning, but without the threat of health risk and development impairments to learning and behavior in the classroom.

Broader recommendations also apply, related to reducing the physiological vulnerability to exposures, reduce allostatic load and build physiological resiliency through high quality nutrition, reducing exposure to toxicants and infectious agents, and reducing stress (Herbert and Weintraub 2012), all of which can be implemented safely based upon presently available knowledge.

3. Build an environmentally physiologically centered research program in ASDs as a platform for investigating the EMR/RFR-ASD linkage

This review has been structured around the physiological parallels between ASDs and the impacts of EMF/RFR. What is missing from the autism research agenda is some cross-study of these two bodies of research evidence. To do this we will need both a recognition of the importance of these risks, and a collaborative multi-site research program centered around a "middle-out" physiological approach that can incorporate the the gene-brain-behavior agenda that has dominated ASD research into a broader framework (Herbert 2013). While the middle-out approach is an emerging framework in systems biology that can incorporate complexity and nonlinear, multileveled modeling (Cristofolini et al. 2008; de Graaf et al. 2009; Majumder and Mukherjee 2011; Vinga et al. 2010; Walker and Southgate 2009), the gene-brain-behavior approach has been based on an expectation of linear mapping across the levels on which it focuses, but instead the systems involved appear to be much more complex, and the physiological levels largely

left out of this linear approach are critically important to helping people with ASDs because they will help not only with understanding how environment impacts function but also with identifying leverage points.

4. Take the evidence as a call to action

Both EMF and RFR exposures are already classified as IARC 2B Possible Human Carcinogens. The substantial scientific literature on EMF and RFR effects on DNA, on immune and blood-brain barrier disruption, on stress proteins, on circadian rhythms and hormone disregulation, and on cognition, sleep, disruption of neural control and altered brainwave activity all argue for reduction of exposures now, and better coordinated research in these areas.

All relevant environmental conditions should be given weight in defining and implementing prudent, precautionary actions to protect public health, including EMF and RFR. Evidence is sufficient to add EMF/RFR prominently to the list of exposures that can degrade the human genome, and impair normal development, health and quality of our physiology. With the rising numbers people with ASDs and other childhood health and developmental disorders, we cannot afford to ignore this component of risk to our children and vulnerable populations. When the risk factors are largely avoidable or preventable, ignoring clear evidence of large-scale health risks to global populations poses unnecessary and unacceptable risks. Taking this evidence as a call to action will be challenging and disruptive in the short term, but constructive in the longer term as we learn to use EMF/RFR in healthier ways.

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SECTION 22

Precaution in Action – Global Public Health Advice Following BioInitiative 2007

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I. INTRODUCTION

This section highlights some major milestones in documentation of potential health effects of low-intensity electromagnetic fields and radiofrequency radiation, and subsequent national and international actions taken to address the problem. The categories of response are divided into Publications and Health Agency Advisories, Local and National Country Actions, Expert Research Group and Physicians' Advisories and the formal classification by the World Health Organization International Agency for Research on Cancer for RFR as a 2B Possible Human Carcinogen.

II. PUBLICATIONS AND HEALTH AGENCY ADVISORIES (2007 – 2012)

The BioInitiative Report (2007)

The BioInitiative Report (1) is a 650+ page report documenting the evidence for bioeffects and adverse health effects (the science and public health consequences of that body of scientific evidence) from electromagnetic field and radiofrequency (microwave) radiation. It was written by an independent international research group to give an overview of what is known of biological effects that occur at low-intensity EMFs exposures (for both radiofrequency radiation RFR and power-frequency ELF-EMF), and various forms of combined exposures that are now known to be bioactive). The Report examines the research and current standards and finds that these standards are far from adequate to protect public health. The report presents solid science on this issue, and makes recommendations to decision-makers and the public.

The BioInitiative Working Group was composed of scientists, researchers and public health policy professionals. In 2007, the Working Group documented information from over 2000 published scientific studies and reviews reporting bioeffects and adverse health impacts of electromagnetic fields and radiofrequency radiation at exposure levels far below current public safety standards that should be considered in the international debate about the adequacy (or inadequacy) of existing public exposure standards.

Eleven chapters documented key scientific studies and reviews identifying low-intensity effects of electromagnetic fields. Sections 16 and 17 were prepared by public health and policy experts. These sections discuss the standard of evidence which should be applied in public health and environmental planning, how the scientific information should be evaluated in the context of prudent public health policy, and the basis for taking precautionary and preventative actions that are proportionate given this evidence.

European Environment Agency (2007)

European Environmental Agency Executive Director Jacqueline McGlade, PhD provided early support for the BioInitiative Report (2007). The Agency's Head of Communications and Corporate Affairs issued a news release on the publication of the BioInitiative Report, and the EEA contributions to it on September 17, 2007, two weeks after the Report was published on the web. It stated (2):

> *"A new report raising concerns about the effects of electromagnetic fields (EMF) on human health calls for tougher safety standards to regulate radiation from mobile phones, power lines and many other sources of exposure in daily life. The report, 'Bioinitiative: A Rationale for a Biologically-Based Public Exposure Standard for Electromagnetic Fields' was compiled by the BioInitiative Working Group, an international group of scientists, researchers and public health policy professionals. The EEA has contributed to this new report with a chapter drawn from the EEA study 'Late lessons from early warnings: the precautionary principle 1896–2000' published in 2001."*
>
> *"The EEA study reviews the histories of a selection of public and environmental hazards, such as asbestos, benzene and PCBs, from the first scientifically based early warnings about potential harm, to subsequent precautionary and preventive measures. Cases on tobacco smoking and lead in petrol are forthcoming."*
>
> *"Although the EEA does not have specific expertise in EMF, the case studies of public hazards analyzed in the 'Late Lessons from Early Warnings' publication show that harmful exposures can be widespread before there is both 'convincing' evidence of harm from long-term exposures, and biological understanding of how that harm is caused."*
>
> *"There are many examples of the failure to use the precautionary principle in the past, which have resulted in serious and often irreversible damage to health and environments. Appropriate, precautionary and proportionate actions taken now to avoid plausible and potentially serious threats to health from EMF are likely to be seen as prudent and wise from future perspectives. We must remember that precaution is one of the principles of EU environmental policy*."
>
> Professor Jacqueline McGlade, Executive Director, EEA.

In the fall of 2007, the EEA Director responsed to strong media and industry attention to the BioInitiative Report, defending the EEA's position to declare 'early warnings' appropriate with respect to the evidence on mobile phone radiofrequency radiation and possible health hazards. The Director defended EEA recommendations for prudent public health action, based on the scientific evidence presented in the BioInitiative Report. (3)

> *"The BioInitiative report draws attention to some of the emerging evidence of potential harm from the long term effects of non-ionising radiations from electro and magnetic fields (EMF), particularly from the radio frequency (RF) exposures that arise from mobile phone telecommunications."*
>
> *"The Bioinitiative report, however, is only one of several reports reviewing the risks from the*

thermal and non-thermal effects of EMF that have been published over recent years."

"These include reports from the NIEHS, the EU, the WHO, the UK National Radiological Protection Board and others The EEA's contribution to the BioInitiative report was a chapter on the history and general application of the precautionary principle to a number of well known hazards for which there had been, and in some cases still is, much scientific uncertainty. The chapter summarised the main messages from our report, "Late Lessons from Early Warnings: the Precautionary Principle 1896-2000", (EEA 2001)."

"The point of our chapter for the BioInitiative report was to illustrate how past uncertainties had been dealt with so as to provide lessons that may be helpful in dealing with current hazards for which there is both scientific uncertainty and high stakes, both health and economic."

"It is because this accumulating evidence on RF is of increasing scientific concern, and because the exposure of the public, particularly vulnerable groups, is widespread and generally rising, that we judged it was timely to draw wider attention to the possibly serious hazards from EMF".

"In our judgement, the human and experimental evidence, taken together, is "clear" enough to support using the precautionary principle to justify reducing exposures, where feasible, and to review the evidence for the existing exposure limits, which, as you know, are based on thermal effects only."

EEA Director Jacqueline McGlade to Wolfram Konig, Nov 27, 2007

<u>*European Parliament (2007)*</u>

In September 26, 2007 Carolyn Lucas, MEP, introduced the topic of the BioInitiative Report recommendations to the European Parliament (4) and asked the European Commission what action the Commission is taking in response to the report, its conclusions and endorsement by the European Environment Agency.

"As the Commission will be aware, on 31 August 2007 the international BioInitiative Working Group of renowned scientists and public health policy experts published a report called "A Rationale for a Biologically-Based Public Exposure Standard for Electromagnetic Fields (ELF and RF)".

"This report documents evidence that ELFs are a risk factor for both childhood and adult cancers, and sets out how wireless technologies which rely on RF to send emails and voice communications are thousands of times stronger than levels reported to cause sleep disorders, headaches, problems with memory and concentration and other physical symptoms. It notes the unprecedented levels of exposure to ELFs being created by the "explosion of new sources" and raises serious scientific concerns over the health risks posed by long-term and cumulative exposure."

"The report concludes that current safety limits regulating the levels of ELF permitted from power lines, mobile phones and other sources are highly inadequate, and that a much more cautious approach should be taken to further deployment of risky technologies."

"The European Environment Agency (EEA) contributed a chapter to the report, concerning the consequences of previous failures to apply the precautionary principle in the face of public and environmental hazards. Following publication of the study the EEA's Executive Director has publicly stressed the importance of precaution where potentially serious future consequences may be involved, and called for actions to reduce exposures to ELF, particularly where vulnerable groups are concerned."

"What action is the Commission taking in response to this report, its conclusions and endorsement by the EEA? Does the Commission agree that the balance of evidence points to the need to revise public safety standards regulating radiation levels from sources of day-to-day ELF exposure, as well as policies on the testing and deployment of new telecommunications technologies?"

European Parliament 2008

The European Parliament issued advice on the Communication from the Commission to the Council, the European Parliament and the European Economic and Social Committee regarding the mid-term review of the European Environment and Health Action Plan 2004-2010 (COM(2007)0314). See Appendix A for full text, but in part, it stated:

21. Is greatly concerned at the Bio-Initiative international report (8) concerning electromagnetic fields, which summarises over 1500 studies on that topic and which points in its conclusions to the health risks posed by emissions from mobile-telephony devices such as mobile telephones, UMTS, Wifi, Wimax and Bluetooth, and also DECT landline telephones;

22. Notes that the limits on exposure to electromagnetic fields which have been set for the general public are obsolete, since they have not been adjusted in the wake of Council Recommendation 1999/519/EC of 12 July 1999 on the limitation of exposure of the general public to electromagnetic fields (0Hz to 30 GHz) (9, obviously take no account of developments in information and communication technologies, of the recommendations issued by the European Environment Agency or of the stricter emission standards adopted, for example, by Belgium, Italy and Austria, and do not address the issue of vulnerable groups, such as pregnant women, newborn babies and children;

23. Calls, consequently, upon the Council to amend its Recommendation 1999/519/EC in order to take into account the Member States' best practices and thus to set stricter exposure limits for all equipment which emits electromagnetic waves in the frequencies between 0.1 MHz and 300 GHz

Pathophysiology Journal Publication - Special Issue on EMF (2009)

As a direct result of the BioInitiative Report, a special, peer-reviewed issue of Pathophysiology (6) was published in March 2009 and contained most of the BioInitiative content (some chapters updated from 2006 to 2009 published works) including a chapter on public health implications of wireless technologies (7). It also extended the scope of coverage to include RF impacts on the blood-brain barrier, effects of cell towers on wildlife, and reproduction effects in animal studies. It provided assurance of the high scientific quality of the BioInitiative Report analysis and conclusions, and buttressed the need for new EMF safety standards in a respected, peer-reviewed scientific journal.

"Bioelectromagnetics, the study of biological effects of electromagnetic fields (EMF), is an interdisciplinary science with a technical literature that is not easily accessible to the non-specialist. To increase access of the public to the technical literature and to the health implications of the scientific findings, the Bioinitiative Report was organized by an international group of scientists and published online at www.bioinitiative.org on August 31, 2007. The report has been widely read, and was cited in September 2008 by the European Parliament when it voted overwhelmingly that the current EMF safety standards were obsolete and needed to be reviewed. "

"DNA shows biological effects at the sub-cellular level that occur at very low EMF thresholds and across frequency ranges of the EM spectrum. Interactions with DNA may account for many of the effects of EMF, and they raise the possibility that genetic damage due to EMF can lead to cancer."

"The brain is exposed to radiation from mobile phone antennas, and laboratory studies show that the radiation causes leakage of the protective blood–brain barrier, as well as the death of neurons in the brain. Radiation emitted from base stations can affect all who are in the vicinity. Epidemiological studies have shown a relation between exposure to mobile phones, base-stations and the development of brain tumors. Some epidemiological studies have significant flaws in design, and the risk of brain cancer may be greater than reported in the published results."

"In addition to the risk of brain cancer, EMF in the environment may contribute to diseases like Alzheimer's dementia and breast cancer in humans, as well as reproductive and developmental effects in animals in the wild. EMF affects the biochemical pathways and immunological mechanisms that link the different organ systems in our bodies and those of animals. The human body can act as an antenna for RF signals, and a small percentage of the population appears to be so sensitive to EMF that it interferes with their daily lives. In addition to the growing presence of EMF signals in the environment, the complexity of the signals may be important in altering biological responses. These are among the many factors that must be considered in approaching EMF safety issues."

Preface, Pathophysiology, Guest Editor Martin Blank, PhD

Media coverage of the Pathophysiology Journal in 2009 highlighted the everyday problems of EMF and wireless exposures in society. For the typical person on the street, the message of the BioInitiative Report and its subsequent contributions to a scientific journal were broken down into examples more familiar to them (8).

"Public health concerns and scientific evidence for risks from cell phones and other wireless devices is published today in the journal Pathophysiology. International researchers have urged quick precautionary action to address a possible epidemic of brain tumors and many other health risks. Over four billion people around the world now use cell phones. They are rapidly eliminating the use of traditional land-line phones throughout the world. Health researchers from six countries give findings in fifteen (15) chapters covering health risks to humans and wildlife from electromagnetic fields and radiofrequency radiation."

"The global rollout of wireless technologies and devices like cell phones, cordless phones, cell towers (masts) and many other sources greatly increases our EMF exposure in daily life. The enormous popularity of new communication devices that allow email, texting, and access to the Internet from any city street has placed the issue squarely before government agencies like the FDA and the FCC, and also parents and school administrators. Parents must decide whether possible health risks to their children outweigh the convenience of keeping track of them. School officials and teachers care because of disruption and distraction in the classroom from cell phone use. National safety officials in the US face public criticism about highway collisions and road deaths from cell phone use while driving. Federal railway officials are

still coping with the problem of illicit texting by US railroad personnel that lead to the catastrophic collision of two trains in Chatsworth, California in 2008 killing 24 and injuring 135 more."

Reba Goodman, PhD (Columbia University) commented: "*cells in the body react to EMFs as potentially harmful, just like to other environmental toxins including heavy metals and toxic chemicals. The DNA in living cells recognizes electromagnetic fields at very low levels of exposure, and produces a biochemical stress response."*

David O. Carpenter, MD, Co-Editor of the BioInitiative Report and Director of the University of Albany, Institute of Health and the Environment concluded: "*the existing FCC and international limits do not do enough to protect people, especially children, from daily exposures to electromagnetic fields and radiofrequency radiation. The existing safety limits did not anticipate these new kinds of technologies affecting the health of people living with and using wireless devices on a daily basis. These effects are now widely reported to occur at exposure levels significantly below most current national and international limits."*

Brain tumor specialist Dr. Lennart Hardell, MD, PhD works as both an oncologist and a researcher at Orebro University Hospital in Sweden. He is an expert on cell phones and brain tumors.

"The evidence for risks from prolonged cell phone and cordless phone use is quite strong. For people who have used these devices for 10 years or longer, and when they are used mainly on one side of the head, the risk of malignant brain tumor is doubled for adults and is even higher for persons with first use before the age of 20 years."

Swedish researcher Olle Johansson, PhD (Karolinska Institute) said: "*most worrisome to me are the constant and unavoidable EMF exposures (from cell and DECT phones, power lines, new wireless technologies like WIMAX and WI-FI, etc.) everywhere in our daily life that may affect the overall health of this and coming generations. I worry especially about the impacts on the immune system, our only real line of defense against disease."*

Wildlife biologist Alfonso Balmoro, PhD of Valladolid, Spain voiced his concern that: *"electromagnetic radiation is a form of environmental pollution which may hurt wildlife. Phone masts located in their living areas are irradiating continuously some species that could suffer long-term effects, like reduction of their natural defenses, deterioration of their health, problems in reproduction and reduction of their useful territory through habitat deterioration. Therefore microwave and radiofrequency pollution constitutes a potential cause for the decline of animal populations and deterioration of health of plants living near phone masts."*

Co-Editor of the BioInitiative Report Cindy Sage observed: *"Prolonged exposure to radiofrequency and microwave radiation from cell phones, cordless phones, cell towers, WI-FI and other wireless technologies has been linked to interference with short-term memory and concentration, sleep disruption, headache and dizziness, fatigue, immune disruption, skin rashes and changes in cardiac function."*

"*these effects can happen with even very small levels of exposure if they occur on a daily basis. Cell phone use is likely to be more harmful in children whose brain and nervous system development can last into late adolescence*"

"The public health implications of billions of people who are exposed makes this a matter of critical concern to policy-makers around the world."

The European Environment Agency Director's Statement (2009)

Two years following the publication of the BioInitiative Report, and just months after publication of the special issue of Pathophysiology on EMF, the EEA updated its comments on potential health

risks of EMF and concern over the adequacy of public safety limits for emerging wireless technologies. The EEA issued a Statement on Mobile Phones for the September, 2009 conference 'Cell Phones and Health: Science and Public Policy Questinos, Washington DC. In part, the comments read (9):

> *"This event and the related Senate Hearings yesterday, have been, in part, stimulated by the BioIntiative Report, (2007), which helped increase public awareness of the potential hazards of electromagnetic fields, not least from mobile phones. The European Parliament responded to this debate with its resolution earlier this year which, among other things, called for lowering exposure to electromagnetic fields and for new exposure limits that would better protect the public. We fully share these recommendations."*

The EEA provides data, information and knowledge on the environment, including its impacts on public health, to EU institutions (the European Parliament, European Commission, and European Council of Ministers), to the 32 Member Countries of the EEA, and to the general public.

> *"The intention of the EEA to promote the use of mobile telephony in this way increases its responsibility to provide information that can help ensure the safety of the public when using mobile phones, especially vulnerable groups such as children, the elderly, and the immuno- compromised. This is the reason why the EEA issued an early warning about the potential hazards of EMF on 17 September 2007."*
>
> *"In this we drew attention to the BioInitiative report and to the other main references relevant to this debate (from the EU, the WHO, and the UK National Radiological Protection Board) which, taken together, provided the basis for our early warning on EMF."*
>
> *"Specifically, we noted that there are many examples of the failure to use the precautionary principle in the past, which have resulted in serious and often irreversible damage to health and environments. Appropriate, precautionary and proportionate actions taken now to avoid plausible and potentially serious threats to health from EMF are likely to be seen as prudent and wise from future perspectives".*
>
> *"This is the reason why the EEA issued an early warning about the potential hazards of EMF on 17 September 2007."*

EEA Recommendations based on current evidence (2009)
The evidence is now strong enough, using the precautionary principle, to justify the following steps:

1. *For governments, the mobile phone industry, and the public to take all reasonable measures to reduce exposures to EMF, especially to radio frequencies from mobile phones, and particularly the exposures to children and young adults who seem to be most at risk from head tumours. Such measures would include stopping the use of a mobile phone by placing it next to the brain. This can be achieved by the use of texting; hands free sets; and by the use of phones of an improved design which could generate less radiation and make it convenient to use hands free sets.*
2. *To reconsider the scientific basis for the present EMF exposure standards which have serious limitations such as reliance on the contested thermal effects paradigm; and simplistic assumptions about the complexities of radio frequency exposures.*
3. *To provide effective labeling and warnings about potential risks for users of mobile phones.*
4. *To generate the funds needed to finance and organise the urgently needed research into the health effects of phones and associated masts. Such funds could include grants from industry and possibly a small levy on the purchase and or use of mobile phones. This idea of a research levy is*

a practice that we think the US pioneered in the rubber industry with a research levy on rubber industry activities in the 1970s when lung and stomach cancer was an emerging problem for that industry. The research funds would be used by independent bodies.

European Parliament 2009

On April 2, 2009, the European Parliament adopted the "European Parliament resolution of 2 April 2009 on health concerns associated with electromagnetic fields (2008/2211(INI))" (10). The Document was based on the "Report on health concerns associated with electromagnetic fields", Rapporteur: Frederique Ries (11) Committee on the Environment, Public Health and Food Safety. See Appendix B for full text. It part, the resolution says:

H. (W)hereas, however, there are some points that appear to be the subject of general agreement, in particular the idea that reactions to microwave exposure vary from one person to another, the need, as a matter of priority, to conduct exposure tests under actual conditions in order to assess the non-thermal effects associated with radio-frequency (RF) fields, and the fact that children exposed to EMFs are especially vulnerable (9) ,

1. Urges the Commission to review the scientific basis and adequacy of the EMF limits as laid down in Recommendation 1999/519/EC and report to the Parliament; calls for the review to be undertaken by the Scientific Committee on Emerging and Newly Identified Health Risks;

2. Calls for particular consideration of biological effects when assessing the potential health impact of electromagnetic radiation, especially given that some studies have found the most harmful effects at lowest levels; calls for active research to address potential health problems by developing solutions that negate or reduce the pulsating and amplitude modulation of the frequencies used for transmission;

5. Invites the Member States and local and regional authorities to create a one-stop shop for authorisation to install antennas and repeaters, and to include among their urban development plans a regional antenna plan

6. Urges the authorities responsible for authorising the siting of mobile telephony antennas to reach agreement, jointly with the operators in that sector, on the sharing of infrastructure, in order to reduce the volume thereof and the exposure of the public to EMFs;

15. Draws attention in this context to the appeal for caution from the coordinator of the Interphone study, Elisabeth Cardis, who, in the light of existing knowledge, recommends, as far as children are concerned, that mobile phones should not be used beyond reasonable limits and that landlines should be preferred;

21. Calls on the Commission, in recognition of the public concern in many Member States, to work with all relevant stakeholders, such as national experts, non-governmental organisations and industrial sectors, to improve the availability of, and access to, up-to-date information understandable to non-specialists on wireless technology and protection standards;

24. Proposes that the EU's indoor air quality policy should encompass the study of "wireless" domestic appliances, which, like Wi-Fi for Internet access and digital enhanced cordless telecommunications (DECT) telephones, have been widely adopted in recent years in public places and in the home, with the result that citizens are being continuously exposed to microwave emissions;

29. Instructs its President to forward this resolution to the Council, the Commission, the

This revision essentially neutralized the chance for an independent and unbiased review of health effects and assessment of the adequacy of the ICNIRP/FCC thermally-based public health standards by designating the SCENIHR Committee to be the arbiter. The SCENIHR Committee ignored the non-thermal science and public health issues on EMF in past reviews. Appointing SCENIHR to provide the 'official' report to Parliament on health effects of EMF essentially guaranteed the outcome would be ineffectual for precautionary action, that the standard of evidence for judging would be "causal" evidence; and a public health standard for judging the evidence would not prevail. Reaching the very high bar of establishing 'causal evidence of risk' is not in line with precautionary, prudent public health decision-making. It will delay necessary actions for avoidance long past the 'early warning' stage when such actions may reasonably prevent substantial health harm.

However many points adopted in the resolution are in favour of public health and must not be dismissed.

Seletun Statement 2009

In November, 2009, a scientific panel met in Seletun, Norway, for three days of intensive discussion on existing scientific evidence and public health implications of the unprecedented global exposures to artificial electromagnetic fields (EMF). The Scientific Panel recognized that the body of evidence on EMF requires a new approach to protection of public health; the growth and development of the fetus, and of children; and argues for strong preventative actions. The study concluded that "new, biologically-based public exposure standards are urgently needed to protect public health worldwide" (12).

The Seletun Statement was published in 2010 in the journal Reviews on Environmental Health. It was titled *Scientific panel on electromagnetic field health risks: Consensus points, recommendations, and rationales*. Scientific Meeting: Seletun, Norway, November 17-21, 2009. (12).

Specific Recommendations from the Seletun Scientific Panel are:

"Extremely Low Frequency (Fields from Electrical Power)

- *Based on the available evidence, the Seletun Scientific Panel recommends a 0.1 uT (1 mG) exposure limit for all new installations based on findings of risk for leukemia, brain tumours,*

Alzheimer's, ALS, sperm damage and DNA strand breaks. This exposure limit does not include a safety margin;

- *For all newly installed, or newly upgraded electrical power distribution, the Panel recommends a 0.1 uT (1 mG) set-back distance, from residences, hospitals, schools, parks, and playgrounds schools (and similar locations occupied by children) [A 0.1 uT (1 mG) time-weighted average (TWA) using peak loading for transmission lines to ensure that average is about half of this for typical exposures; or equivalent for long-term exposure in interior EMF environments (wiring, trans-formers, appliances, others).];*

- *For all newly constructed residences, offices, schools (and other facilities with children), and hospitals there shall be a 0.1 uT (1 mG) max. 24 hour average exposure limit;*

- *For all new equipment (e.g. transformers, motors, electronic products), where practical, the Panel recommends a 0.1 uT (1 mG) max. 24 hour average exposure limit. Where not practical (e.g. large power transformers), there should be a fence, or boundary marker, with clearly written warning labels that states that within the boundary area the 0.1 uT (1 mG) maximum, 24 hour average exposure limit is exceeded;*

- *The Panel recommends all countries should adopt electrical code requirements to disallow conduction of high-frequency voltage transients back into electrical wiring systems;*

- *All new electronic devices including compact fluorescent lamps (CFLs) should be constructed with filters to block high-frequency voltage transients from being conducted back onto electrical wiring systems;*

- *The Panel recommends electric field reductions from electrical wiring in buildings based on evidence of increased cancer risk from prolonged or repetitive electric field exposure. The United States National Electrical Code (NEC) and other govern-mental codes relating to building design and construction should be revised so that all new electrical wiring is enclosed in a grounded metal shield;*

- *The United States NEC and other govern-mental codes that disallow net current on electrical wiring should be better enforced, and ground fault interrupters (GFIs) should be installed on all electrical circuits in order to reduce net current.*

<u>Radiofrequency/Microwave Radiation Exposure Limit Recommendations</u>

- *Present guidelines, such as IEEE, FCC, and ICNIRP, are not adequate to protect humans from harmful effects of chronic EMF exposure. The existing scientific knowledge is, however, not sufficient at this stage to formulate final and definite science-based guidelines for all these fields and conditions, particularly for such chronic exposure as well as contributions of the different parameters of the fields, e.g. frequency, modulation, intensity, and window effects. The values suggested below are, thus, provisional and may be altered in the future.*

- *For whole-body (in vivo experiments) or cell culture-based exposure, the Seletun Scientific Panel finds sufficient evidence to establish a scientific benchmark for adverse health effect at 0.0166 W/kg based on at least 32 scientific studies reporting low-intensity effects (defined as studies reporting effects at exposures of 0.1 W/kg or lower) /8-39/.*

- *The Panel recommends a provisional whole-body limit of 0.00033 W/kg by incorporation of an additional 50-fold safety margin applied to the scientific benchmark of 0.0166 W/kg. This is consistent with both ICNIRP and IEEE/FCC safety factors. An additional 10-fold reduction is applied to take prolonged exposure into account (because 29 of the 32 studies are acute exposure only), giving a final whole-body limit of 0.000033 W/kg (33 μW/kg). No further safety margin or provision for sensitive populations is incorporated. This may need to be lowered in the future.*

- *Based on power density measurements, the Seletun Scientific Panel finds sufficient evidence for a whole-body scientific bench-mark for adverse health effect exists down to 85 mW/m^2 (0.0085 mW/cm^2 or 8.5 μW/cm^2) based on at least 17 scientific studies reporting low-intensity effects on humans. Taking more recent human studies conducted near base stations, or at base-station RF levels, Kundi and Hutter /57/ report that the levels must exceed 0.5-1.0 mW/m^2 (0.05 to 0.1 uW/cm^2) for effects to be seen; /40-57/.*

- *The Panel recommends a provisional whole-body (far-field) limit of 1.7 mW/m^2 (also = 0.00017 mW/cm^2 = 0.17 μW/cm^2) by incorporation of an additional 50-fold safety margin applied to the scientific benchmark of 85 mW/m^2. This is consistent with both ICNIRP and IEEE/FCC safety factors. This may need to be lowered in the future.*

- *It can be argued that a further 10-fold reduction is not justified since 13 of the 17 studies are already testing for long-term RF exposure. However, considering that the latest human population studies as reported by Kundi & Hutter (2009) do not show effects below 0.5-1.0 mW/m2, it can also then be argued that an additional 10-fold reduction on precautionary grounds is justified. If another 10-fold reduction is applied, the recommended level would then be 0.17 mW/m^2 (also 0.000017 mW/cm^2 = 0.017 μW/cm^2);*

- *The Seletun Scientific Panel recommends these numeric limits to governments and health agencies for adoption in place of ICNIRP, IEEE/FCC and other outdated public safety guidelines and limits in use around the world. This approach is based on traditional public health principles that support taking actions to protect public health when sufficient evidence is present. Sufficient scientific evidence and public health concern exist today based on increased risk for cancer, adverse fertility and reproductive outcomes, immune disruption, neurological diseases, increased risk of road collisions and injury-producing events, and impairment of cognition, behaviour, performance, mood status, and disruption of sleep;*

- *Numeric limits recommended here do not yet take into account sensitive populations (EHS, immune-compromised, the fetus, developing children, the elderly, people on medications, etc). Another safety margin is, thus, likely justified further below the numeric limits for EMF exposure recommended here;*

- *The Scientific Panel acknowledges that numeric limits derived here for new biologically-based public exposure standards are still a billion times higher than natural EMF levels at which all life evolved.*

<u>Specific Recommendations for mobile (cell) and cordless phone use</u>

- *The Seletun Scientific Panel recommends that users keep mobile (cell) phones away from head and body;*

- *The Seletun Scientific Panel recommends that users keep mobile (cell) phones and PDAs* switched off if worn or carried in a pocket or holster, or on a belt near the body. *PDA is generic for any type of Personal Digital Assistant or hand-held computer device;*

- *The Panel strongly recommends against the use of mobile (cell) and cordless phones and PDAs by children of any age;*

- *The Panel strongly recommends against the use of mobile (cell) and cordless phones and PDAs by pregnant women;*

- *The Panel recommends that use of mobile (cell) and cordless phones and PDAs be curtailed near children or pregnant women, in keeping with preventative and precautionary strategies. The most vulnerable members of society should have access to public places without fear of harm to health;*

- *Public access to public places and public transportation should be available without undue risk of*

EMF exposure, particularly in enclosed spaces (trains, airplanes, buses, cars, etc) where the exposure is likely to be involuntary;

- *The Panel recommends wired internet access in schools, and strongly recommends that schools do not install wireless internet connections that create pervasive and prolonged EMF exposures for children;*

- *The Panel recommends preservation of existing land-line connections and public telephone networks;*

- *The Panel recommends against the use of cordless phones (DECT phones) and other wireless devices, toys and baby monitors, wireless internet, wireless security systems, and wireless power transmitters in SmartGrid-type connections that may produce unnecessary and potentially harmful EMF exposures;*

- *The Panel recognizes that wired internet access (cable modem, wired Ethernet connections, etc) is available as a substitute;*

- *The Panel recommends use of wired headsets, preferably with hollow-tube segments;*

- *The Panel recommends avoidance of wireless (Bluetooth-type) headsets in general;*

- *The Panel encourages the removal of speakers from headsets on wireless phones and PDAs;*

- *The Panel encourages _auto-off switches' for mobiles (cells) and PDAs that automatically turn off the device when placed in a holster;*

- *The Panel strongly discourages the technology that allows one mobile (cell) phone to act as a repeater for other phones within the general area. This can increase exposures to EMF that are unknown to the person whose phone is ―piggy-backed upon without their knowledge or permission;*

- *The Panel recommends the use of telephone lines (land-lines) or fiber optic cables for SmartGrid type energy conservation infra-structure. Utilities should choose options that do not create new, community-wide exposures from wireless components of SmartGrid-type projects. Future health risks from prolonged or repetitive wireless exposures of SmartGrid-type systems may be avoided by using telephone lines or fiber-optic cable. The Panel endorses energy conservation but not at the risk of exposing hundreds of millions of families in their homes to a new, involuntary source of wireless radiofrequency radiation."*

<u>Ten Key points had been identified:</u>

- *"The global populations are insufficiently protected, thus currently at risk;*

- *Sensitive Populations are extra vulnerable;*

- *Government actions are urgently warranted now, based on evidence of serious disruption to biological systems;*

- *The Burden of Proof for the safety of radiation-emitting technologies should fall on Producers and Providers, not Consumers;*

- *EMF Exposures should be reduced in advance of complete understanding of mechanisms of action;*

- *The current operative measure of Radiation Risk - the specific absorption rate (SAR) - is inadequate, and misguides on safety and health risks;*

- *An international Disease Registry is needed to track Time Trends of the incidence of Illnesses to correlate the illnesses with exposures;*

- *Pre-market health testing and safety demonstration is needed for all radiation-emitting technologies;*
- *Parity is needed for occupational exposure standards, compared to those for the general public;*
- *Persons with Electrohypersensitivity need the classification Functionally Impaired.*
- *The scientists recommend specific exposure limits for different frequency fields, including microwaves, used in wireless communications, and ELF electric fields and magnetic fields."*

Collegium Ramazzini Publication (2010)

The 400 page review of non-thermal EMF effects by the Ramazzini Institute, and sponsored by the International Commission for Electromagnetic Safety, and the National Institute for the Study and Control of Cancer and Environmental Diseases 'Bernardino Ramazzini' in 2010 provided a substantial evidence foundation for the relationship between low-intensity EMF (ELF-EMF and RFR) exposure and potential health risks (13). Taken as a whole, the two-volume report provides a compelling scientific basis on which to take precautionary, prudent public health actions. The EEA relied heavily on the Collegium Ramazzini publication to buttress their Statement on Mobile Phones, when addressing the Council of Europe the following year.

European Environment Agency (2011)

Dr. Jacqueline McGlade, Executive Director of the European Environment Agency provided key guidance to the Council of Europe in her *Statement on Mobile Phones and the Potential Head Cancer Risk for EMF* to the Council of Europe, Paris, February 25th 2011 (14). It read:

> *"The European Parliament[1] has responded to this public concern with a resolution on EMF in 2009 which, among other things, called for lowering exposure to electromagnetic fields and for lower exposure limits that would better protect the public from health hazards. We share these recommendations."*

[1] European Parliament resolution of 2 April 2009 on health concerns associated with electromagnetic fields (2008/2211(INI))

Further, she urged the Council of Europe take interim actions to protect public health, particularly for children, with the following:

> *"The EU Commission and the EEA sees the precautionary principle as central to public policymaking where there is scientific uncertainty and high health, environmental and economic costs in acting, or not acting, when faced with conflicting evidence of potentially serious harm."*
>
> *"This is precisely the situation that characterises EMF at this point in its history. Waiting for high levels of proof before taking action to prevent well known risks can lead to very high health and economic costs, as we have seen with asbestos, leaded petrol and smoking."*

Council of Europe 2011

[1] European Parliament resolution of 2 April 2009 on health concerns associated with electromagnetic fields (2008/2211(INI))

On May 27, 2011 the Standing Committee, acting on behalf of the Parliamentary Assembly of the Council of Europe (PACE), adopted the Resolution 1815 (2011) "The potential dangers of electromagnetic fields and their effect on the environment" (15) based on the Doc. 12608, report of the Committee on the Environment, Agriculture and Local and Regional Affairs, rapporteur: Mr Huss (16). The Parliamentary Assembly of the Council of Europe come from the national parliaments of the Organization's 47 member states and speak for the 800 million Europeans who elected them. The texts adopted by PACE – recommendations, resolutions and opinions – serve as guidelines for the Committee of Ministers, national governments, parliaments and political parties (17).

Recommendations given by the PACE Resolution 1815:

> *"8. In light of the above considerations, the Assembly recommends that the member states of the Council of Europe:*
>
> ***8.1. in general terms:***
>
> *8.1.1. take all reasonable measures to reduce exposure to electromagnetic fields, especially to radio frequencies from mobile phones, and particularly the exposure to children and young people who seem to be most at risk from head tumours;*
>
> *8.1.2. reconsider the scientific basis for the present standards on exposure to electromagnetic fields set by the International Commission on Non-Ionising Radiation Protection, which have serious limitations, and apply ALARA principles, covering both thermal effects and the athermic or biological effects of electromagnetic emissions or radiation;*
>
> *8.1.3. put in place information and awareness-raising campaigns on the risks of potentially harmful long-term biological effects on the environment and on human health, especially targeting children, teenagers and young people of reproductive age;*
>
> *8.1.4. pay particular attention to "electrosensitive" people who suffer from a syndrome of intolerance to electromagnetic fields and introduce special measures to protect them, including the creation of wave-free areas not covered by the wireless network;*
>
> *8.1.5. in order to reduce costs, save energy, and protect the environment and human health, step up research on new types of antenna, mobile phone and DECT-type device, and encourage research to develop telecommunication based on other technologies which are just as efficient but whose effects are less negative on the environment and health;*
>
> ***8.2. concerning the private use of mobile phones, DECT wireless phones, WiFi, WLAN and WIMAX for computers and other wireless devices such as baby monitors:***
>
> *8.2.1. set preventive thresholds for levels of long-term exposure to microwaves in all indoor areas, in accordance with the precautionary principle, not exceeding 0.6 volts per metre, and in the medium term to reduce it to 0.2 volts per metre;*
>
> *8.2.2. undertake appropriate risk-assessment procedures for all new types of device prior to licensing;*

8.2.3. introduce clear labelling indicating the presence of microwaves or electromagnetic fields, the transmitting power or the specific absorption rate (SAR) of the device and any health risks connected with its use;

8.2.4. raise awareness on potential health risks of DECT wireless telephones, baby monitors and other domestic appliances which emit continuous pulse waves, if all electrical equipment is left permanently on standby, and recommend the use of wired, fixed telephones at home or, failing that, models which do not permanently emit pulse waves;

8.3. concerning the protection of children:

8.3.1. develop within different ministries (education, environment and health) targeted information campaigns aimed at teachers, parents and children to alert them to the specific risks of early, ill-considered and prolonged use of mobiles and other devices emitting microwaves;

8.3.2. for children in general, and particularly in schools and classrooms, give preference to wired Internet connections, and strictly regulate the use of mobile phones by schoolchildren on school premises;

8.4. concerning the planning of electric power lines and relay antenna base stations:

8.4.1. introduce town planning measures to keep high-voltage power lines and other electric installations at a safe distance from dwellings;

8.4.2. apply strict safety standards for the health impact of electrical systems in new dwellings;

8.4.3. reduce threshold values for relay antennae in accordance with the ALARA principle and install systems for comprehensive and continuous monitoring of all antennae;

8.4.4. determine the sites of any new GSM, UMTS, WiFi or WIMAX antennae not solely according to the operators' interests but in consultation with local and regional government authorities, local residents and associations of concerned citizens;

8.5. concerning risk assessment and precautions:

8.5.1. make risk assessment more prevention oriented;

8.5.2. improve risk-assessment standards and quality by creating a standard risk scale, making the indication of the risk level mandatory, commissioning several risk hypotheses to be studied and considering compatibility with real-life conditions;

8.5.3. pay heed to and protect "early warning" scientists;

8.5.4. formulate a human-rights-oriented definition of the precautionary and ALARA principles;

8.5.5. increase public funding of independent research, in particular through grants from industry and taxation of products that are the subject of public research studies to evaluate health risks;

8.5.6. create independent commissions for the allocation of public funds;

8.5.7. make the transparency of lobby groups mandatory;

8.5.8. promote pluralist and contradictory debates between all stakeholders, including civil society (Århus Convention)."

European Environment Agency 2011

In October 12 2011, the European Environment Agency (EEA), an agency of the European Union. based in Copenhagen, Denmark, recommends again to take a precautionary approach to policy making in the EMF area (18). The Agency notes:

"The precautionary principle.

Because the evidence on mobile phones and cancer presents a mixed picture, the EEA recommends using the precautionary principle (PP), as recommended in the EU Treaty, to better manage the risk. There is no clear legal definition of the PP so the EEA has produced a working definition:

The precautionary principle provides justification for public policy actions in situations of scientific complexity, uncertainty and ignorance, where there may be a need to avoid, or reduce, potentially serious or irreversible threats to health and the environment, using an appropriate strength of scientific evidence, and taking into account the pros and cons of action and inaction.

The PP requires us to weigh evidence in a different way. This is not new - societies are used to using different strengths of evidence for different reasons, based on the costs of being wrong.
For example, criminals must be found guilty 'beyond all reasonable doubt' before they are convicted; injured people in compensation cases need only show a balance of evidence in order to win compensation for negligence; while doctors only need slight evidence of a serious illness to prescribe treatment. Such precautionary approaches are justified where it is not yet possible to establish causality beyond reasonable doubt.

Implications for policy makers and the mobile phone industry.

Citizens could be better informed about the risks of mobile phone use, as recommended by the EEA in September 2007. There is sufficient evidence of risk to advise people, especially children, not to place the handset against their heads: text messaging, or hands-free kits lead to about ten times lower radiation levels, on average, than when the phone is pressed to the head.

Governments may also wish to label mobile handsets as a 'possible carcinogen', in line with the IARC decision. In addition, more independent research is needed. The cost of these measures is very low, but the potential costs of inaction may be very high."

US Government Accountability Office (2012)

The US Government Accountability Office published a report in 2012 urging the US Federal Communications Commission to revisit the outdated safety standards for the exposures from wireless devices. (19)

The rapid adoption of mobile phones has occurred amidst controversy over whether the technology poses a risk to human health as a result of long-term exposure to RF energy from mobile phone use.

FCC and FDA share regulatory responsibilities for mobile phones. GAO was asked to examine several issues related to mobile phone health effects and regulation. Specifically, this report addresses:

1. *(1) what is known about the health effects of RF energy from mobile phones and what are current research activities,*
2. *(2) how FCC set the RF energy exposure limit for mobile phones, and*
3. *(3) federal agency and industry actions to inform the public about health issues related to mobile phones, among other things.*
4. *GAO reviewed scientific research; interviewed experts in fields such as public health and engineering, officials from federal agencies, and representatives of academic institutions, consumer groups, and the mobile phone industry; reviewed mobile phone testing and certification regulations and guidance; and reviewed relevant federal agency*
websites and mobile phone user manuals.

The Report noted that the FCC's RF energy exposure limit may not reflect the latest research. Redundant and overlapping jurisdiction over the setting of public safety limits is highlighted where the GAO Report notes:

> *"FCC told GAO that it relies on the guidance of federal health and safety agencies when determining the RF energy exposure limit, and to date, none of these agencies have advised FCC to change the limit. However, FCC has not formally asked these agencies for a reassessment. By not formally reassessing it's current limit, FCC cannot ensure it is using a limit that reflects the latest research on RF energy exposure. FCC has also not reassessed it's testing requirements to ensure that they identify the maximum RF energy exposure a user could experience. Some consumers may use mobile phones against the body, which FCC does not currently test, and could result in RF energy exposure higher than the FCC limit." (US GAO, 2012)*

The GAO Report recommends to the FCC that it formally reassess, and, if appropriate, change it's current RF energy exposure limit and mobile phone testing requirements related to likely usage configurations, particularly when phones are held against the body. FCC noted that a draft document that is now under consideration by the FCC has the potential to address GAO's recommendations. (US GAO, 2012)

European Environment Agency: Late Lessons II - Mobile Phone Chapter (2012)

The European Environment Agency (EEA) has Late Lessons from Early Warnings: Science, Precaution, Innovation (20). It includes a new chapter on Mobile Phone Use and Brain Tumor Risk (Hardell et al., 2012 (21). It addresses the early 'lessons' learned about carcinogenicity of EMF hazards from power lines and visual display units or VDUs. ELF-EMF was classified in 2001 by IARC as a 2B Possible Human Carcinogen. It provides a chronology of the publication of studies,

including the Final Interphone Report, the combined Hardell et al. papers (1999-2011) on brain tumor risks, and finally the classification in 2011 by IARC of radiofrequency radiation also to be a Group 2B Possible Human Carcinogen. The paper includes a section on risks to children. It shows that for children who start using a mobile phone in their early teenage years, by the time these children are in the 20-29 age group, they have a 500%+ increased risk of glioma and a 600%+ increased risk of acoustic neuroma when they are young adults. The risks for adults (ipsilateral, 10+ years of mobile phone use are roughly 200% or doubled.

III. EXPERT RESEARCH GROUP AND PHYSICIANS' ADVISORIES (2007 – 2012)

American Academy of Environmental Medicine Statement

In a landmark statement adopted early 2012, the American Academy of Medicine (AAEM) signaled it's opposition to the California Public Utilities Commission proposal to install wireless utility meters in California that create new sources of elevated radiofrequency radiation wherever buildings have electrical meters (22 and Appendix C). The letter stated:

> *"The American Academy of Environmental Medicine opposes the installation of wireless 'smart meters' in homes and schools based on a scientific assessment of the current medical literature (references available on request). Chronic exposure to wireless radiofrequency radiation is a preventable environmental hazard that is sufficiently well-documented to warrant immediate preventative public health action."*

The American Academy of Environmental Medicine was founded in 1965, and is an international association of physicians and other professionals interested in the clinical aspects of humans and their environment. The Academy is interested in expanding the knowledge of interactions between human individuals and their environment, as these may be demonstrated to be reflected in their total health. The AAEM provides research and education in the recognition, treatment and prevention of illnesses induced by exposures to biological and chemical agents encountered in air, food and water. This represents the first national physician's group to look in-depth at wireless health risks; and to advise the public and decision-makers about preventative public health actions that are necessary. The AAEM based its opinion in part on the established scientific evidence, and on the recent classification by the WHO International Agency for Research on Cancer (IARC) that radiofrequency radiation, like ELF-EMF is a Group 2B Possible Human Carcinogen. The rationale for widespread public exposure to a new source of radiofrequency radiation in every home and classroom, after being designated a Possible Human Carcinogen, is clearly unacceptable from a medical and public health standpoint. The full text of the letter is Appendix A.

International Doctors´ Appeal (2012)

In 2002 more than 1000 physicians signed the "Freiburg Appeal" (23). It was translated into many languages. As many as 36,000 people from all over the world support its warning about the dangers of wireless communication. Ten years later, in October 2012 the 'International Doctors´ Appeal 2012' was published (24).

"As physicians and scientists, we hereby call on our colleagues and the wider global community to support us with their signature in our fight for the protection of life. However, we also appeal to the politicians to ensure that the people are protected by the following precautionary measures, which also include fundamental human rights:

- *Protect the inviolability of the home by minimizing radio-frequency exposure levels, which penetrate through the walls of one's own home.*
- *Considerably lower radio-frequency radiation exposures as well as exposure limits to a level that reliably protects humans and nature from adverse biological effects of electromagnetic fields.*
- *Convert devices/transmitters that transmit continuously (e.g. cordless phones, wireless Internetaccess (Wi-Fi), and wireless meters) to technologies that only emit radio-frequency radiation on demand when being used.*
- *Children and adolescents need special protection: Children below the age of 8 should not use cell phones and cordless phones; children and adolescents between the ages 8 and 16 should not use cell phones or only use them in the case of an emergency.*
- *Attach clearly visible warning labels and safety guidelines for lowering the radiation exposure on cell phones and other wireless devices, including instruction manuals. An important reminder: Try not to carry a cell phone right next to your body when it is turned on.*
- *Identify and clearly mark protected zones for electrohypersensitive people; establish public areas without wireless access or coverage, especially on public transport, similar to smoke-free areas for nonsmokers.*
- *Promote the development of communication technologies and electricity use that is more compatible with health. Prefer wired solutions for home use and public facilities. Expand fiberoptic networks as the foundation of a modern, sustainable, and performance-based technology that meets the ever-increasing demand for higher data transmission rates.*
- *Provide government funding for industry-independent research and education that do not dismiss strong scientific and medical findings of potential risks, but rather work to clarify those risks.*

We also call on you as an individual: Prefer wired communication technologies. Inform yourself and pass this information on to your family, neighbors, friends, and politicians. You can make a difference by sharing information and making precautionary choices so that the protection of human health and the environment is not left to and limited by commercial interests."

American Academy of Pediatrics (July 2012)

The American Academy of Pediatrics (AAP), a non-profit professional organization of 60,000 primary care pediatricians, pediatric medical subspecialists, and pediatric surgical specialists in the

United States dedicated to the health, safety and well-being of infants, children, adolescents, and young adults strongly supports the proposal for a formal inquiry into radiation standards for cell phones and other wireless products. The Academy encourages the Federal Communications Commission (FCC) to vote to move forward with it's proposed inquiry into the adequacy of the existing FCC public safety limits (25 and Appendix D).

> *"The FCC has not assessed the standard for cell phone radiation since 1996. According to industry groups, approximately 44 million people had mobile phones when the standard was set; today, there are more than 300 million mobile phones in use in the United States. While the prevalence of wireless phones and other devices has sky-rocketed, the behaviors around cell phone uses have changed as well. The number of mobile phone calls per day, the length of each cell phone call, and the amount of time people use mobile phones has increased, while cell phone and wireless technology has undergone substantial changes. Many more people, especially adolescents and young adults, now use cell phones as their only phone line and they begin using wireless phones at much younger ages."*
>
> *"The AAP believes the inquiry to reassess the radiation standard presents an opportunity to review its impacts on children's health and well-being. In the past, such standards have generally been based on the impact of exposure on an adult male. Children, however, are not little adults and are disproportionately impacted by all environmental exposures, including cell phone radiation. In fact, according to IARC, when used by children, the average RF energy deposition is two times higher in the brain and 10 times higher in the bone marrow of the skull, compared with mobile phone use by adults. While the Academy appreciates that the FCC is considering investigating whether the emission standards should be different for devices primarily used by children, it is essential that any new standard for cell phones or other wireless devices be based on protecting the youngest and most vulnerable populations to ensure they are safeguarded throughout their lifetimes."*
>
> *"Finally, in reviewing the SAR standard, the FCC has the opportunity to highlight the importance of limiting media use among children. The Academy has found potentially negative effects and no known positive effects of media use by children under the age of two, including television, computers, cell phones, and other handheld wireless devices. In addition, studies consistently show that older children and adolescents utilize media at incredibly high rates, which potentially contributes to obesity and other health and developmental risks. In reviewing the SAR limit, the FCC has the opportunity to improve the health of our nation by highlighting the importance of limiting screen time and media use for children and adolescents."*

IV. LOCAL AND NATIONAL COUNTRY ACTIONS (2007 – 2012)

City of Brussels

The order of 1 March 2007 on the protection of the environment against the potentially harmful effects and nuisances caused by non-ionizing radiation, established a new regional framework legislation. Installations emitting electromagnetic radiation in the Brussels-Capital Region need environmental permits to be issued by Brussels Environment (26). The ordinance defines a standard of 3 V/m (also ~ 24 mW/m² ~ 2.4 µW/cm²) is not exceeded by the transmitting mobile phone antennas. Compliance with this standard is applied since 14 March 2009.

"Environmental permit for antennas: The steps of the procedure (27)

1. *Introduction of the permit application*
   The application of the *environment permit is introduced by the operator of the antenna to Brussels Environment includes a technical dossier containing plans from a simulation of the electromagnetic field in a radius of influence of 200 meters from the transmitting antenna.*
   This simulation takes into account the technical characteristics of the antenna and the surrounding environment (presence of buildings ...). It aims to ensure that 25% of the 3 V/m standard (also ~ 24 mW/m² ~ 2.4 µW/cm²) [given as power density = 1.5 V ~ 6 mW/m² ~ 0.6 µW/cm²/m] *is not exceeded in any place accessible to the public.*
2. *Site visit and review of the record*
   A Brussels Environment agent reviews the application and conducts a site visit to see if the simulation is correct and if the environmental situation close to the antenna described in the application file corresponds reality given. If this is the case, the file is submitted to public inquiry.
3. *Public Inquiry*
   The application is submitted to a 15 days public inquiry to notify you and allow you to give your opinion. Public inquiry was announced by red posters usual affixed near the place of the antenna location. Any citizen can go to municipal services concerned to take note of the case.
4. *Decision*
   The environmental permit is granted or refused by Brussels Environment. This license ensures that all measures for safety and protection of the environment and residents are provided."

Principality of Liechtenstein

In 2008 in the Principality of Liechtenstein a new environmental law came into effect including regulations and legal limits for cellular transmitters (28). The complete text for article 31 and 34 is given below. Article 31 defines locations with sensitive use where site specific limits have to be applied. However article 34, paragraph 4 (0.6 V/m limit) had been repealed in 2009 after business associations had initiated a national referendum (29).

Article 31 - Places of Sensitive Use

Regarded as places of sensitive use:

a) rooms in buildings where people stay regularly over a long period;
b) playgrounds and rest places of schools, kindergartens and nursery schools operated by the public;
c) fixed outdoor workplaces where work-related to the same person is shown during more than 800 hours a year. Including, in particular fixed sales stands and Jobs at permanently installed equipment, but not outside areas of restaurants and construction sites;
d) those areas of undeveloped land in construction zones on which uses are permitted by letters a and b.

Article 34 transmitters for cellular and wireless local loops

Site specific limits

1) For transmitters of mobile cellular networks and transmitters for wireless local loops with a total effective radiated power of at least 6 watts, the site specific limits under paragraph 2 and 4 apply. They do not apply for radio relay systems, the wireless network security "Polycom" and other radio networks of security and rescue organizations.
2) The site specific limit for the effective value (rms) of the electric field strength is:
a) for installations transmitting exclusively in the frequency range of 900 MHz: 4.0 V/m (also =

42 mW/m² = 4.2 µW/cm²);
b) for facilities that broadcast exclusively in the frequency range of 1800 MHz or in a higher frequency range: 6.0 V/m (also ~ 100 mW/m² = 10 µW/cm²).;
c) for facilities that broadcast in both frequency ranges specified in letters a and b: 5.0 V/m (also = 66 mW/m² = 6.6 µW/cm²).

3) *Whereas the operative mode and the maximum call and data traffic is at maximum transmission power.*
4) *Holder of a broadcast system are required to reduce the actual electric filed strength to the lowest technically feasible value, using appropriate measures and to accomplish by the end of 2012 an actual electric field strength of 0.6 V/m (also ~ 1 mW/m² ~ 0,1 µW/cm²) on average.*
5) *The Government shall provide further details by ordinance.*

Italy – Autonomous Province of Bolzano - South Tyrol (2009)

In a Decree dated April 29, 2009, the governor of the Autonomous Province Bolzano issued Regulation No. 24 concerning telecommunications infrastructure. In the autonomous province of Bolzano radio- and cellular transmitter sites have to be operated that take health aspects into account (30, 31). In practice e.g. radio transmitters had been aggregated on tall mast sites preferably outside residential areas on mountains. The population exposure from cellular antenna sites is calculated with help of predictive software and the best possible sites are evaluated. Each site has to be approved by a communications commission. The national limit for the sum of all RF sources in Italy is 6 V/m (also ~ 100 mW/m² ~ 10 µW/cm²). In the autonomous province of Bolzano the competent authority - State Agency for Environment - negotiates each cellular site with the relevant operator(s) in order to achieve a site specific exposure of 3 V/m (also ~ 24 mW/m² ~ 2.4 µW/cm²) and lower (32).

Austria – Ministry of Health 2010

In December 2010 the document "Aspects of the current health assessment of mobile communications - Recommendation of the Supreme Health Council" was published (33). Some of the recommendations are listed below.

"... Radio equipment, which leads to a prolonged exposure of people should be set up using a precautionary target value, since long-term effects can not be excluded with sufficient certainty. This target value should be set for high-frequency effects at least a factor of 100 below the limit for the power density of the ÖNORM E 8850 (note by the author: similar to ICNIRP 1998). In addition, legal measures should be taken, that
a) in case that various electromagnetic fields acting simultaneously, all relevant frequencies of different emitters are not to exceed the limits and
b) operators are encouraged to minimize exposure from electromagnetic fields well below the limit values during planning and operation."

,, ... In view of the many pending issues, the rational use of mobile phones should be taken generally, which seeks to have meaningful use and avoid unnecessary exposure. This is especially true for children and adolescents, since they will be predictable more exposed over their lifetime and

the organ-specific exposure through anatomical and developmental differences in certain tissues may be higher than in adults."

Nine specific recommendations were given by the Austrian Supreme Health Council:

1. *"If possible, do not call, when the reception is poor.*
2. *Keep calls short.*
3. *In situations where you can choose between mobile and fixed-line, use the landline.*
4. *Make calls in the car as little as possible.*
5. *With GSM (2 G) phones, wait a little time while connecting, before you run the phone to your head. Exposure by UMTS (3 G) mobile phones is usually much lower. Make sure to set the connection in multi-band-mobiles preferably via UMTS (3 G)*
6. *Use headsets or speakerphones.*
7. *When buying a cell phone mind low SAR values.*
8. *Wear the mobile not directly on the body.*
9. *Send an SMS instead of calling."*

France (2010)

In 2010 in France the Environmental Law some regulations concerning EMF issues had been supplemented (34, 35). Some excerpts are given below:

Article 183

- *Wireless terminals that are intended to be connected with a public telephone network may not be placed on the market without additional equipment, which allows to limit the exposure of the head during communication.*
- *The Higher Audiovisual Council shall ensure that the development of the sector of audiovisual communication goes along with an increased level of protection of the environment and the health of the population.*
- *Any advertising, about what aid whatsoever, with the direct aim to promote the sale, the provision or the use of a mobile phone by children under 14 is prohibited.*
- *The payment or free circulation of goods which contain a radio equipment and their use is specifically designed for children under six may be banned by decree of the Minister of Health, in order to avoid excessive exposure of children.*
- *Individuals who are responsible for the transport of electrical energy have to carry out a regular control of the electromagnetic fields, which are induced by power lines. The result of these measurements is to report annually to the French Agency for Sanitary Safety of environment and labor, which will publish them.*
- *In kindergarten (pre-), in the primary schools and in secondary schools (secondary) the use of a mobile phone is prohibited by a student during the entire lesson and at the designated places given in the house rules.*

Article 184

For any mobile telephone that is offered for sale [in France], the specific absorption rate is legible and in French. It must also provide a recommendation for the use of additional equipment, by means

of which the radio exposure of the head can be limited during the communication, as in the fifth Paragraph of point I of Article 183 of this law provided.

Austria – Austrian Medical Association (2012)

In 2012 the Austrian Medical Association published the "Guideline of the Austrian Medical Association for the diagnosis and treatment of EMF-related health problems and illnesses (EMF syndrome)"(36). The guideline is recommended to doctors of all disciplines in Austria. The guideline says in part:

"There has been a sharp rise in unspecific, often stress-associated health problems that increasingly present physicians with the challenge of complex differential diagnosis. A cause that has been accorded little attention so far is increasing electrosmog exposure at home, at work and during leisure activities, occurring in addition to chronic stress in personal and working life. It correlates with an overall situation of chronic stress that can lead to burnout.

How can physicians respond to this development?

The Austrian Medical Association has developed a guideline for differential diagnosis and potential treatment of unspecific stress-related health problems associated with electrosmog. Its core element is a patient questionnaire consisting of a general assessment of stress symptoms and a specific assessment of electrosmog exposure. The guideline is intended as an aid in diagnosing and treating EMF-related health problems."

Key elements of the guideline are:

1. *History of health problems and EMF exposure*
2. *Examination and findings*
3. *Measurement of EMF exposure*
4. *Prevention or reduction of EMF exposure*
5. *Diagnosis*
6. *Treatment*

Russian National Committee on Non-Ionizing Radiation (2011 and 2012)

On March 3, 2011 the Russian National Commitee on Non-Ionizing Radiation Protection approved the "Resolution: Electromagnetic Fields from Mobile Phones: Health Effects on Children and Teenagers" (37 and Appendix E). Parts of the resolution are given below.

"The Resolution evolved from scientific statements adopted by RNCNIRP in 2001, 2004, 2007, 2008 and 2009, taking into account contemporary views and actual scientific data. The Resolution represents a viewpoint of the professional scientific community and is meant for public dissemination, for the consumers of the mobile telecommunications services, as well as for the legislative and executive authorities who develop and implement health protection, environmental, communication, scientific and safety policies."

In 2012, the RCNIRP issued an update to this Resolution, calling on all countries to halt the use of wireless technologies in the school classrooms, and to move quickly to replace wireless with wired internet and teaching technologies (38 and Appendix F).

V. INTERNATIONAL HEALTH AGENCY ACTION

WHO International Agency for Research On Cancer – Formal Classification (2011)

On May 31, 2011 the WHO/International Agency for Research on Cancer (IARC) classified radiofrequency electromagnetic fields as possibly carcinogenic to humans (Group 2B), based on an increased risk for glioma, a malignant type of brain cancer, associated with wireless phone use (39, 40).

A group of 30 researchers, scientists and medical doctors were invited to participate in an assessment of the scientific literature on radiofrequency radiation carcinogenicity in Lyon, France. Under the auspices of IARC, this IARC Monograph Working Group on RFR conducted a comprehensive scientific assessment of RF studies and determined:

> *"In view of the limited evidence in humans and in experimental animals, the Working Group classified RF- EMF as "possibly carcinogenic to humans" (Group 2B). This evaluation was supported by a large majority of Working Group members."*
>
> *"The Working Group concluded that the (Interphone Final Report) findings could not be dismissed as reflecting bias alone, and that a causal interpretation between mobile phone RF-EMF exposure and glioma is possible. A similar conclusion was drawn from these two studies for acoustic neuroma, although the case numbers were substantially smaller than for glioma."*

It is important to recognize that the IARC RF Working Group did not find the evidence insufficient to classify (Group 3) or not a carcinogen (Group 4). Both of these possible outcomes to the scientific assessment could have rendered a substantially weaker conclusion. Where there has been the necessity of a virtual scientific paradigm shift to accommodate ANY consideration of both ELF-EMF and RFR to the status where legitimate scientific attention is achieved is a notable achievement. There is a very high bar set to show that non-chemical carcinogens warrant IARC carcinogenicity evaluation - it greatly exceeds that necessary for chemicals and other toxins.

The WHO press release No° 208 states

> *"The IARC Monograph Working Group discussed the possibility that these exposures might induce long-term health effects, in particular an increased risk for cancer. This has relevance for public health, particularly for users of mobile phones, as the number of users is large and growing,*

particularly among young adults and children."

The corresponding monograph has not been published as of October 2012. On request, IARC clarified the frequency range covered by the monograph (41).

> *"The IARC Monographs classification of Radiofrequency Electromagnetic Fields (RF-EMF) covers the entire radiofrequency segment of the electromagnetic spectrum (30 kHz-300 GHz). Within this spectrum, the electromagnetic fields around (or the radiation emitted by) mobile telephones represent the most intense and most wide-spread exposure situation, for which a small increase in risk for glioma and acoustic neuroma has been found in the group of 'heavy users'. Other devices that emit the same type of RF radiation - base-station antennas, radio/tv antennas, WiFi stations, smart meters - fall under the same evaluation. However, because the exposure levels for many of these other devices and exposure situations are so much lower than the exposure to someone who has a functioning cell phone against her/his ear, the risk will be considerably less (although the hazard still exists)."*

VI. CONCLUSIONS

1) The European Environmental Agency (2007) concludes that: "(*T)here are many examples of the failure to use the precautionary principle in the past, which have resulted in serious and often irreversible damage to health and environments. Appropriate, precautionary and proportionate actions taken now to avoid plausible and potentially serious threats to health from EMF are likely to be seen as prudent and wise from future perspectives. We must remember that precaution is one of the principles of EU environmental policy*."

2) The European Parliament, the Council of Europe and various governmental agencies in Europe, Scandinavia, Israel, North America, India and Asia have called for better warnings, to reduce or eliminate exposures from wireless devices, to label devices with health warnings, to develop new, lower public safety standards, to protect sensitive subgroups (children, people who are sensitized to EMF and wireless radiation already (electrosensitivity), and to inform and protect pregnant women and their young from unnecessary exposures. The countries of France, Italy, Belgium, the Principality of Liechtenstein, Switzerland, Austria, the United Kingdom, and others have led in proposing new restrictions on wireless exposures, based on scientific and public health reviews of the evidence. The US Government Accountability Office has called for review of American (FCC) safety limits for wireless devices.

3) Physicians and health advisory groups around the world have called for prudent public health actions that include reducing or eliminating ELF and RFR exposures, especially for pregnant women and for the developing fetus, and children, and particularly where other options are available (in the case of wireless exposures in particular). Some of these groups include the Austrian Ministry of Health, the Russian National Committee on Non-Ionizing Radiation, the American Academy of Environmental Medicine, the American Academy of Pediatrics, the British Chief Medical Officer, and many more governmental agencies across Europe, Scandinavia, North America, India and Asia.

4) Physicians and researchers who have published in-depth reviews on the science and public health policy implications of ELF and RFR risks to health include Pathophysiology, Vol 16 (2,3); 2009; the two-volume *Non Thermal effects and Mechanisms of interaction between Electromagnetic Fields and Living Matter*. eds Giuliani L and Soffritti, M, ICEMS, Ramazzini Institute, Bologna, Italy., 2010; the World Health Organization INTERPHONE Final Report, 2010; and the WHO International Agency for Research on Cancer RFR Monograph (Baan et al, 2011) designating RFR

as a Group 2B Possible Human Carcinogen.

5) Overall, these provide support for warnings and advice to consumers and the public that the body of evidence for bioeffects from daily exposure levels of ELF and RFR can reasonably be presumed to result in adverse health impacts with chronic exposure. The studies on which these warnings rely establish that bioeffects from exposure to ELF and RFR are established, not speculative or weak. Further, they establish that existing ICNIRP and FCC public safety limits are inadequate to protect public health; and underscore the need for new, biologically-based public exposure standards.

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VIII. APPENDICES

APPENDIX A Full Text of European Parliament Statement - 2008

"The European Parliament ,

– having regard to the Communication from the Commission to the Council, the European Parliament and the European Economic and Social Committee on the mid-term review of the European Environment and Health Action Plan 2004-2010 (COM(2007)0314),

– having regard to its resolution of 23 February 2005 on the European Environment and Health Action Plan 2004-2010(1) ,

– having regard to the World Health Organisation (WHO) report of 27 July 2007 entitled 'Principles for evaluating health risks in children associated with exposure to chemicals',

– having regard to Articles 152 and 174 of the EC Treaty targeting a high level of protection for human health and the environment,

– having regard to Decision No 1350/2007/EC of the European Parliament and of the Council of 23 October 2007 establishing a second programme of Community action in the field of health (2008-13)(2) ,

– having regard to Rule 45 of its Rules of Procedure,

– having regard to the report of the Committee on the Environment, Public Health and Food Safety (A6-0260/2008),

A. noting with interest the fact that, since 2003, the EU has based its health-protection policy on closer cooperation between the health, environment and research sectors, so that it may be hoped that a coherent and integrated European environmental health strategy will eventually be introduced,

B. whereas the courses of action currently being followed by the EU as part of its first environment and health action plan (2004-2010) (COM(2004)0416) - namely, the preparation of indicators, the development of integrated monitoring, the collection and evaluation of relevant data as well as an increase in the volume of research - will allow greater insight into the interactions between sources of pollution and health effects but are known to be inadequate as a means of reducing the growing number of diseases related to environmental factors,

C. whereas it is virtually impossible to establish a mid-term assessment of the aforementioned action plan, since the latter pursues no clear, quantified objective and the total budget allocated to it is difficult to determine and definitely insufficient for its efficient promotion,

D. whereas the main objective of the 2008-2013 health programme is to act upon the factors which traditionally determine health (diet, smoking, alcohol consumption and the use of drugs); whereas this 2004-2010 action plan should focus on certain new health challenges and in addition address the determining environmental factors which affect human health, such as indoor and outdoor air quality, electromagnetic waves, nanoparticles and chemicals which are a cause for serious concern (substances classed as carcinogenic, mutagenic or toxic to reproduction [CMR], endocrine disruptors), as well as risks to health arising from climate change,

E. whereas respiratory illnesses rank second as a cause of death and in terms of incidence, prevalence and cost within the EU, whereas they constitute the main cause of death amongst children under the age of five

and whereas such diseases are continuing to progress on account of - in particular - indoor and outdoor air pollution,

F. whereas atmospheric pollution caused, in particular, by fine particles and ground-level ozone, is a significant threat to human health which is affecting the proper development of children and reducing life expectancy in the EU(3) ,

G. whereas, with reference to the issue of urban environmental health, particularly the quality of indoor air, the Community - in accordance with the subsidiarity and proportionality principles - should do more to combat domestic pollution, since Europeans spend on average 90% of their time inside buildings,

H. whereas at the 2004 and 2007 WHO ministerial conferences on health and the environment, attention was drawn to the links between the complex combined influence of chemical pollutants and a number of chronic illnesses and disorders (affecting children in particular); whereas those concerns are also expressed in official documents issued in connection with the United Nations Environment Programme (UNEP) and by the Intergovernmental Forum on Chemical Safety (IFCS),

I. whereas there is increasing scientific evidence that certain cancers, such as cancer of the bladder, bone cancer, lung cancer, skin cancer, breast cancer and others are caused not only by the effects of chemical substances, radiation and airborne particles but also by other environmental factors,

J. whereas these problematic developments in environmental health have been accompanied in recent years by the emergence of new diseases or syndromes, such as multiple chemical hypersensibility, dental-amalgam syndrome, hypersensitivity to electromagnetic radiation, sick-building syndrome and attention-deficit and hyperactivity syndrome in children,

K. whereas the precautionary principle has been enshrined in the Treaty since 1992 and whereas the European Court of Justice has repeatedly specified the substance and the scope of that principle in Community law, which constitutes one of the cornerstones of the protection policy pursued by the Community in the field of health and the environment(4) ,

L. having regard to the highly restrictive - if not to say impracticable - nature of the criteria adopted by the Commission in its 2 February 2000 Communication on the precautionary principle (COM(2000)0001),

M. having regard to the importance of human biological monitoring as a tool for assessing the European population's degree of exposure to the effects of pollution and the determination (repeatedly expressed by Parliament in Paragraph 3 of its aforementioned resolution of 23 February 2005 and in the conclusions issued at the end of the 20 December 2007 Council meeting of Environment Ministers) to expedite the introduction of a biological-monitoring programme at EU level,

N. whereas it is readily acknowledged that climate change can play an important role in increasing the severity and incidence of certain diseases and in particular that heat-wave frequency, flooding and wildfires as the most frequent natural disasters in the EU can lead to additional diseases, poor sanitation and deaths, while at the same time recognising the beneficial effects on health of measures to alleviate climate change,

O. whereas climate change will have significant effects on human health, inter alia by encouraging the development of certain infectious and parasitic diseases mainly because of changes in temperature and humidity and their impact on ecosystems, animals, plants, insects, parasites, protozoa, microbes and viruses,

P. whereas Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy(5) and its daughter directives contain clear provisions concerning the preservation and restoration of healthy waters,

Q. whereas environmental medicine is a new medical discipline based on university teaching which is still too fragmentary and unevenly distributed amongst the Member States and which thus deserves to be supported and promoted within the EU,

R. whereas the number of persons suffering as a result of environmental factors is increasing and epidemiologies should be developed in order to obtain a full picture of diseases which are caused wholly or in part by environmental factors,

1. Acknowledges the efforts made by the Commission since the action plan was launched in 2004, particularly in terms of improving the chain of information concerning health and the environment, integrating and expanding European research in this area and cooperating with specialist international organisations such as the WHO;

2. Considers, however, that such an action plan is bound to fail at least in part, since it is designed solely to accompany existing Community policies, it is not based upon a preventive policy intended to reduce illnesses linked to environmental factors, and it pursues no clear, quantified objective;

3. Draws the Commission's attention to the fact that a programme has already been carried out under the aegis of the WHO as part of which the WHO Member States established their own national and local environmental health action plans comprising specific objectives and implementation plans; recommends to the Commission therefore that it review this WHO programme as a possible model which could also serve as a useful example to the Union in the future;

4. Deeply regrets the fact that the Commission (and in particular its Research DG) has not provided sufficient funding for human biological monitoring in 2008 to enable it (as it had promised Parliament and the Member States) to introduce a consistent approach to biological monitoring within the EU;

5. Calls upon the Commission to respond by 2010 to two essential objectives which the Commission set itself in 2004 and to establish and carry out a practicable communication strategy for these objectives, namely to make members of the general public aware of environmental pollution and the impact thereof on their health, and to reconsider and adapt European risk-reduction policy;

6. Strongly recommends that the Commission and Member States meet their obligations as regards implementation of Community legislation;

7. Stresses that, when it comes to assessing the impact of environmental factors on health, consideration should be given first and foremost to vulnerable groups such as pregnant women, newborn babies, children and the elderly;

8. Calls for special attention to be given to vulnerable groups, who are the most susceptible to pollutants, by introducing measures to reduce exposure to indoor environmental contaminants in healthcare facilities and schools through the adoption of sound indoor air quality management practices;

9. Urges the Commission, when drafting proposals for the revision of existing laws, not to weaken those laws under pressure from lobbies or regional or international organisations;

10. Points that the EU needs to apply a continuous dynamic and flexible approach to the Action Plan; considers that it is therefore of paramount importance to acquire specific expertise on the subject of environmental health, to be based on transparency and on a multidisciplinary and adversarial approach which would thus enable the general public's distrust of official agencies and committees of experts to be countered; points to the importance of improving the training of health experts by means, in particular, of exchanges of best practice at Community level;

11. Points out that in recent years there have been genuine advances in environmental policy in the form of (for example) a reduction in air pollution, an improvement in water quality, the collection and recycling of waste, the monitoring of chemicals and a ban on leaded petrol, but notes at the same time that EU policy still lacks a comprehensive preventive strategy and fails to apply the precautionary principle;

12. Calls, therefore, on the Commission to revise the criteria laid down in its aforementioned Communication as regards recourse to the precautionary principle pursuant to European Court of Justice case-law, in order to ensure that an action and security principle based on the adoption of provisional and proportionate measures lies at the heart of Community health and environment policies;

13. Considers that shifting the burden of proof onto producers or importers and requiring them to demonstrate that a product is harmless would make it possible for a policy based on prevention to be promoted (as provided for in European Parliament and Council Regulation (EC) No 1907/2006 of 18 December 2006 concerning the registration, evaluation, authorisation and restriction of chemicals (REACH) and establishing a European Chemicals Agency(6)), and encourages the Commission to extend that obligation to Community legislation concerning all products; considers that any increase in animal testing under the Action Plan should be avoided and full regard should be paid to the development and use of alternative methods;

14. Calls once again upon the Commission to come forward as soon as possible with concrete measures on indoor air quality which would ensure a high level of protection of health and safety indoors to be established, in particular when revising Council Directive 89/106/EEC of 21 December 1988 on the approximation of laws, regulations and administrative provisions of the Member States relating to construction products(7) , and to propose measures to increase the energy efficiency of buildings and the safety and the harmlessness of chemical compounds used in equipment and furnishings;

15. Recommends that, in order to reduce damaging effects of the environment on health, the Commission should call upon Member States, by means of tax concessions and/or other economic incentives, to interest market operators in improving the quality of indoor air and reducing exposure to electromagnetic radiation in their buildings, branch establishments and offices;

16. Recommends that the Commission draft appropriate minimum requirements to guarantee the quality of indoor air in buildings to be newly built;

17. Recommends that, in awarding individual European Union support, the Commission bear in mind its impact on the quality of indoor air, exposure to electromagnetic radiation and the health of particularly endangered sections of the population in the projects concerned in a similar way to that in which attention is devoted to environmental protection criteria;

18. Calls for environmental quality standards for priority substances in water to be laid down in accordance with the latest scientific knowledge and regularly brought into line with current scientific thinking;

19. Points out that certain Member States have successfully introduced mobile analysis laboratories (or "green ambulances") to enable habitat pollution in public and private places to be diagnosed swiftly and reliably; considers that the Commission could promote such a practice within the Member States which have not yet acquired such a means of direct intervention at a polluted site;

20. Is concerned about the lack of specific legal provisions to ensure the safety of consumer products containing nanoparticles and the relaxed attitude of the Commission with regard to the need to review the regulatory framework for the use of nanoparticles in consumer products in light of the increasing number of consumer products containing nanoparticles being put on the market;

21. Is greatly concerned at the Bio-Initiative international report(8) concerning electromagnetic fields, which summarises over 1500 studies on that topic and which points in its conclusions to the health risks posed by emissions from mobile-telephony devices such as mobile telephones, UMTS, Wifi, Wimax and Bluetooth, and also DECT landline telephones;

22. Notes that the limits on exposure to electromagnetic fields which have been set for the general public are obsolete, since they have not been adjusted in the wake of Council Recommendation 1999/519/EC of 12 July 1999 on the limitation of exposure of the general public to electromagnetic fields (0Hz to 30 GHz)(9) , obviously take no account of developments in information and communication technologies, of the recommendations issued by the European Environment Agency or of the stricter emission standards adopted, for example, by Belgium, Italy and Austria, and do not address the issue of vulnerable groups, such as pregnant women, newborn babies and children;

23. Calls, consequently, upon the Council to amend its Recommendation 1999/519/EC in order to take into account the Member States' best practices and thus to set stricter exposure limits for all equipment which emits electromagnetic waves in the frequencies between 0.1 MHz and 300 GHz;

24. Takes a very serious view of the multiple health risks created by global warming on EU territory and calls for enhanced cooperation between the WHO, the Member States" monitoring authorities, the Commission and the European Centre for Disease Prevention and Control in order to bolster the early-warning system and thus to curb the harmful effects which climate change has on health;

25. Highlights that this Action Plan would benefit from being extended to cover negative impacts of climate change on human health by elaborating on effective adaptation measures necessary at Community level, such as:

- *systematic public education programmes and awareness-raising;*
- *integration of climate change adaptation measures into public health strategies and programmes, such as communicable and non-communicable diseases, workers' health and animal diseases hazardous to health;*
- *proper surveillance aiming at the early detection of disease outbreaks;*
- *health-related early warning systems and response;*
- *coordination of existing environmental data monitoring networks with disease outbreak networks;*

26. Calls on Member States and the Commission to respond adequately to the new threats posed by climate change such as the increased presence of emerging viruses and undetected pathogens and therefore implement new existing pathogen reduction technologies that reduce known and undetected viruses and other pathogens transmitted by blood;

27. Regrets that the current cost benefit impact assessment of the '20 20 by 2020 Europe's Climate Change Opportunity' (COM(2008)0030) only considers the health benefits of reduced air pollution at a 20% reduction of greenhouse gas emissions by 2020; calls on the Commission to ensure that the (ancillary) co-benefits to health of various levels of ambition, in line with the International Panel on Climate Change recommendations of domestic 25% to 40% as well as possibly 50% or more of greenhouse gas emission reduction by 2020, are urgently investigated and modelled into an impact assessment by the Commission;

28. Calls on the Commission to pay attention to the serious problem of mental health, considering the number of suicides in the EU, and to devote more resources to the development of adequate prevention strategies and therapies;

29. Reiterates that the Commission and the Member States should support the WHO Children's Environment and Health Action Plan in Europe, to encourage it both through EU and bilateral development policy, and to encourage similar processes outside the WHO Europe Region;

30. Calls on the Commission to reincorporate into its second action plan the initiative SCALE (Science, Children, Awareness, Legal instruments, Evaluation) relating to the reduction of exposure to pollution, as set out in the European Environment and Health Strategy (COM(2003)0338);

31. Urges the Commission to work on and provide instruments that would foster the development and promotion of innovative solutions, as stressed within the Lisbon agenda framework, in order to minimise major health risks from environmental stressors;

32. Urges the Council to take a decision without delay on the proposal for a regulation establishing the Union Solidarity Fund, as Parliament adopted its position as long ago as 18 May 2006(10) ; considers that the new regulation, which, together with other measures, will lower thresholds for the entry into force of the Union Solidarity Fund, will make it possible to alleviate more effectively, flexibly and quickly damage caused by natural or man-made disasters; stresses that such a financial instrument is very important, particularly because it is assumed that natural disasters will occur more frequently in future, partly on account of climate change;

33. Recommends, as SMEs are of decisive economic importance in Europe, that the Commission should provide technical support to SMEs to make it possible, and help them, to comply with binding environmental health regulations and encourage them to make other changes which are positive from the point of view of environmental health and affect the operation of enterprises;

34. Advises the Commission to envisage (by 2010 and under the "second cycle" of the health and environment action plan) refocusing its initiatives on vulnerable populations and to devise new methods of risk assessment, taking into account the fundamental fact that children, pregnant women and older people are particularly vulnerable;

35. Urges the Commission and Member States therefore to acknowledge the advantages of the prevention and precautionary principles and to develop and implement tools enabling potential environmental and health threats to be anticipated and countered; recommends that the Commission cost the 'second cycle' of this action plan and make provision for appropriate funding covering a larger number of practical measures to reduce environmental impact on health and to implement prevention and precautionary measures;

36. Instructs its President to forward this resolution to the Council, the Commission, the governments and parliaments of the Member States and the WHO.

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(2) OJ L 301, 20.11.2007, p. 3.

(3) Europe's environment, the fourth assessment, summary, European Environment Agency (10.10.2007).

(4) Judgment of 23 September 2003 in Case C-192/01, Commission/Denmark, ECR 2003, p. I-9693; judgment of 7 September 2004 in Case C-127/02, Landelijke Vereniging tot Behoud van de Waddenzee and Nederlandse Vereniging tot Bescherming van Vogels, ECR 2004, p. I-7405.

(5) OJ L 327, 22.12.2000, p. 1.

(6) OJ L 396, 30.12.2006, p. 1; corrected version in OJ L 136, 29.5.2007, p. 3.

(7) OJ L 40, 11.2.1989, p. 12.

(8) Published by a group of independent scientists on 31 August 2007. For details, see: www.bioinitiative.org.

(9) OJ L 199, 30.7.1999, p. 59.

(10) OJ C 297 E, 7.12.2006, p. 331.

APPENDIX B Full Text of European Parliament Resolution – 2009

European Parliament 2009

On April 2, 2009, the European Parliament adopted the "European Parliament resolution of 2 April 2009 on health concerns associated with electromagnetic fields (2008/2211(INI))" (10). The Document was based on the "Report on health concerns associated with electromagnetic fields", Rapporteur: Frederique Ries (11) Committee on the Environment, Public Health and Food Safety.

A. whereas electromagnetic fields (EMFs) exist in nature and have consequently always been present on earth; whereas, however, in recent decades, environmental exposure to man-made sources of EMFs has risen constantly, driven by demand for electricity, increasingly more specialised wireless technologies, and changes in the organisation of society; whereas the end effect is that every individual is now being exposed to a complex mixture of electric and magnetic fields of different frequencies, both at home and at work,

B. whereas wireless technology (mobile phones, Wi-Fi/WiMAX, Bluetooth, DECT landline telephones) emits EMFs that may have adverse effects on human health,

C. whereas most European citizens, especially young people aged from 10 to 20, use a mobile phone, an object serving a practical purpose and as a fashion accessory, and whereas there are continuing uncertainties about the possible health risks, particularly to young people whose brains are still developing,

D. whereas the dispute within the scientific community regarding the potential health risks arising from EMFs has intensified since 12 July 1999, when exposure limits for fields in the 0 Hz to 300 GHz range were laid down in Recommendation 1999/519/EC,

E. whereas the fact that the scientific community has reached no definite conclusions has not prevented some national or regional governments, in China, Switzerland, and Russia, as well as in at least nine EU Member States, from setting what are termed "preventive" exposure limits, that is to say, lower than those advocated by the Commission and its independent scientific committee, the Scientific Committee on Emerging and Newly Identified Health Risks(7) ,

F. whereas actions to limit the exposure of the general public to EMFs should be balanced against improvements to quality of life, in terms of safety and security, brought about by devices transmitting EMFs,

G. whereas among the scientific projects arousing both interest and controversy is the Interphone epidemiological study, financed by an EU contribution of EUR 3 800 000, primarily under the Fifth RTD Framework Programme(8) , the findings of which have been awaited since 2006,

H. whereas, however, there are some points that appear to be the subject of general agreement, in particular the idea that reactions to microwave exposure vary from one person to another, the need, as a matter of priority, to conduct exposure tests under actual conditions in order to assess the non-thermal effects associated with radio-frequency (RF) fields, and the fact that children exposed to EMFs are especially vulnerable(9) ,

I. whereas the EU has laid down exposure limits to protect workers from the effects of EMFs; whereas on the basis of the precautionary principle such measures should also be taken for the sections of population concerned, such as residents and consumers,

J. whereas the Special Eurobarometer report on Electromagnetic Fields (No 272a of June 2007) indicates that the majority of citizens do not feel that the public authorities inform them adequately on measures to protect them from EMFs,

K. whereas it is necessary to continue investigations into intermediate and very low frequencies so that conclusions can be drawn as to their effects on health,

L. whereas the use of Magnetic Resonance Imaging (MRI) must not be threatened by Directive 2004/40/EC as MRI technology is at the cutting edge of research, diagnosis and treatment of life-threatening diseases for patients in Europe,

M. whereas the MRI safety standard IEC/EN 60601-2-33 establishes limit values for EMFs which have been set so that any danger to patients and workers is excluded.

1. Urges the Commission to review the scientific basis and adequacy of the EMF limits as laid down in Recommendation 1999/519/EC and report to the Parliament; calls for the review to be undertaken by the Scientific Committee on Emerging and Newly Identified Health Risks;

2. Calls for particular consideration of biological effects when assessing the potential health impact of electromagnetic radiation, especially given that some studies have found the most harmful effects at lowest levels; calls for active research to address potential health problems by developing solutions that negate or reduce the pulsating and amplitude modulation of the frequencies used for transmission;

3. Maintains that as well as, or as an alternative to, amending European EMFs limits, the Commission, working in coordination with experts from Member States and the industries concerned (electricity companies, telephone operators and manufacturers of electrical appliances including mobile phones), should draw up a guide to available technology options serving to reduce exposure to EMFs;

4. Notes that industry stakeholders as well as relevant infrastructure managers and competent authorities can already influence certain factors, for example setting provisions with regards to the distance between a given site and the transmitters, the height of the site in relation to the height of the base station, or the direction of a transmitting antenna in relation to living environments, and, indeed, should obviously do so in order to reassure, and afford better protection to, the people living close to such facilities; calls for optimal placement of masts and transmitters and further calls for the sharing of masts and transmitters placed in this way by providers so as to limit the proliferation of poorly positioned masts and transmitters; calls on the Commission and Member States to draw up appropriate guidance;

5. Invites the Member States and local and regional authorities to create a one-stop shop for authorisation to install antennas and repeaters, and to include among their urban development plans a regional antenna plan

6. Urges the authorities responsible for authorising the siting of mobile telephony antennas to reach agreement, jointly with the operators in that sector, on the sharing of infrastructure, in order to reduce the volume thereof and the exposure of the public to EMFs;

7. Acknowledges the efforts of mobile communications and other EMF-transmitting wireless technologies to avoid damaging the environment, and in particular to address climate change;

8. Considers that, given the increasing numbers of legal actions and measures by public authorities having the effect of a moratorium on the installation of new EMF-transmitting equipment, it is in the general interest to encourage solutions based on negotiations involving industry stakeholders, public

authorities, military authorities and residents" associations to determine the criteria for setting up new GSM antennas or high-voltage power lines, and to ensure at least that schools, crèches, retirement homes, and health care institutions are kept clear, within a specific distance determined by scientific criteria, of facilities of this type;

9. Calls on the Member States to make available to the public, jointly with the operators in the sector, maps showing exposure to high-voltage power lines, radio frequencies and microwaves, and especially those generated by telecommunications masts, radio repeaters and telephone antennas. Calls for that information to be displayed on an internet page so that it can easily be consulted by the public, and for it to be disseminated in the media;

10. Proposes that the Commission consider the possibility of using funding from the Trans-European Energy Networks to investigate the effects of EMFs at very low frequencies, and particularly in electrical power lines,

11. Calls on the Commission, during the 2009-2014 parliamentary term, to launch an ambitious programme to gauge the electromagnetic compatibility between waves created artificially and those emitted naturally by the human body with a view to determining whether microwaves might ultimately have undesirable consequences for human health;

12. Calls on the Commission to present a yearly report on the level of electromagnetic radiation in the EU, its sources, and actions taken in the EU to better protect human health and the environment;

13. Calls on the Commission to find a solution enabling Directive 2004/40/EC to be implemented more rapidly and thus ensure that workers are properly protected against EMFs, just as they are already protected under two other Community acts against noise(10) and vibration(11) and to introduce a derogation for MRI under Article 1 of that Directive.

14. Deplores the fact that, as a result of repeated postponements since 2006, the findings of the Interphone study have yet to be published, the purpose of this international epidemiological study being to establish whether there is a link between use of mobile phones and certain types of cancer, including brain, auditory nerve, and parotid gland tumours;

15. Draws attention in this context to the appeal for caution from the coordinator of the Interphone study, Elisabeth Cardis, who, in the light of existing knowledge, recommends, as far as children are concerned, that mobile phones should not be used beyond reasonable limits and that landlines should be preferred;

16. Believes in any event that it is up to the Commission, which has an important contribution to the financing of this global study, to ask those in charge of the project why no definitive findings have been published and, should it receive an answer, to inform Parliament and the Member States without delay;

17. Also suggests to the Commission, to make for efficiency in policy and budget terms, that the Community funding earmarked for studies on EMFs be partly switched to finance a wide-ranging awareness campaign to familiarise young Europeans with good mobile phone techniques, such as the use of hands-free kits, keeping calls short, switching off phones when not in use (such as when in classes) and using phones in areas that have good reception;

18. Considers that such awareness-raising campaigns should also familiarise young Europeans with the health risks associated with household devices and the importance of switching off devices rather than leaving them on stand-by;

19. Calls on the Commission and Member States to increase research and development funding for the evaluation of potential long-term adverse effects of mobile telephony radio frequencies; calls also for an increase in public calls for proposals for investigation of the harmful effects of multiple exposure to different sources of EMFs, particularly where children are concerned;

20. Proposes that the European Group on Ethics in Science and New Technologies be given the additional task of assessing scientific integrity in order to help the Commission forestall possible cases of risk, conflict of interests, or even fraud that might arise now that competition for researchers has become keener;

21. Calls on the Commission, in recognition of the public concern in many Member States, to work with all relevant stakeholders, such as national experts, non-governmental organisations and industrial sectors, to improve the availability of, and access to, up-to-date information understandable to non-specialists on wireless technology and protection standards;

22. Calls on the International Commission on Non-Ionising Radiation Protection and the World Health Organisation (WHO) to be more transparent and open to dialogue with all stakeholders in standard setting;

23. Condemns certain particularly aggressive marketing campaigns by telephone operators in the run-up to Christmas and other special occasions, including for example the sale of mobile phones designed solely for children or free call time packages aimed at teenagers;

24. Proposes that the EU's indoor air quality policy should encompass the study of "wireless" domestic appliances, which, like Wi-Fi for Internet access and digital enhanced cordless telecommunications (DECT) telephones, have been widely adopted in recent years in public places and in the home, with the result that citizens are being continuously exposed to microwave emissions;

25. Calls, given its constant concern to improve consumer information, for the technical standards of the European Committee for Electrotechnical Standardisation to be amended with a view to imposing labelling requirements whereby the transmitting power would have to be specified and every wireless-operated device accompanied by an indication that it emitted microwaves;

26. Calls on the Council and Commission, in coordination with the Member States and the Committee of the Regions, to encourage the introduction of a single standard designed to ensure that local residents are subjected to as low a degree of exposure as possible when high-voltage grids are extended;

27. Is greatly concerned about the fact that insurance companies are tending to exclude coverage for the risks associated with EMFs from the scope of liability insurance policies, the implication clearly being that European insurers are already enforcing their version of the precautionary principle;

28. Calls on Member States to follow the example of Sweden and to recognise persons that suffer from electrohypersensitivity as being disabled so as to grant them adequate protection as well as equal opportunities;

29. Instructs its President to forward this resolution to the Council, the Commission, the governments and parliaments of the Member States, the Committee of the Regions, and the WHO.

(1) OJ L 199, 30.7.1999, p. 59.
(2) OJ L 159, 30.4.2004, p. 1.

(3) OJ L 91, 7.4.1999, p. 10.

(4) OJ L 374, 27.12.2006, p. 10.

(5) Texts adopted, P6_TA(2008)0410.

(6) OJ C 175, 21.6.1999, p. 129.

(7) Opinion of 21 March 2007 adopted at the 16th plenary meeting of the Committee.

(8) Quality of life programme, contract No QLK4-1999-01563.

(9) March 2001 STOA study on "The physiological and environmental effects of non-ionising EMR", PE297.574.

(10) Directive 2003/10/EC of the European Parliament and of the Council of 6 February 2003 on the minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (noise) (OJ L 42, 15.2.2003, p. 38).

(11) Directive 2002/44/EC of the European Parliament and of the Council of 25 June 2002 on the minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (vibration) (OJ L 177, 6.7.2002, p. 13).

APPENDIX C American Academy of Environmental Medicine

American Academy of Environmental Medicine

6505 E Central • Ste 296 • Wichita, KS 67206
Tel: (316) 684-5500 • Fax: (316) 684-5709
www.aaemonline.org

January 19, 2012

Decision Proposed Decision of Commissioner Peevy (Mailed 11/22/2011)
BEFORE THE PUBLIC UTILITIES COMMISSION OF THE STATE OF CALIFORNIA
On the proposed decision 11-03-014

Dear Commissioners:

The Board of the American Academy of Environmental Medicine opposes the installation of wireless "smart meters" in homes and schools based on a scientific assessment of the current medical literature (references available on request). Chronic exposure to wireless radiofrequency radiation is a preventable environmental hazard that is sufficiently well documented to warrant immediate preventative public health action.

As representatives of physician specialists in the field of environmental medicine, we have an obligation to urge precaution when sufficient scientific and medical evidence suggests health risks which can potentially affect large populations. The literature raises serious concern regarding the levels of radio frequency (RF - 3KHz – 300 GHz) or extremely low frequency (ELF – 300Hz) exposures produced by "smart meters" to warrant an immediate and complete moratorium on their use and deployment until further study can be performed. The board of the American Board of Environmental Medicine wishes to point out that existing FCC guidelines for RF safety that have been used to justify installation of "smart meters" only look at thermal tissue damage and are obsolete, since many modern studies show metabolic and genomic damage from RF and ELF exposures below the level of intensity which heats tissues. The FCC guidelines are therefore inadequate for use in establishing public health standards. More modern literature shows medically and biologically significant effects of RF and ELF at lower energy densities. These effects accumulate over time, which is an important consideration given the chronic nature of exposure from "smart meters". The current medical literature raises credible questions about genetic and cellular effects, hormonal effects, male fertility, blood/brain barrier damage and increased risk of certain types of cancers from RF or ELF levels similar to those emitted from "smart meters". Children are placed at particular risk for altered brain development, and impaired learning and behavior. Further, EMF/RF adds synergistic effects to the damage observed from a range of toxic chemicals. Given the widespread, chronic, and essentially inescapable ELF/RF exposure of everyone living near a "smart meter", the Board of the American Academy of Environmental Medicine finds it unacceptable from a public health standpoint to implement this technology until these serious medical concerns are resolved. We consider a moratorium on installation of wireless "smart meters" to be an issue of the highest importance.

The Board of the American Academy of Environmental Medicine also wishes to note that the US NIEHS National Toxicology Program in 1999 cited radiofrequency radiation as a potential Carcinogen. Existing safety limits for pulsed RF were termed 'not protective of public health' by the Radiofrequency Interagency Working Gropu (a federal interagency working group includeing the FDA, FCC, OSHA, the EPA and others). Emissions given off by 'smart meters' have been classified by the World Health Organization International Agency for Research on Cancer (IARC) as a Possible Human Carciongen.

Hence, we call for:

- An immediate moratorium on "smart meter" installation until these serious public health issues are resolved. Continuing with their installation would be extremely irresponsible.
- Modify the revised proposed decision to include hearings on health impact in the second proceedings, along with cost evaluation and community wide opt-out.
- Provide immediate relief to those requesting it and restore the analog meters.

Members of the Board
American Academy of Environmental Medicine

APPENDIX D American Academy of Pediatrics Statement

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

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Elk Grove Village, IL 60007-1019
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E-mail: kidsdocs@aap.org
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Homer Building, Suite 400 N
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July 12, 2012

The Honorable Julius Genachowski
Commissioner
Federal Communications Commission
445 12th Street SW
Washington, DC 20554

Dear Chairman Genachowski:

The American Academy of Pediatrics (AAP), a non-profit professional organization of 60,000 primary care pediatricians, pediatric medical sub-specialists, and pediatric surgical specialists dedicated to the health, safety and well-being of infants, children, adolescents, and young adults strongly supports the proposal for a formal inquiry into radiation standards for cell phones and other wireless products. The Academy encourages the Federal Communications Commission (FCC) to vote to move forward with this inquiry in an expeditious manner.

The FCC has not assessed the standard for cell phone radiation since 1996. According to industry groups, approximately 44 million people had mobile phones when the standard was set; today, there are more than 300 million mobile phones in use in the United States. While the prevalence of wireless phones and other devices has sky-rocketed, the behaviors around cell phone uses have changed as well. The number of mobile phone calls per day, the length of each cell phone call, and the amount of time people use mobile phones has increased, while cell phone and wireless technology has undergone substantial changes. Many more people, especially adolescents and young adults, now use cell phones as their only phone line and they begin using wireless phones at much younger ages.

The FCC standard for maximum radiation-exposure levels are based on the heat emitted by mobile phones. These guidelines specify exposure limits for hand-held wireless devices in terms of the Specific Absorption Rate (SAR), which measures the rate the body absorbs radiofrequency (RF). The current allowable SAR limit is 1.6 watts per kilogram (W/kg), as averaged over one gram of tissue. Although wireless devices sold in the United States must ensure that they do not exceed the maximum allowable SAR limit when operating at the device's highest possible power level, concerns have been raised that long-term RF exposure at this level affects the brain and other tissues and may be connected to types of brain cancer, including glioma and meningioma.

In the past few years, a number of American and international health and scientific bodies have contributed to the debate over cell phone radiation and its possible link to cancer. The International Agency for Research on Cancer (IARC), part of the

United Nations' World Health Organization, said in June 2011 that a family of frequencies that includes mobile-phone emissions is "possibly carcinogenic to humans." The National Cancer Institute has stated that although studies have not demonstrated that RF energy from cell phones definitively causes cancer, more research is needed because cell phone technology and cell phone use are changing rapidly. While a definitive link between cell phone radiation and brain cancer has not been established, these studies and others clearly demonstrate the need for further research into this area and highlight the importance of reassessing the current SAR to determine if it is protective of human health.

The AAP believes the inquiry to reassess the radiation standard presents an opportunity to review its impacts on children's health and well-being. In the past, such standards have generally been based on the impact of exposure on an adult male. Children, however, are not little adults and are disproportionately impacted by all environmental exposures, including cell phone radiation. In fact, according to IARC, when used by children, the average RF energy deposition is two times higher in the brain and 10 times higher in the bone marrow of the skull, compared with mobile phone use by adults. While the Academy appreciates that the FCC is considering investigating whether the emission standards should be different for devices primarily used by children, it is essential that any new standard for cell phones or other wireless devices be based on protecting the youngest and most vulnerable populations to ensure they are safeguarded throughout their lifetimes.

Finally, in reviewing the SAR standard, the FCC has the opportunity to highlight the importance of limiting media use among children. The Academy has found potentially negative effects and no known positive effects of media use by children under the age of two, including television, computers, cell phones, and other handheld wireless devices. In addition, studies consistently show that older children and adolescents utilize media at incredibly high rates, which potentially contributes to obesity and other health and developmental risks. In reviewing the SAR limit, the FCC has the opportunity to improve the health of our nation by highlighting the importance of limiting screen time and media use for children and adolescents.

The AAP supports the proposal for a formal inquiry into radiation standards for cell phones and other wireless products and the Academy encourages the FCC to vote in favor of moving forward with this investigation. If you have questions or concerns, please contact Kristen Mizzi in the AAP's Washington Office at 202/347-8600.

Sincerely,

Robert W. Block, MD FAAP President

Appendix E RCNIRP Resolution: Electromagnetic Fields from Mobile Phones: Health Effects on Children and Teenagers

"The Resolution evolved from scientific statements adopted by RNCNIRP in 2001, 2004, 2007, 2008 and 2009, taking into account contemporary views and actual scientific data. The Resolution represents a viewpoint of the professional scientific community and is meant for public dissemination, for the consumers of the mobile telecommunications services, as well as for the legislative and executive authorities who develop and implement health protection, environmental, communication, scientific and safety policies."

" ... Thus, for the first time in the human history, children using mobile telecommunications along with the adult population are included into the health risk group due to the RF EMF exposure. A situation has emerged that cumulative EMF exposure of children may be comparable to adult exposure and may be equal to the levels of occupational exposure of workers. At the same time, the society, with all its administrative and social structures, remain in a "waiting" position."

"Priority measures aimed at protection of children and teenagers

Taking into account the RNCNIRP position and the precautionary measures suggested by WHO, the Committee considers that urgent measures must be taken because of the inability of children to recognize the harm from the mobile phone use and that a mobile phone itself can be considered as an uncontrolled source of harmful exposure.

1. *It is required that the information that a mobile phone is a source of RF EMF is clearly shown on the phone's body (or any other telecommunication device).*
2. *It is required that the "User's Guide" contains information that a mobile phone (personal wireless communication tool using electromagnetic communication method, etc.) is a source of harmful RF EMF exposure. Usage of a mobile phone by children and adolescents under 18 years old is not recommended by the Sanitary Rule SanPiN 2.1.8/2.2.4.1190-03, and mobile phone use requires implementation of precautionary measures in order to prevent health risks. Mobile phone use by pregnant women is not recommended in order to prevent risk for a fetus.*
3. *The easiest way to reduce RF EMF exposure is to move the mobile phone away from one's head during the phone call which may be achieved by using the hands-free sets (protection by distance). Shortening the call duration is another way to reduce the exposure (protection by time).*
4. *The RNCNIRP considers it is reasonable to develop mobile phones with reduced EMF exposure (with hands-free sets, included limitation functions, such as limitation of the number of daily phone calls, possibility of forced limitation of phone call duration, etc.).*
5. *It is required to include courses on mobile phones use and issues concerning EMF exposure in the educational program in schools.*
6. *It is reasonable to set limits on mobile telecommunications use by children and adolescents, including ban on all types of advertisement of mobile telecommunications for children (teenagers) and with their participation.*
7. *The RNCNIRP is ready to assist the mass-media in their awareness-raising work and educational activities in the area of EMF and, in particular, to provide information about the newest research of the impact of EMF on human health and the measures to curb the negative impact of this physical agent.*
8. *Better safety criteria for children and teenagers are required in the nearest term. Features of the developing organism should be taken into account, as well as the significance of bioelectric processes for human life and activities, present and future conditions of EMF, prospects of technological and technical development should be addressed in a document of legal status.*
9. *Development of a funded national program for studying possible health effects from chronic EMF exposure of the developing brain is necessary."*

Appendix F RCNIRP Resolution to Regulate the Use of WI-FI in Schools

RUSSIAN NATIONAL COMMITTEE
ON NON-IONIZING RADIATION PROTECTION

June 19, 2012 *Moscow, Russia*

Recommendations

of the Russian National Committee on Non-Ionizing Radiation Protection of the necessity to regulate strictly the use of Wi-Fi in kindergartens and schools

Mobile cellular communication is getting more popular among children of different ages. Children excel adult population in the mobile phone calls use. At the same time, there is a daily brain exposure of EMF RF. In addition, all children are constantly exposed of EMF RF from base stations. The problem of the children's health maintenance in the development of wireless communications was set up as priority by World Health Organization.

Electromagnetic radiation from Wi-Fi creates an additional burden for the child brain, whose body is in a state of development and the formation of mental activity. During this period, children are most susceptible to adverse environmental factors (WHO, publication number 3, April 2003).

It is necessary to note that the existing standards have been developed, without consideration of this additional exposure of EMF.

RussCNIRP consider necessary:

1. Ministry of Health and other organizations, responsible for the population safety (including children), should pay attention to the regulation of Wi-Fi use in kindergartens and schools; to the strengthening of sanitary control of the Wi-Fi using and to the development of an appropriate regulatory framework.
2. To recommend the usage of wired networks in schools and educational institutions, rather than a network using wireless broadband systems, including Wi-Fi.

Chairman of RussCNIRP,
Professor

Yury G. Grigoriev

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SECTION 23

The Precautionary Principle

"Late Lessons from Early Warnings: Towards Realism and Precaution with EMF?"

David Gee, European Environment Agency
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Disclaimer.: The views expressed are those of the author and do not represent the views of the EEA or its Management Board. The author has no competing financial interest in the matters dealt with.

Prepared for the BioInitiative Working Group

2007

TABLE OF CONTENTS

I. INTRODUCTION

The histories of selected public and environmental hazards, from the first scientifically based early warnings about potential harm, to the subsequent precautionary and preventive measures, have been reviewed by the European Environment Agency.("Late Lessons from Early Warnings: the Precautionary Principle 1896-2000", EEA,2001). This paper summarises some of the definitional and interpretative issues that arise from the report and subsequent debates, such as the contingent nature of knowledge; the definitions of precaution, prevention, risk, uncertainty, and ignorance; the use of differential levels of proof; and the nature and main direction of the methodological and cultural biases within the environmental health sciences. These issues are relevant to EMF.

II. THE TWELVE "LATE LESSONS FROM EARLY WARNINGS

The paper does not address the specifics of EMF hazards, leaving it to the reader to apply, or not, the "Twelve late Lessons" that conclude the report. These lessons attempt to synthesise the fourteen historical experiences from the very different case study chapters into generic knowledge that can help inform policy-making on current issues such as GMO,, nanotechnologies, mobile phones, and endocrine disrupting substances where the luxuries of hindsight are not yet available but where exposures are already widespread and rising.

The idea of the twelve late lessons is to make the most of past experience to help anticipate future surprises whilst recognising that history never exactly repeats itself. When adopted alongside the best available science the lessons aim to help minimize hazards without compromising innovation. The "lessons" are reproduced below.

A. "Identify/Clarify the Framing and Assumptions"

1. Manage "risk", "uncertainty" and "ignorance"
2. Identify/reduce "blind spots" in the science
3. Assess/account for all pros and cons of action/inaction
4. Analyse/evaluate alternative options

5. Take account of stakeholder values
6. Avoid "paralysis by analysis" by acting to reduce hazards via the precautionary principle.

B. "Broaden Assessment Information"

7. Identify/reduce interdisciplinary obstacles to learning
8. Identify/reduce institutional obstacles to learning
9. Use "lay", local as well as specialist knowledge
10. Identify/anticipate "real world" conditions
11. Ensure regulatory and informational independence
12. Use more long-term (ie. decades) monitoring and research

III. EARLY USE OF PRECAUTION

The Vorsorgeprinzip, or "foresight" principle, only emerged as a specific policy tool during the German debates on the possible role of air pollution as a cause of "forest death" in the 1970-80s. However, John Graham, one of Bush's science policy advisors, and trenchant critic of the precautionary principle, has noted that:

> *"Precaution, whether or not described as a formal principle, has served mankind well in the past and the history of public health instructs us to keep the spirit of precaution alive and well"*. (Graham 2002).

Graham might have been thinking of the cholera episode of 1854 when precaution did indeed serve the people of London well. Dr. John Snow, a London physician, used the spirit of precaution to advise banning access to the polluted water of the Broad St. pump which he suspected was the cause of the cholera outbreak. He based his recommendation on the evidence he had been accumulating for some years including his study of S. London populations served by both piped and well water. Snow's views on cholera causation were not shared by The Royal College of Physicians who considered Snow's thesis and rejected it as 'untenable' as they and other "authorities" of the day believed that cholera was caused by airborne contamination. This particular scientific "certainty" soon turned out to be certainly mistaken, with the last remaining doubt being removed when Koch in Germany isolated the cholera vibrio in 1883.

From the *association* between exposure to water polluted with human faeces, and cholera, observed by Snow in 1854, to Koch's discovery of the *"mechanism of action"*, took 30 years of further scientific inquiry. Such a long time lag between acknowledging compelling associations and understanding their mechanisms of action is a common feature of scientific inquiry, as the histories of TBT, PCBs, DES, the Great Lakes pollution, beef hormones and the other cases in the EEA report illustrate.

IV. KNOWLEDGE AND IGNORANCE REQUIRES BOTH PREVENTION AND PRECAUTION

The Broad St. pump, TBT, DES, PCBs and Great Lakes Pollution examples described here also serve to illustrate the contingent nature of knowledge. Today's scientific certainties can be tomorrow's mistakes, and today's research can both reduce and increase scientific uncertainties, as the boundaries of the "known" and the unknown expand. Waiting for the results of more research before taking action to reduce threatening exposures may not only take decades but the new knowledge may identify previously unknown sources of both uncertainty and ignorance, as awareness of what we do not know expands, thereby supplying further reasons for inaction. "Paralysis by Analysis " can then follow.

"The more we know, the more we realise what we don't know" is not an uncommon scientific experience. Socrates observed some time ago:
"I am the wisest man alive, for I know one thing, and that is that I know nothing". (Plato's Apology 1.21).

This was an early lesson in humility that has been lately forgotten by many scientists and politicians, who often put what turns out to be "misplaced certainty" in today's scientific knowledge: or assume that uncertainty can only be reduced, and not increased, by further research.

The distinction between uncertainty and ignorance is important. (Stirling, 1999) Ignorance is knowing that today's knowledge is very limited: it is the source of scientific surprises, such as the hole in the ozone layer, the mesothelioma cancer from asbestos, imposex in sea snails etc. It is distinct from the uncertainties that arise from

gaps in knowledge and from variances in sampling and monitoring; parameter variability; model assumptions; and from the other attempts to approximate, model and predict unfolding realities.

Foreseeing and preventing hazards in the context of ignorance presents particular challenges to decision-makers. At first sight it looks impossible to do anything to avoid or mitigate "surprises". And ignorance ensures that there will always be surprises. However, some measures that could help limit the consequences of ignorance and the impacts of surprises are:

- using intrinsic properties as generic predictors for unknown but possible impacts e.g. the persistence, bioaccumulation and spatial range potential of chemical substances. (Stroebe et al., 2004)
- reducing specific exposures to potentially harmful agents on the basis of credible 'early warnings' of *initial* harmful impacts, thus limiting the size of any other 'surprise' impacts from the same agent, such as the asbestos cancers that followed asbestosis; and the PCB neurotoxicological effects that followed its wildlife impacts.
- promoting a diversity of robust and adaptable technological and social options to meet needs, which limits technological 'monopolies' (such as those like asbestos, CFCs, PCBs etc.), and therefore reduces the scale of any 'surprise' from any one technological option.
- using more long-term research and monitoring of what appear to be "surprise sensitive sentinels", such as frogs and foetuses.

A. Prevention and Precaution

The distinction between *prevention* and *precaution* is also important. Preventing hazards from "known" risks is relatively easy and does not require precaution. Banning smoking, or asbestos, today requires only acts of prevention to avoid the well-known risks. However, it would have needed precaution, (or foresight, based on a sufficiency of evidence), to have justified acts to avoid exposure to the then uncertain hazards of asbestos in the 1930s –50s, or of tobacco smoke in the 1960's). Such precautionary acts then, if implemented successfully, would have saved many more lives in Europe than today's bans on asbestos and smoking are doing. As

Cogliano has recently pointed out, the difference between prevention and precaution can be further illustrated by showing that *prevention* is used to justify the restriction of exposure to an IARC Category 1 carcinogen whereas *precaution* is necessary to justify restricting exposure to a Category 2A or B carcinogen, where the evidence is less strong. The section below. on different levels of proof , further elaborates this point.
For EMF, the question is, does the existing strength of evidence justify *precautionary* actions now? Or will exposure reduction be delayed until the evidence is clear enough to justify the more belated and overall less protective *prevention* of "known" causes, so that EMF replicates the fate of asbestos ,smoking and most of the other cases in the EEA report?

Some commentators, who have a long and distinguished history in preventing occupational and environmental risks, have queried the added value of the precautionary principle in the field of public health, with its long traditions of prevention. (Goldstein, 2007).

The key to understanding the added value of the PP requires a) acknowledging the distinction between prevention and precaution described above; b) an appreciation of the further distinctions between the primary, secondary and tertiary preventative *measures* that have long between adopted in public health, and the prior *justification* for any such measure, which the PP brings; and c) a recognition of the increased legitimacy and transparency that arises from the articulation and adoption of the PP in legal texts, international agreements and conventions, as opposed to being merely part of general practice.

More empirically, the evidence that many scientific disciples, legal scholars (de Sadeleer, 2007),and international policymakers, have, since the 1970s, recognised the need for legitimising the PP as a new policy tool that is better able to deal with systems complexities, ignorance and uncertainties, suggests that the PP brings added value to the protection of the environment and the public.

There is much discussion generated by the different meanings often attached to the common terms “prevention”, “precaution”, “risk”, “uncertainty” and “ignorance”. **Table 1** attempts to clarify these so as to help reduce unnecessary argumentation.

Table 1: Clarification of Key Terms

Situation	***State and dates of knowledge***	***“Nature of the justification for Action”***
Risk	**‘Known’ impacts; ‘known’ probabilities e.g. asbestos**	**Prevention: action taken to reduce known hazards e.g. eliminate exposure to asbestos dust**
Uncertainty	**‘Known’ impacts; ‘unknown’ probabilities e.g. antibiotics in animal feed and associated human resistance to those antibiotics**	**Precautionary prevention: action taken to reduce exposure to potential hazards**
Ignorance	**‘Unknown’ impacts and therefore ‘unknown’ probabilities eg the ‘surprises’ of chlorofluorocarbons (CFCs), pre 1974**	**Precaution: action taken to anticipate, identify and reduce the impact of ‘surprises’**

Source: Reproduced, with amendment, from the Late Lessons Report, EEA 2001.

V. THE PRECAUTIONARY PRINCIPLE: DEFINITIONS AND INTERRPRETATIONS

There are some relatively rare but successful acts of “precautionary prevention” in the EEA report such as on cholera in1854, on TBT in France in the 1980s, and on CFCs in the 1970s. Together with the many other examples of the failure to use the precautionary principle in the other case studies (EEA, 2001), these illustrate the wisdom of taking appropriate precautionary actions to avoid plausible and serious threats to health or environments, especially when the impacts are irreversible and likely to be much more costly to society than the precautionary measures.

Some commentators have stressed the need for policymakers to take account of the foreseeable, or plausible, countervailing (secondary) costs of otherwise genuine precautionary attempts to protect the environment and health. (Rushton, 2007). This

consideration of countervailing costs has long been recognised by the better policymakers, even if it is difficult in practice to anticipate and account for all consequences of actions. And of course there are the secondary benefits of precautionary actions as well, which tend to be less stressed, such as the benefit of reduced respiratory and cardiovascular disease from the reduced combustion of fossil fuels: a large and early secondary benefit of that climate change measure.

The outcomes of some controversial actions based on the PP, such as the EU ban on antibiotics as growth promoters, which is a Late Lessons case study, have since been scrutinised, and have been considered sound ,or unsound, depending on the science used and its interpretation by different interests. (Cox, 2007, Angulo et al., 2004).

Any policy effectiveness analysis of measures taken to deal with such multi-causal and long term hazards as antibiotics as growth promoters is fraught with methodological difficulties and is hampered by long latencies and complex biological systems: untangling the causal impact of one stressor amongst many inter-dependent ones is virtually impossible. The value of applying more probabilistic and value of information data to such conundrums is recognised by many risk managers. However, this cannot remove the need for scientific and political judgment about how to take appropriate and proportionate action in the face of irreducible uncertainties, ignorance and plausible hazards which could have serious, widespread and irreversible impacts and for which probabilities are not possible at the time when they are most needed. This is the current case with many EMF exposures.

A. Some Definitions and Interpretations of the Precautionary Principle

The increasing awareness of complexity and uncertainty during the 1980/90's led to the German debates on the Vorsorgeprinzip shifting to the international level, initially in the field of conservation (World Charter for Nature UN 1982), but then particularly in marine pollution, where an overload of data accompanied an insufficiency of knowledge. (Marine Pollution Bulletin, 1997). This generated the need to act with precaution to reduce the large amounts of chemical pollution entering the North Sea. Since then many international treaties have included the PP (including the often cited version from the Third North Sea Ministerial Conference, 1990, have included

reference to the precautionary principle, or, as they refer to it in the USA, the precautionary approach.

The N.Sea declaration called for *"action to avoid potentially damaging impacts of substances, even where there is no scientific evidence to prove a causal link between emissions and effects"*.

This definition has often, and sometimes mischievously, been used to deride the precautionary principle by claims that it appears to justify action even when there is "no scientific evidence" that associates exposures with effects. However, the N. Sea Conference definition clearly links the words "no scientific evidence" with the words. "to prove a causal link". We have already seen with the Broad St. pump and TBT examples that there is a significant difference between evidence about an "association" and evidence that is robust enough to establish a "causal" link. (Hill, 1965).

The Treaty of the European Union also cites the precautionary principle, as well as the other key principles of sound public policy on health:

> "*Community policy on the environment … shall be based on the precautionary principle and on the principles that preventive action should be taken, that environmental damage should, as a priority, be rectified at the source and the polluter should pay*" (Treaty on European Union, 1992).

Other parts of the EU Treaty ,and cases taken at the European Court of Justice, make it clear that these principles also apply to environmental and consumer protection issues.

These principles, as well as the important and legally required *proportionality principle*, which limits disproportion between the costs and benefits of prevention, are not defined in the Treaty but are illuminated by their practical application in case law. However, all serious applications of the precautionary principle require some scientific evidence of a plausible association between exposures and current, or potential, impacts.

There is still much disagreement and discussion about the interpretation and practical application of the precautionary principle, due, in part, to this lack of clarity and consistency over its definition. For example, many definitions in the Treaties and Conventions use a double negative to define the precautionary principle: that is, they

identify reasons that cannot be used to justify not acting, but without specifying that a sufficiency of evidence is needed to justify taking action.

B. Reasonable Grounds for Concern?

The Communication from the EU on the precautionary principle (European Commission 2000) does specify that "reasonable grounds for concern" are needed to justify action under the precautionary principle, but it does not make explicit that these grounds will be case specific: nor does it explicitly distinguish between risk, uncertainty and ignorance. Since the EC Communication, the EU Council of Misisters, EU case law, and the regulation establishing the new European Food Safety Authority, EFSA, (General Food Law Regulation, EC No 178/2002), have further clarified the circumstances of use and application of the precautionary principle.
For example, the judgement of the European Court of Justice in the BSE case contained a general definition which authoritative commentators think contain many of the necessary elements of the precautionary principle that are applicable in all areas of the EC law:

> "*Where there is uncertainty as to the existence or extent of risks to human health, the institutions may take protective measures without having to wait until the reality and seriousness of those risks become fully apparent*" (Christoforou, 2002).

The WHO Declaration from the Fourth Ministerial Conference on Environment and Health (WHO, 2004a) refers explicitly to the precautionary principle with the recommendation:

> *"that it should be applied where the possibility of serious or irreversible damage to health or the environment has been identified and where scientific evaluation, based on available data, proves inconclusive for assessing the existence of risk and its level but is deemed to be sufficient to warrant passing from inactivity to policy alternatives"* (WHO, 2004b).

The American Public Health Association (APHA) affirmed endorsement of the precautionary principle as a cornerstone of public health for the protection of children's health. In a 2000 policy statement, the APHA encouraged governments, the private sector and health professionals to promote and use the precautionary principle to protect the health of developing children (APHA, 2001).

C. The EEA working definition of the Precautionary Principle.

The working definition used in the European Environment Agency that has been developed during debates since 2001 is explicit about specifying both uncertainty and ignorance, as contexts for applying the principle, and in acknowledging that a case-specific sufficiency of scientific evidence is needed to justify public policy actions:

> '*The Precautionary Principle provides justification for public policy actions in situations of scientific complexity, uncertainty and ignorance, where there may be a need to act in order to avoid, or reduce, potentially serious or irreversible threats to health or the environment, using an appropriate level of scientific evidence, and taking into account the likely pros and cons of action and inaction*' (Gee, 2006).

The definition is also explicit about the trade off between action and inaction, and widens the conventionally narrow, and usually quantifiable, interpretation of costs and benefits to embrace the wider and sometimes unquantifiable, "pros and cons". Some of these wider issues, such as loss of the ozone layer, or of public trust in science, are unquantifiable, but they can sometimes be more damaging to society than the quantifiable impacts: and they need to be included in any comprehensive risk assessment. The EEA definition is proving to be useful in clarifying the use and interpretation of the PP, especially in emerging issues such as EMF.

VI. DIFFERENT LEVELS OF PROOF FOR DIFFERENT PURPOSES

The level of proof (or strength of scientific evidence) that would be appropriate to justify public action in each case varies with the pros and cons of action or inaction. These include the nature and distribution of potential harm; the justification for, and the benefits of the agent or activity under suspicion; the availability of feasible alternatives; and the overall goals of public policy. Such policy goals can include the achievement of the "high levels of protection" of public health, of consumer safety, and of the environment, required by the EU Treaty.

The use of different levels of proof is not a new idea: societies often use different levels of proof like for different purposes.

For example, a high level of proof (or strength of evidence) such as “beyond all reasonable doubt” is used to achieve good science where A is seen to cause B only when the evidence is very strong. Such a high level of proof is also used to minimise the costs of being wrong in the criminal trial of a suspected murderer, where it is usually regarded as better to let several guilty men go free than it is to wrongly convict an innocent man. However, in a different, civil trial setting, where, say, a citizen seeks compensation for neglectful treatment at work, which has resulted in an accident or ill health, the court often uses a lower level of proof commensurate with the costs of being wrong in this different situation. I n compensation cases an already injured party is usually given the benefit of the doubt by the use of a medium level of proof, such as “balance of evidence or probability”. It is seen as being less damaging (or less costly in the wider sense) to give compensation to someone who was *not* treated negligently than it is to *not* provide compensation to someone who was treated negligently. The “broad shoulders” of insurance companies are seen as able to bear the costs of mistaken judgements rather better than the much narrower shoulders of an injured citizen. In each of these two illustrations it is the nature and distribution of the costs of being wrong that determines the level of proof (or strength of evidence) that is “appropriate” to the particular case.

Bradford Hill, cited above, was very concerned about the social responsibility of scientists and he concluded his classic 1965 paper on association and causation in environmental health , which was prepared at the height of the smoking controversy, with a “call for action” in which, *inter alia*, he also proposed the concept of case specific and differential levels of proof. His three examples ranged from “relatively slight” to “very strong” evidence, depending on the nature of the potential impacts and of the pros and cons in each specific case, i.e., possibly teratogenic medicine for pregnant women; a probable carcinogen in the workplace; and government restrictions on public smoking or diets. (Bradford Hill 1965).

Identifying an appropriate level of proof has also been an important issue in the climate change debates. The International Panel on Climate Change (IPCC) discussed

at length this issue before formulating their 1995 conclusion that “on the balance of evidence” mankind is disturbing the global climate. They further elaborated on this issue in their 2001 report where they identified 7 levels of proof (or strengths of evidence) that can be used to characterise the scientific evidence for a particular climate change hypothesis.

Table 2 provides the middle 5 of these levels of proof from the IPPC and illustrates their practical application to a variety of different societal purposes. In the cancer field the International Agency for Research on Cancer also uses several strengths of evidence to characterise the scientific evidence on carcinogens. (Cogliano, 2007)

Different Levels of Proof for Different Purposes: Some Examples and Illustrations

Probability	Quantitative descriptor (Probability bands based on IPCC 2001)	Qualitative Descriptor	Illustrations
100 % probability	Very likely (90-99 %)	• "Statistical significance"	• Part of strong scientific evidence for "causation"
		• "Beyond all reasonable doubt"	• Most criminal law. And the Swedish Chemical law, 1973, for evidence of "safety" of substances under suspicion-burden of proof on manufacturers
90 %	Likely (66-90 %)	• "Reasonable certainty"	• Food Quality Protection Act, 1996 (US)
		• "Sufficient scientific evidence"	• To justify a trade restriction designed to protect human, animal or plant health under World Trade Organisation Sanitary and Phytosanitary (SPS) Agreement, Art. 2.2, 1995
50 %	Medium Likelihood (33-66 %)	• "Balance of evidence"	• Intergovernmental Panel on Climate Change 1995 & 2001
		• "Balance of probabilities"	• Much Civil and some administrative law
		• "Reasonable grounds for concern"	• European Commission Communication on the Precautionary Principle 2000
		• "Strong possibility"	• British Nuclear Fuels occupational radiation compensation scheme, 1984 (20-50% probabilities triggering different awards up to 50% +, which then triggers full compensation)
	Low Likelihood (10-33 %)	• "Scientific suspicion of risk"	• Swedish Chemical law, 1973, for sufficient evidence to take precautionary action on potential harm from substances-burden of proof on regulators
0 %		• "Available pertinent information"	• To justify a provisional trade restriction under WTO SPS Agreement, Art. 5.7 where "scientific information is insuffiicient"
	Very Unlikely (1-10 %)	• Low risk	• Household fire insurance
0 % probability		• "Negligible and insignificant"	• Food Quality Protection Act, 1996 (US)

Source: EEA, 2001

VII. FALSE NEGATIVES AND FALSE POSITIVES.

All of the 14 case studies (tributylin or TBT, benzene, PCBs, CFCs, MTBE, SO_2. Great Lakes pollution. DES, and beef hormones. asbestos. medical x-rays, BSE and Fisheries are all examples of "false negatives" in the sense that the agents or activities were regarded as not harmful for some time before evidence showed that they were indeed hazardous.

We tried to include a "false positive" case study in the report (i.e., where actions to reduce potential hazards turned out to be unnecessary), but failed to find either authors or sufficiently robust examples to use. Providing evidence of "false positives" is more difficult than with "false negatives" (Mazur, 2004). How robust, and over what periods of time, does the evidence on the absence of harm have to be before concluding that a restricted substance or activity is without significant risk?

Volume 2 of "Late Lessons", which the EEA intends to publish in 2008, will explore the issues raised by false positives. including lessons to be learned from such apparent examples as the EU ban on food irradiation and hazardous labelling on saccharin in the US. The Y2K computer bug story may also carry some interesting lessons.

Why are there so many "false negatives" to write about, and how might this be relevant to EMF? Conclusions based on the first Late lessons volume of case studies point to two main answers: the bias within the health and environmental sciences towards avoiding "false positives", thereby generating more "false negatives", and the dominance within decision-making of short-term, specific, economic and political interests over the longer term, diffuse, and overall welfare interests of society.

The latter point needs to be further explored, particularly within the political sciences. Researchers could examine the ways in which society's long-term interests can be more effectively located within political and institutional arrangements that have, or could have, an explicit mandate to look after the longer term welfare of society, and thereby to better resist the short-term pressures of particular economic or political interests. The judiciary in democracies can play part of this role, as can long running

and independent advisory bodies, such as the Royal Commission on Environmental Pollution (UK), or the German Advisory Council on Global Change.

The current and increasing dominance of the short-term in markets and in parliamentary democracies makes this an important issue. The experiments we are conducting with planet earth, its eco-systems and the health of its species, including humans, require, *inter alia*, more long-term monitoring of "surprise-sensitive" parameters which could, hopefully, give us early warnings of impending harm. Such long-term monitoring requires long-term funding, via appropriately designed institutions: such funding and institutions are in short supply. The case studies in Vol. 1 of "Late Lessons" illustrate both the great value, (e.g. in the TBT, DES, Great Lakes and CFCs stories), yet relative paucity, of long-term monitoring of both health and environments. Such monitoring can contribute to the "patient science" that slowly evolving natural systems require for their better understanding.

Since the publication of "Late Lessons" we have further explored the second cause of "false negatives" i.e. the issue of bias within the health and environmental sciences. Table 3 lists sixteen common features of methods and culture in the environmental and health sciences and shows their main directions of error. Of these, only three features tend towards generating "false positives" whereas twelve tend towards generating "false negatives". (Clearly, the weighting of these different biases would be the next step but has not yet been tried).

Table 3

ON BEING WRONG:
Environmental and Health Sciences and Their Directions of Error

SCIENTIFIC STUDIES	SOME METHODOLOGICAL FEATURES	MAIN[1] DIRECTIONS OF ERROR-INCREASES CHANCES OF DETECTING A:
Experimental	High doses	False positive
Studies	Short (in biological terms) range of doses	False negative
(Animal	Low genetic variability	False negative
Laboratory)	Few exposures to mixtures	False negative
	Few Foetal-lifetime exposures	False negative
	High fertility strains	False negative (Developmental/reproductive endpoints)
Observational	Confounders	False positive
Studies	Inappropriate controls	False positive/negative
(Wildlife &	Non-differential exposure misclassification	False negative
Humans)	Inadequate follow-up	False negative
	Lost cases	False negative
	Simple models that do not reflect complexity	False negative
Both	Publication bias towards positives	False positive
Experimental And	Scientific cultural pressure to avoid false positives	False negative
Observational Studies	Low statistical power (e.g. From small studies)	False negative
	Use of 5 % probability level to minimise chances of false positives	False negative

Source: Gee, 2006

[1] Some features can go either way (e.g. inappropriate controls) but most of the features mainly err in the direction shown in the table

The general bias towards the null helps to produce robust science, basing it on strong foundations of knowledge, but this bias can encourage poor public health or environmental policy. The goals of science and public policy-making on health and environmental hazards are different: science puts a greater priority on avoiding "false positives" by accepting only very high levels of proof of "causality", whereas public policy tries to prioritize the avoidance of "false negatives" on the basis of a sufficiency of evidence of potential harm.

Table 3 is derived from papers presented to a conference on the precautionary principle organised by the Collegium Ramazzini, the EEA, the WHO and NIEHS in 2002. (Grandjean et al., 2003). It provides a first and tentative step in trying to capture and communicate the main directions of this bias within the environmental and health sciences, a bias which decision makers and the public should be aware of. As they debate the evidence on emerging hazards such as EMF.

The appropriate balance between false negatives and positives was addressed at a JRC/EEA workshop on the precautionary principle and scientific uncertainty which was held during the "Bridging the Gap" Conference, 2001, organised by the Swedish Presidency of the EU, in partnership with the EEA and DG Research. It drew the following conclusion:

> *"Improved scientific methods to achieve a more ethically acceptable and economically efficient balance between the generation of "false negatives" and "false positives" are needed"*. (Swedish EPA 2001).

VIII. SOME CRITERIA FOR ESTABLISHING CAUSATION

Bradford Hill established nine criteria for helping to move from association to causation in environmental health which have been, and still are, widely used in debates on issues such as EMF

Two of the apparently more robust of the "criteria" may not be so robust in the context of multi-causality, complexity and gene/host variability.

For example, ***"consistency"*** of study findings is not always to be expected. As Prof. Needleman, who provided the first of what could be called the second generation of early warnings on lead in petrol in 1979 has observed:

> *"Consistency in nature does not require that all or even a majority of studies find the same effect. If all studies of lead showed the same relationship between variables, one would be startled, perhaps justifiably suspicious"* (Needlemann , 1995).

It follows that the *presence* of consistency of results between studies on the same hazard can provide robust evidence for a causal link, but the *absence* of such consistency may not provide very robust evidence for the absence of a real association. In other words, the "criterion" of consistency is asymmetrical, like most of the other Bradford Hill "criteria".

Similarly, the criterion of ***"temporality",*** which says that the putative cause X of harm Y must come before Y appears, is robust in a simple, uni-causal world. In a multi-causal, complex world of common biological end points that have several chains of causation this may not necessarily be so. For example, falling sperm counts can have multiple, co-causal factors, some of which may have been effective at increasing the incidence of the biological end point in question in advance of the stressors in focus, thereby confusing the analysis of temporality. The resulting overall sperm count trends could then be rising, falling or static, depending on the combined direction and strengths of the co-causal factors and the time lags of their impacts. It follows that say, chlorine chemicals, may or may not be co-causal factors in falling sperm counts: but the use of the "temporality" argument by the WHO, who observed that sperm counts began to fall before chlorine chemistry production took off, does not provide robust evidence that they are not causally involved.

The presence of "temporality", like "consistency" may be robust evidence *for* an association being causal, but its *absence* may not provide robust evidence *against* an association. Bradford Hill was explicitly aware of the asymmetrical nature of his "criteria": his followers have not always been so aware.
During 2005, the 40th anniversary year of the Bradford Hill "criteria", the EEA convened a panel of experts to review the "criteria" and their use in light of advances in knowledge, particularly multi-causality, since 1965. A report will be published in 2007.

How this goal can be achieved without compromising science remains to be explored, (Grandjean 2004; Grandjean et al., 2004). It is clearly necessary, particularly when dealing with EMF, for scientific methods to not only take account of thisfalse negative/positive bias in methodologies but also to more clearly reflect other realities such as multi-causality; thresholds; timing of dose; sensitive sub-populations, such as children, (Jarosinska and Gee, 2007); sex, age, and immune conditions of the host; information physics; effects below the thresholds of "acute" impacts, such as tissue heating; non-linear dose/response relationships; "low dose" effects; and the effects arising from disturbing the balance between opposing elements in complex biological systems. The evidence on EMF needs to take full account of these realities, as well as of the methodological biases of Table 3.

1X. PUBLIC PARTICIPATION IN RISK ANALYSIS

Choosing an appropriate level of proof for a particular case is clearly based, *inter alia*, on value judgements about the acceptability of the costs, and of their distribution, of being wrong in both directions, i.e. of acting or not acting to reduce threatening exposures. This is why it is necessary to involve the public in decisions about serious hazards and their avoidance: and to do so for all stages of the risk analysis process.

Three of the "twelve late lessons" (number 5, number 9 and number 10) explicitly invite early involvement of the public and other stakeholders at all stages of risk analysis, a development which has been actively encouraged in many other influential reports during the last decade. (NRC 1994; US Presidential Commission on Risk Assessment and Risk Management 1997; Royal Commission on Environmental Pollution 1998; CEC Communication on the Precautionary Principle 2000; German Advisory Council on Global Change 2001).

The best available science is therefore only a necessary but not a sufficient condition for sound public policy making on potential threats to health and the environment. Where there is scientific uncertainty and ignorance "it is primarily the task of the risk managers to provide risk assessors with guidance on the science policy to apply in their risk assessments." (Christoforou, 2003). The content of this science policy advice, as well as the nature and scope of the questions to be addressed by the risk

assessors, need to be formulated by the risk managers and relevant stakeholders at the initial stages of the risk analysis.

Involving the public in not only all stages of risk analysis, but also in helping to set research agendas and technological trajectories, (Wilsdon and Willis, 2004) is not easy. Many experiments, in both Europe and the USA, with focus groups, deliberative polling, citizens' juries, and extended peer review, (Funtovicz and Ravetz, 1990/92) are exploring appropriate ways forward.

The issue of time is also a critical issue for risk analysis and application of the precautionary principle. For example, the time from the first scientifically based early warnings (1896 for medical X rays, 1897 for benzene, 1898 for asbestos) to the time of policy action that effectively reduced damage was often 30-100 years. Some consequences of the failures to act in good time (e.g. on CFCs or asbestos) continue to cause damage over even longer time periods. For example, the ozone hole will cause many thousands of extra skin cancers in today's children but the cancers will only peak around the middle of this century because of the long latent period between exposure and effect. Such long-term but foreseeable impacts raise liability and compensation issues, including appropriate discount rates (if any) on future costs and benefits, which being value-laden choices. need also to be discussed by stakeholder groups. Again, experience in the climate change field with these long-term issues may be helpful in managing them with respect to electromagnetic fields (ELF and RF).

The wider involvement of stakeholders has also been recognised more recently by the International Risk Governance Council (IRGC, 2005) and the EU report on Science and Governance, (Wynne et al., 2007). Whether wider involvement of stakeholders results in better and more acceptable decisions needs to studied: early indications (Beierle, 2002), and lessons from history, suggests that is. In many cases several decades will be necessary to confidently judge outcomes, given latencies and complexities.

X. SOME EXAMPLES OF EARLY WARNINGS

The 14 case studies in the Late Lessons Report (EEA 2001) include examples some chemicals (tributylin or TBT, benzene, PCBs, CFCs, MTBE, SO_2 and Great Lakes pollution); two other pharmaceuticals (DES, and beef hormones); two physical agents (asbestos and medical x-rays); one pathogen (BSE); and Fisheries (overfishing).

The main issues discussed so far, such as the contingent nature of knowledge; ignorance and "surprises"; appropriate levels of evidence for policy actions; and public participation in risk analysis are critical to the successful application of both scientific knowledge and the precautionary principle to public policy-making. They are therefore relevant to discussions about the potentially new hazards that are now emerging e.g. from nanotechnology, (Royal Society 2003); from the non-ionising radiations arising from the use of mobile phones, (Stewart Reports 2000, 2004), and from endocrine disrupting substances or EDSs. (WHO, 2002).

With such newly emerging hazards it can be helpful to use historical examples to illustrate what a scientifically based early warning looks like as it is often difficult to properly recognise such warnings at the time they occur. A good example is that provided by the UK Medical Research Council's Swann Committee in 1969. They were asked to assess the evidence for risks of resistance to antibiotics in humans following the prolonged ingestion of trace amounts of antibiotics arising from their use as growth promoters in animal feed. (Edqvist and Pedersen 2001). They concluded that:

> *"Despite the gaps in our knowledge .. we believe … on the basis of evidence presented to us, that this assessment is a sufficiently sound basis for action .. The cry for more research should not be allowed to hold up our recommendations'….'sales/use of AFA should be strictly controlled via tight criteria, despite not knowing mechanisms of action, nor foreseeing all effect"*. (Swann 1969).

A. Antibiotics in Animal Feed

The Swann Committee also concluded that it would be more rewarding and innovative to improve animal husbandry as a means of encouraging disease free animal growth rather than to the cruder approach of diets containing antimicrobials. Despite the gaps in knowledge, the need for much more research, and considerable ignorance about the mechanisms of action, a sufficiency of evidence was identified and described by the Swann Report that justified the need for public authorities to restrict the possibility of exposures to antibiotics from animal growth promoters. This early warning was initially heeded, but was then progressively ignored by the pharmaceutical companies and regulatory authorities, who wanted more scientific justification for restricting anti-microbial growth promoters. However, in 1985 in Sweden, and then in the EU in 1999, the use of antibiotics as growth promoters was finally banned. Pfizer, the main supplier of such antibiotics in Europe, appealed against the European Commission banning decision, pleading, *inter alia*, an insufficiency of scientific evidence. They lost this case at the European Court of Justice (Case T-13/99-Pfizer 2002), a case which further clarified the proper use and application of the precautionary principle in circumstances of scientific uncertainty and of widespread, if low, public exposures to a potentially serious threat.

B. Lead in Gasoline

A US example of an early warning comes from the lead in gasoline story: a warning that was largely ignored for over 50 years, resulting in much damage to the intelligence and behaviour of children in America, Europe and the rest of the motorised world. Yandell Hendersson, Chair of the Medical Research Board, US Aviation Service, who had been asked to look at the scientific evidence on the possible hazards of tetraethyl lead during the temporary ban on lead in petrol, in 1925, concluded:

> *"It seems likely that the development of lead poisoning will come on so insidiously that leaded gasoline will be in nearly universal use … before the public and the government awakens to the situation"*. (Rosner and Markowitz, 2002).

Motorised societies would have gained much in dollars, brainpower and social cohesion had they heeded this foresight.

C. Tributylin (TBR) – A Marine Antifoulant for Ships

The case study on tributylin (TBT) and DES illustrate the surprises that arise from real life complexities and which may carry some lessons for the EMF debate. For example, the unfolding of the TBT story was accompanied by an increased appreciation of scientific complexity arising from the discoveries that adverse impacts were caused by very low doses (i.e. in parts/trillion); that high exposure concentrations were found in unexpected places e.g. in the marine micro-layer; and that bioaccumulation in higher marine animals, including sea-food for human consumption, was greater than expected. The early actions on exposure reduction in France and the UK in 1982-85 were based on a 'strength of evidence' for the 'association' only: knowledge about 'causality', **'**mechanisms of action' and other the complexities above came much later.

We were lucky in some ways with the TBT story: a highly specific, initially uncommon impact (imposex) was quickly linked to one chemical, TBT. This relatively easily identified linkage is not likely to be repeated for the more common and multi-causal impacts where, for example, neurodevelopmental diseases and dysfuntions, or common cancers, are the impacts under suspicion.

D. Diethylstilbestrol (DES)

Key lessons from the DES story are also instructive, as it provides the clearest example of endocrine disruption in humans. Diethylstilbestrol, commonly referred to as DES, is a synthetic estrogen . It was originally prescribed to prevent miscarriage, but did not. Later, sons and daughters of mothers given DES to prevent miscarriage developed cancers, reproductive tract anomalies, and had more pre-term babies themselves as a result. The effects of DES include the absence of visible and immediate teratogenic effects **not** being robust evidence for the absence of reproductive toxicity; and the **'**timing of the dose clearly determining the poison', in contrast to the 'dose determines the poison' dictum of Paracelsus. Timing is also relevant to other biological end points:

> *"the time of life when exposures take place may be critical in defining dose-response relationships of EDSs for breast cancer as well as for other health effects",* (WHO/IPCS, 2002).

Although the exposure levels were higher than the usual environmental levels of other EDSs, the DES story provides a clear warning about the potential dangers of perturbing the endocrine system with synthetic chemicals.

With over 20,000 publications, DES is now a well-studied compound, yet many doubts persist about its mechanisms of action. Since no dose-effect relationship has been found in humans, it cannot be excluded that DES could have been toxic at low doses, and that other less potent xenoestrogens could have similar effects.

If we still have few certainties about DES after so much time and research, what should our attitude be towards emerging hazards, such as other endocrine disrupting substances (EDSs) and EMF?

XI. CONCLUSION

The lessons of history from the EEA report, and subsequent debates and events, indicate that they have much relevance to the EMF issue, as well as to other emerging issues such as nanotechnology, (Royal Society, 2003) and endocrine disrupting substances or EDSs (WHO, 2002). The public health assessment of EMF could apply these lessons, approaches, terms of discussion and interpretations to the precautionary and preventative actions on the different parts of the EMF exposure problem.

There are of course large differences between smoking and EMF. The smoking hazard had at least 10 times the relative risk increase in the exposed population compared to the leukaemia risk from power line exposure; and the size of the smoking exposed population, and its exposure above that needed to generate a doubling of the risk, are both very much greater than with power lines. The larger relative risk for smoking and lung cancer seems to arise from comparing smokers with non, or never, smokers whilst the relative risk of 2 to 3 that arises between moderate and heavy smokers, or between second hand smokers and non smokers, is more relevant to the EMF issue,

where there is an absence of unexposed controls. The lower relative risks of 2 or 3 for EMF are biased towards the null to unknown extent by the absence of such controls (Milham, 1998). However, the parallel between the slow recognition of the smoking hazard and power line EMF hazard is interesting.

The parallel with the history of X rays is also pertinent. The initial discovery, by Alice Stewart in the early 50s, that a few x rays of a pregnant woman in the sensitive period of her pregnancy gave a 2 fold excess of leukaemia, was greeted with much strident disbelief, particularly from the male doctors whose latest toy was under threat. It took another 20 years or so before her result became generally accepted, and only after several negative studies that were conducted in the early response to her study. Many studies of X rays in pregnant women now exist, and, as with the power line studies, the relative risk remains at about 2. (EEA, 2001) What will the history of EMF look like in 2020?

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SECTION 23

The Precautionary Principle

2012 Supplement

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Disclaimer.: The views expressed are those of the author and do not represent the views of the EEA or its Management Board. The author has no competing financial interest in the matters dealt with.

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I. INTRODUCTION

In 2007, the evidence for EMF, and in particular radiofrequency radiation (RFR) from the use of mobile phones, was a focus for discussion in the BioInitiative Report (2007). It arose from growing scientific evidence of possible health risks, with a very large global population that could presumably be affected by the outcome.

Illustrating the importance of observing 'early warnings' of environmental and public health risks arising from emerging scientific studies and direct observation of impacts to peoples' health, this author wrote about the importance of applying 'lessons learned' from the histories of selected public and environmental hazards, from the first scientifically based early warnings about potential harm, to the subsequent precautionary and preventive measures, as reviewed by the European Environment Agency in Late Lessons from Early Warnings: the Precautionary Principle 1896-2000 (EEA, 2001). In considering the evidence on mobile phones and head cancers the EEA concluded that it would be prudent and timely to issue an "early warning" on the issue, in September, 2007. Five years on, this note briefly updates our opinion on this issue.

II. NEED FOR PRECAUTIONARY ACTIONS ON MOBILE PHONES

The communication leaflet for publication of "Late Lessons from Early Warnings 2: Science, Precaution, Innovation." (EEA, 2012) includes this message:

> *"In the context of scientific uncertainty and ignorance, the decision-makers responsible for incentivising and regulating innovation face a significant challenge in balancing opportunities against risks. The precautionary principle can help to better manage such choices. It requires actions to prevent potentially serious harm before the likelihood or severity of an innovation's impacts become all too clear."*

Volume 2 of 'Late Lessons' includes a chapter on mobile phones and brain tumour risk by Hardell, Carlberg and Gee. Inclusion of a full chapter on the science and public health implications of the mobile phone-brain cancer issue underscores the importance to the European Environmental Agency that mobile phone radiation is a possible health threat. This position is supported by the 2011 classification by the World Health

Organization International Agency for Research on Cancer (IARC) of radiofrequency radiation as a Group 2B Possible Human Carcinogen (Baan et al, 2011).

The evidence in 2012 is stronger than in 2007, and based essentially on two large population studies, the Hardell group in Sweden and the Interphone Study Group which involved 13 countries (WHO Interphone Final Report, 2010; Cardis & Radetski 2010? Hansson Mild et al, 2007; Hardell et al, 2006a, 2006b, 2006c; Hardell et al, 2008; Hardell et al, 2009a, 2009b; Hardell et al, 2010; Hardell et al, 2011a, 2011b; Hardell et al, 2012a in press; Hardell et al, 2012b in press). Are all 12 refs from Hardell needed? Looks like overkill…how about those from 2009?

Some researchers have identified in the last five years "*a consistent pattern of increased risk of glioma and acoustic neuroma associated with use of mobile phones and cordless phones.*" (Hardell et al, 2012b in press), a view that is essentially supported by the leader of the Interphone study. (Cardis & Radetski)

The European Environmental Agency's view on the need for precautionary measures on mobile phones is more warranted in 2012, than it was in 2007, or even early 2011, prior to the IARC decision, when we last reviewed the evidence for a presentation to the Council of Europe (EEA, 2011).

Precautionary actions that can be taken to reduce exposures to RFR would be consistent with actions that have been recommended for other emerging environmental and health issues, for example some uses of the common plastic, BPA, some nanotechnologies, and some food chain additives or contaminants, such as antibiotics, beef hormones, and GMOs. The 25 or so more historical case studies in the 'Late Lessons' volumes such as those on the Minamata Bay disaster, asbestos, leaded petrol, and tobacco illustrate the huge costs of not taking robust early warnings seriously.

Precautionary measures are of particular importance in regard to children, who are generally more biologically sensitive, may be unable to protect themselves; and for whom such exposures may carry greater life-time health risks than they do for adults.

The evidence for a brain tumour risk from mobile phones is still not well established

amongst all researchers in the field and there is much scientific controversy about what the current evidence means. The debate is not helped by what might be termed 'trial by media' where some scientific advocates leap into the lay press to argue their own case just as, or even before, their research is published. The effects of this behaviour would be minimized if the results of genuine differences of scientific opinion were made transparent when they were published, with clear explanations about the origins of divergent views, such as the scientific paradigms used ("tissue heating" or "information physics" ?); assumptions made; evidence rejected; and values chosen. This does not tend to happen. Divergent scientific views are often smoothed over with the use of what one respected commentator on the reporting of the Interphone results called "oracular " sentences (Saracci & ?? 2010 ?) which thereby give the media and others the opportunity to report quite opposite conclusions from the same study,as was the case with the Interphone study.

We note that countries including France, Germany, Belgium, Austria, Italy, Russia, India and others have moved toward cautionary warnings and some have revised some target exposure levels for new wireless facilities in line with recommendations issued in 2007. Further actions appear now to be warranted, especially in light of the authoritative 2011 IARC cancer classification.

The IARC, and the EEA , may be wrong to suggest there could be a brain tumour risk from the extensive use of mobile phones, and we dearly hope we are wrong. However, it is worth noting that during over 30 years of classifying cancer risks, covering around 900 agents, IARC very rarely downgrades its judgements: in most cases tentative carcinogens become more certain carcinogens as time since first exposures and further research accumulates. Is it not worth gambling that mobile phones will be one of those very rare cases where IARC has over-classified an agent? We think not. The human cost of getting such a gamble wrong would be too great, especially in light of the relatively low cost of reducing exposures significantly.

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SECTION 24

Key Scientific Evidence and Public Health Policy Recommendations

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Table of Contents

I. KEY SCIENTIFIC EVIDENCE

Exposure to electromagnetic fields (EMF) has been linked to a variety of adverse health outcomes. The health endpoints that have been reported to be associated with ELF and/or RF include childhood leukemia, adult brain tumors, childhood brain tumors, genotoxic effects (DNA damage and micronucleation), neurological effects and neurodegenerative disease, immune system disregulation, allergic and inflammatory responses, breast cancer in men and women, miscarriage and some cardiovascular effects.

Effects are not specifically segregated for ELF or RF, since many overlapping exposures occur in daily life; and because this is an artificial division based on frequencies as defined in physics that has little bearing on the biological effects. Both ELF and RF, for example have been shown to cause cells to generate stress proteins, a universal sign of distress in plant, animal and human cells.

The number of people exposed to elevated levels of EMF has been estimated in various studies, and there is general agreement among them. In the United States, few people have chronic or prolonged exposures over 4 mG (0.4 μT) (Kheifets et al, 2005b). Section 20 has information on average residential and occupational ELF levels. The highest exposure category in most all studies is $\geq$ 4 mG ($\geq$ 0.4 μT). Many people have daily exposures to ELF in various ways, some of them up to several hundred milligauss for short periods of time, but relatively few people with the exception of some occupational workers habitually experience ELF exposures greater than 1-2 mG (0.2 – 0.3 μT - App. 20-A).

The exposure of children to EMF has not been studied extensively; in fact, the FCC standards for exposure to radiofrequency radiation are based on the height, weight and stature of a 6-foot tall man, not scaled to children or adults of smaller stature. They do not take into account the unique susceptibility of growing children to exposures (SCENIHR, 2007; Jarosinska and Gee, 2007), nor are there studies of particular relevance to children.

Differences in exposure patterns between infants, children and adults; 2) special susceptibilities of infants and children to the effects of EMF; and 3) interactions between chemical contaminants

and EMF are lacking; as are studies on chronic exposure for both children and adults. There is reason to believe that children may be more susceptible to the effects of EMF exposure since they are growing, their rate of cellular activity and division is more rapid, and they may be more at risk for DNA damage and subsequent cancers. Growth and development of the central nervous system is still occurring well into the teenage years so that neurological changes may be of great importance to normal development, cognition, learning, and behavior. Prenatal exposure to EMF have been identified as possible risk factor for childhood leukemia. Children are largely unable to remove themselves from exposures to harmful substances in their environments. Their exposure is involuntary.

Like second-hand smoke, EMF is a complex mixture, where different frequencies, intensities, durations of exposure(s), modulation, waveform and other factors is known to produce variable effects. Many years of scientific study has produced substantial evidence that EMF may be considered to be both carcinogenic and neurotoxic. The weight of evidence is discussed in this report, including epidemiological evidence and studies on laboratory animals.

Relative risk estimates associated with some of these endpoints are small and the disease is fairly rare (for childhood leukemia, for example), For other diseases, the risk estimates are small but the diseases are common and EMF exposures at levels associated with increased risks are widespread and chronic so the overall public health impacts may be very large.

A. Weight of Evidence Assessment and Criteria for Causality

A weight-of-evidence approach has been used to describe the body of evidence between health endpoints and exposure to electromagnetic fields (ELF and RF).

The number and quality of epidemiological studies, as well as other sources of data on biological plausibility are considered in making scientific and public health policy judgments. Methodological issues that were considered in the review of the epidemiological literature include 1) quality of exposure assessment. 2) sample size of the study, which detects the power to detect an effect, 3) extent to which the analysis or design takes into account potential

confounders or other risk factors, 4) selection bias, 5) the potential for bias in determining exposure. Assessment of the epidemiological literature is consistent with guidelines from Hill (1971), Rothman and Greenland (1998) and the Surgeon General's Reports on Smoking (US DHHS, 2004), and California Air Resources Board (2005). Factors that were considered in reaching conclusions about the weight of evidence overall included strength of the association, consistency of association, temporality, biological plausibility, dose-response and issues with non-linear dose-response, specificity and experimental evidence.

There is a relatively large amount of human epidemiological information with real world exposures, including data from occupational studies. There is less animal data in most cases, except for the genotoxicity studies. Human epidemiological evidence has be given the greatest weight in making judgments about weight-of-evidence, where the results across high quality studies give relatively consistent positive results. Meta-analyses of childhood leukemia, adult leukemia, adult brain tumors, childhood brain tumors, male and female breast cancer and Alzheimer's disease were relied upon in assessing the overall strength of epidemiological study results. Sections 5 – 15 provide analysis of the relevant scientific studies that are key evidence in making public health policy recommendations with respect to exposure to electromagnetic fields (both ELF and RF).

B. Summary of Evidence

1. Childhood Leukemia

Several meta-analyses have been conducted to assess risks of childhood leukemia from exposure to ELF. The results of these studies that combine or pool results of many individual studies (including studies that report both effects and no effects) consistently report increased risks.

Meta-Analysis: Studies of Childhood Leukemia and EMF

Greenland et al., (2000) reported a significantly elevated risk of 1.68 [95% CI 1.23-2.31] based on pooled results from 12 studies using a time-weighted average of exposure greater than 3 mG (0.3 μT). This is a 68% increased risk of childhood leukemia.

Ahlbom et al., (2000) reported a doubling of risk based on a meta-analysis of nine (9) studies. The results reported an elevated risk of 2.0 [95% CI 1.27-3.13] for EMF exposures equal to or greater than 4 mG (0.4 μT) as compared to less than 1 mG (0.1 μT)

Other Relevant Evidence

In 2002, the International Agency for Cancer Research (IARC) designated EMF as a "possible human carcinogen" or Group 2B Carcinogen based on consistent epidemiological evidence. The exposure levels at which increased risks of childhood leukemia are reported in individual studies range from above 1.4 mG or 0.14 μT (Green et al., 1999)for younger children to age six (6) to 4 mG (0.4 μT). Many individual studies with cutpoints of 2 mG or 3 mG (0.2-0.3 μT)) report increased risks. Plausible biological mechanisms exist that may reasonably account for a causal relationship between EMF exposure and childhood leukemia.

Recurrence of Childhood Leukemia and Poorer Survival Rates with Continued EMF Exposure

Foliart reported more than a four-fold (450% increased risk) of adverse outcome (poorer survival rate) for children with acute lymphoblastic leukemia (ALL) who were recovering in EMF environments of 3 mG (0.3 μT) and above (OR 4.5, CI 1.5-13.8). Svendsen reported a poorer survival rate of children with acute lymphoblastic leukemia (ALL) in children exposed to 2 mG (0.2 μT) and above. These children were three times more likely (300% increased risk) to die than children recovering in fields of less than 1 mG (OR 3.0, CI 0.9.8). Children recovering in EMF environments between 1- 2 mG (0.1-0.2 μT) also had poorer survival rates, where the increased risk was 280% (OR 2.8, CI 1.2-6.2).

Higher Lifetime Cancer Risks with Childhood EMF Exposure

Lowenthal (2007) reported that children raised for the first five years in home environments exposed to EMF within 300 meters of a high voltage power line have a five-fold (a 500 percent increased risk of developing some kinds of cancers sometime in later life. For children from newborn to 15 years of age; it is a three-fold risk of developing cancer later in life (Lowenthal et al., 2007). There is suggestive evidence for a link between adult leukemia and EMF exposure.

Attributable Risk

Wartenberg estimates that 8% to 11% of childhood leukemia cases may be related to ELF exposure. This translates into an additional 175 to 240 cases of childhood leukemia based on 2200 US cases per year. The worldwide total of annual childhood leukemias is estimated to be 49,000, giving an estimate of nearly 4000 to 5400 cases per year. Other researchers have estimated higher numbers that could reach to 80% of all cases (Milham, 2001).

2. Childhood Brain Tumors

Childhood Brain Tumors

There is suggestive evidence that other childhood cancers may be related to EMF exposure. The meta-analysis by Wartenberg et al., (1998) reported increased risks for childhood brain tumors. Risks are quite similar whether based on calculated EMF fields (OR = 1.4, 95% CI = 0.8 – 2.3] or based on measured EMF fields (OR = 1.4, 95% CI = 0.8 – 2.4).

3. Adult Brain Tumors

Brain Tumors in Electrical Workers and in Electrical Occupations (Meta-analysis)

A significant excess risk for adult brain tumors in electrical workers and those adults with occupational EMF exposure was reported (Kheifets et al., 1995). This is about the same size risk for lung cancer and second hand smoke (US DHHS, 2006). A total of 29 studies with populations from 12 countries were included in this meta-analysis. The relative risk was reported as 1.16 (CI = 1.08 – 1.24) or a 16% increased risk for all brain tumors. For gliomas, the risk estimate was reported to be 1.39 (1.07 – 1.82) or a 39% increased risk for those in electrical occupations. A second meta-analysis published by Kheifets et al., ((2001) added results of 9 new studies published after 1995. It reported a new pooled estimate (OR = 1.16, 1.08 – 1.01) that showed little change in the risk estimate overall from 1995.

4. Brain Tumors and Acoustic Neuromas in Cell Phone and Cordless Phone Users (Meta-Analysis)

Glioma and Acoustic Neuroma

Hardell et al., (2007) reported in a meta-analysis statistically significant increased risk for glioma with exposure of 10 years or greater in persons using cell phones. Risks were estimated to be 1.2 (0.8 – 1.9) for all use; but when ipsilateral use was assessed (mainly on same side of head) it increased the risk of glioma to 2.0 (1.2 – 3.4) for 10 years and greater use.

For acoustic neuromas, Hardell et al., (2007) reported the increased risk with 10 years or more of exposure to a cell phone at 1.3 (0.6 – 2.8) but this risk increased to 2.4 (1.1 – 5.3) with ipsilateral use (mainly on the same side of the head). There is a consistent pattern of increased risk for brain tumors (glioma) and acoustic neuromas at 10 years and greater exposure to cell phones.

The meta-analysis by Lakhola et al., (2006) reported that brain tumor risk was 1.3 (0.99 – 1.9) for ipsilateral use of a cell phone, but no data was given for exposures at 10 years or greater (all exposures were of shorter duration).

The meta-analysis by Kan et al., (2007) reported "no overall risk" but found elevated risk of brain tumors (RR = 1.25, CI 1.01 – 1.54) $\geq$ 10 years, reinforcing the findings of other pooled

estimates of risk. No estimates of increased risk with ipsilateral use were provided, which would have likely increased reported risks.

5. Neurodegenerative Diseases

Alzheimer's Disease and ALS

Evidence for a relationship between exposure and the neurodegenerative diseases, Alzheimer's and amyotrophic lateral sclerosis (ALS), is strong and relatively consistent. While not every publication shows a statistically significant relationship between exposure and disease, ORs of 2.3 (95% CI = 1.0-5.1 in Qio et al., 2004), of 2.3 (95% CI = 1.6-3.3 in Feychting et al., 2003) and of 4.0 (95% CI = 1.4-11.7 in Hakansson et al., 2003) for Alzheimer's Disease.

Hakansson et al., report more than a doubling of risk for ALS 2.2 (95% CI = 1.0-4.7).

Savitz et al., (1998) reports more than a tripling of risk for ALS (3.1, CI = 1.0 – 9.8).

6. Breast Cancer (Men and Women)

A meta-analysis by Erren (2001) on EMF and breast cancer reported pooled relative risks based on studies of both men and women. A total of 38 publications were reviewed; there were 23 studies on men; 25 studies on women; and 10 studies on both men and women. The pooled relative risk for women exposed to EMF was 1.12 (CI 1.09 – 1.15) or a 12% increased risk, Erren observed that variations between the contributing results are not easily attributable to chance (P = 0.0365). For men and breast cancer, he reported a fairly homogeneous increased risk (a pooled relative risk of 1.37 [CI 1.11 – 1.71]).

This analysis is well conducted. The results were stratified according to measured or assumed intensity of exposure to EMF; and the estimate of risk for the most heavily exposed group was extracted. Independent estimates of RRs were grouped according to gender, type of study (case-control and cohort), country where the study was conducted and method used to assess exposure. Pooled estimates of RRs and their 95% confidence intervals (CI) referring to various combinations of these factors were calculated according to appropriate statistical methods (Greenland, 1987). Misclassification possibilities were thoroughly assessed, and whether the results were sole endpoints or there were multiple endpoints in each study did not affect the RRs.

Erren qualifies his findings by discussing that latencies for cancers can be 20 to 30 years, Further, he notes that studies of total EMF exposures from both home, travel and workplace are rarely available, and these EMF sources are ubiquitous. Both could result in underestimation of risks. Another way in which risks might be masked is by variations in age of study participants. Forssen and colleagues (2000) reported no increased RRs for breast cancer in women of all ages

when they combined residential and occupational EMF exposures (RR = 0.9, CI 0.3 – 2.7). However, when risks for the women younger than 50 years of age were separated out and calculated, the RR increased to 7.3 (CI 0.7 – 78.3) although with wide confidence intervals based on only four cases. Erren notes

"When possibly relevant exposures to EMF in the whole environment are assessed only partially, errors in the categorization of exposure status are likely to occur. If such misclassification is random and thus similar in subrgroups being compared (nondifferential), then the error will tend to introduce bias towards the null. Substantial random misclassification of exposures would then tend to generate spurious reports of 'little or no effect'. Note for example that estimates of smoking-associated lung cancer risks in the early 1950's could have been seriously distorted if exposure assessment had not considered smoking either at work or at home."

"Collectively, the data are consistent with the idea that exposures to EMF, as defined, are associated with some increase in breast cancer risks, albeit the excess risk is small." Erren (2001)

7. Combined Effects of Toxic Agents and ELF

ELF and Toxic Chemical Exposures

There is also the issue of what weight to give the evidence for synergistic effects of toxic chemical exposure and EMF exposure. Juuilainen et al., (2006) reported that the combined effects of toxic agents and ELF magnetic fields together enhances damage as compared to the toxic exposure alone. In a meta-analysis of 65 studies; overall results showed 91% of the *in vivo* studies and 68% of the *in vitro* studies had worse outcomes (were positive for changes indicating synergistic damage) with ELF exposure in combination with toxic agents. The percentage of the 65 studies with positive effects was highest when the EMF exposure preceded the other exposure. The radical pair mechanism (oxidative damage due to free radicals) is cited as a good candidate to explain these results. Reconsideration of exposure limits for ELF is warranted based on this evidence.

II. FALLACIES AND ANSWERS IN THE DEBATE OVER EMF EVIDENCE

There are several arguments (false, in our view) that have been presented by those who minimize the strength of the relationship between exposure to both 50-60Hz ELF and RF EMFs. These are as follows:

A. "Only a small number of children are affected."

This argument is not correct because we do not know precisely how many children are affected. In 1988 Carpenter and Ahlbom attempted to answer this question based on the results of the New York State Powerlines Project and the results of the study of Savitz et al. (1988), and concluded that if the magnetic fields homes in the US were similar to those in Denver, Colorado fully 10 to 15% of US childhood leukemia (about 1,000 cases) could be associated with residential magnetic field exposure. They then concluded that exposure to magnetic fields from non-residential sources (particularly appliances) must be at least equal in magnitude, and that if so these two sources of exposure would account for 20-35% of childhood leukemia.

There have been several meta-analyses of the childhood leukemia data (Wartenberg, 1998; Greenland et al., 2000; Ahlbom et al., 2000). All have concluded that there is a significant association between residential exposure to magnetic fields and elevated risk of leukemia in children. Greenland et al. (2000) performed a meta-analysis of 15 studies of magnetic field or wire code investigations of childhood leukemia, and calculated the attributable fraction of cases of childhood leukemia from residential magnetic field exposure in the US was 3%. Ahlbom et al. (2000) conducted a different meta-analysis that concluded there was a significant 2-fold elevation of risk at exposure levels of 4 mG (0.4 μT) or greater. Kheifets et al. (2006) attempted to calculate the attributable fraction of worldwide childhood leukemia due to EMFs, based on the meta-analyses of Ahlbom et al. (2000) and Greenland et al., (2000). They concluded that the attributable fraction of leukemia was between <1% to 4%. The recent WHO Environmental Health Criteria ELF Monograph #238 (2007) states "(A)ssuming that the association is causal, the number of cases of childhood leukaemia worldwide that might be attributable to exposure can be estimated to range from 100 to 2,400 cases per year. However this represents 0.2 to 4.9% of the total annual incidence of leukaemia cases, estimated to be 49,000 worldwide in 2000. Thus, in a global context, the impact on public health, if any, would be limited and uncertain."

These reports are important, in that they show consistency in there being a clearly elevated risk of leukemia in children with EMF exposure from power line fields in homes. These meta-analyses lead to the conclusion, reflected in the WHO report, that there is an association between childhood cancer and exposure to elevated magnetic fields in homes. We strongly disagree, however, with the overall conclusion that these calculations indicate that the fraction of childhood leukemia attributable to EMFs is so small as to not have serious public health implications.

There are several reasons why the WHO ELF Environmental Health Criteria Monograph conclusion is not justified. These studies all considered either only measured magnetic fields in homes or wire codes from power lines, ignoring exposure from appliances, wireless devices and all exposures outside of the home. Thus these metrics do not come close to accounting for any individual's cumulative exposure to EMFs. If residential magnetic fields cause cancer, then those from other sources will add to the risk. The failure to measure total EMF exposure would tend to obscure the relationship and lead to

gross underestimation of the true relationship between exposure and disease. While the evidence for a relationship between exposure and childhood leukemia may be considered to be definitive at exposure levels of 3 or 4 mG (0.3 or 0.4 μT) or higher; there is evidence from some (but not all) of the other studies for an elevated risk at levels not greater than 2 mG (0.2 μT) (Savitz et al., 1988; Green, 1999). There is absolutely no evidence that exposures at lower levels are "safe", since persons with these exposures are usually the "control" group. Therefore this WHO statement fails to acknowledge the true magnitude of the problem, even when considering only childhood leukemia. The global attributable risk of childhood leukemia as a result of exposure to EMFs must be significantly greater than that calculated from consideration of only residential 50/60 Hz magnetic fields in studies where there is no unexposed control.

As detailed in other chapters in this report (Chapter 10), there is some evidence for a relationship between EMF exposure and brain cancers in children. We have almost no understanding of the mechanisms behind the development of brain cancers, and any cancer in a child is a tragedy. While evidence for a relationship between EMF exposure and childhood brain cancer is not as strong as for leukemia, it is of concern and deserves more study. Of even greater concern, given the clear evidence for elevated risk of childhood leukemia upon exposure to 50/60 Hz EMFs, is the relative lack of a comparable body of information on the effects of radiofrequency EMFs on the health of children. A recent study of South Korean children (1,928 with leukemia, 956 with brain cancer and 3,082 controls) living near to AM radio transmitters reports an OR of 2.15 (95% CI = 1.19-2.11) for risk of leukemia in children living within 2 km of the nearest AM transmitter as compared to those living more than 20 km from it (Ha et al., 2007). No relation was found for brain cancer. This study is consistent with the hypothesis that radiofrequency EMFs have similar effects to 50/60 Hz EMFs, but more study is needed. Since radiofrequency EMFs have higher energy than do power line frequencies, one might expect that they would be even more likely to cause disease. The enormous and very recent increase in use of cell phones by children is particularly worrisome. However there is little information at present on the long-term consequences of cell phone use, especially by children.

B. "There is insufficient evidence that adult diseases are secondary to EMF exposure."

It is correct that the level of evidence definitively proving an association between exposure to EMFs and various adult diseases is less strong that the relationship with childhood leukemia. However there are multiple studies which show statistically significant relationships between occupational exposure and leukemia in adults (see Chapter 11), in spite of major limitations in the exposure assessment. A very recent study by Lowenthal et al. (2007) investigated leukemia in adults in relation to residence near to high-voltage power lines. While they found elevated risk in all adults living near to the high voltage power lines, they found an OR of 3.23 (95% CI = 1.26-8.29) for individuals who spent the first 15 years of life within 300 m of the power line. This study provides support for two important conclusions: adult leukemia is also associated with

EMF exposure, and exposure during childhood increases risk of adult disease. Thus protecting children from exposure should be a priority.

The evidence for a relationship between exposure and breast cancer is relatively strong in men (Erren, 2001), and some (by no means all) studies show female breast cancer also to be elevated with increased exposure (see Chapter 12). Brain tumors and acoustic neuromas are more common in exposed persons (see Chapter 10). There is less published evidence on other cancers, but Charles et al. (2003) report that workers in the highest 10% category for EMF exposure were twice as likely to die of prostate cancer as those exposed at lower levels (OR 2.02, 95% CI = 1.34-3.04). Villeneuve et al. (2000) report statistically significant elevations of non-Hodgkin's lymphoma in electric utility workers in relation to EMF exposure, while Tynes et al. (2003) report elevated rates of malignant melanoma in persons living near to high voltage power lines. While these observations need replication, they suggest a relationship between exposure and cancer in adults beyond leukemia.

Evidence for a relationship between exposure and the neurodegenerative diseases, Alzheimer's and amyotrophic lateral sclerosis (ALS), is strong and relatively consistent (see Chapter 12). While not every publication shows a statistically significant relationship between exposure and disease, ORs of 2.3 (95% CI = 1.0-5.1 in Qio et al., 2004), of 2.3 (95% CI = 1.6-3.3 in Feychting et al., 2003) and of 4.0 (95% CI = 1.4-11.7 in Hakansson et al., 2003) for Alzheimer's Disease, and of 3.1 (95% CI = 1.0-9.8 in Savitz et al., 1998) and 2.2 (95% CI = 1.0-4.7 in Hakansson et al., 2003) for ALS cannot be simply ignored.

In total the scientific evidence for adult disease associated with EMF exposure, given all of the difficulties in exposure assessment, is sufficiently strong that preventive steps are appropriate, even if not all reports have shown exactly the same positive relationship. While there are many possible sources of false positive results in epidemiological studies, there are even more possible reasons for false negative results, depending on sample size, exposure assessment and a variety of other confounders. It is inappropriate to discount the positive studies just because not every investigation shows a positive result. While further research is needed, with better exposure assessment and control of confounders; the evidence for a relationship between EMF exposure and adult cancers and neurodegenerative diseases is sufficiently strong at present to merit preventive actions to reduce EMF exposure.

C. "The risk is low."

This argument is incorrect because at present it is not possible to determine the magnitude of the risk. Clearly as far as EMFs are concerned there is no unexposed population. Therefore one can only compare groups with different levels of exposure. We can perhaps say with confidence that the elevated risk of leukemia from residential exposure of children to magnetic fields is "low" (meaning ORs in the range of 2-4), but this does not consider the child's exposure to appliances, exposure in automobiles and at

daycare or school, exposures in playgrounds and at all of the other places that a child spends time. Even if the risk to one individual is low, the societal impact when everyone is exposed may be very significant.

In addition the exposure assessment is grossly inadequate, even in the best of studies. Most reports deal only with either characterization of the fields within residences or with job titles in occupational settings. Some studies attempt to quantitate other sources of exposure, such as frequency of cell phone usage or use of other appliances, but these studies almost always do not consider residential exposure from power lines. In no investigation has it been possible to follow the exposures of a large number of people over a number of years with accurate monitoring of total exposure to EMFs. This would of course be almost impossible to do for the very good reason that as a person moves through his or her environment the exposures vary from place to place and from moment to moment. However to truly and objectively determine the risk of exposure to EMFs it is essential to consider residential, occupational (or school) and recreational exposures to the full range of the electromagnetic spectrum, including appliances and wireless devices. This has not been accomplished in any study, and without such information it is not possible to determine the overall magnitude of the risk. It is possible, indeed likely, that upon consideration of both childhood and adult diseases that the risk is not low.

D. "There is no animal evidence".

It is correct that there is no adequate animal model system that reproducibly demonstrates the development of cancer in response to exposure to EMFs at the various frequencies of concern. McCann et al. (1997) reviewed the animal studies, and while they found most to be negative there were several that showed suggestive positive results. They also clearly identified issues that need to be improved in further animal carcinogenesis investigations. However Kheifets et al. (2005a) in a policy review noted that "even consistent negative toxicological data cannot completely overcome consistent epidemiological studies. First, a good animal model for childhood leukemia has been lacking. Second, particularly for ELF, the complex exposures that humans encounter on a daily basis and a lack of understanding of the biologically relevant exposure calls into question the relevance of exposures applied in toxicology. Another limitation of toxicologic studies is that animals cannot be exposed to fields that are orders of magnitude more powerful than those encountered by humans, decreasing their power to detect small risks." Further, they conclude that "(A)lthough the body of evidence is always considered as a whole, based on the weight of evidence approach and incorporating different lines of scientific enquiry, epidemiologic evidence, as most relevant, is given the greatest weight."

One positive animal study is that by Rapacholi et al. (1997), who demonstrated that lymphoma-prone transgenic mice developed significantly more lymphoma after exposure to 900 MHz fields (lymphoma being the animal equivalent of human leukemia) than did unexposed animals. More striking is the report from Denver, Colorado using the wire-code characterization originally developed by Wertheimer and Leeper (1979) showing

that pet dogs living in homes characterized as having high or very high wire codes, as compared to those with low or very low wire codes or buried power lines, showed a OR of 1.8 (95% CI = 0.9-3.4) for development of lymphoma after adjustment for potential confounders, whereas dogs that lived in homes with very high wire codes had an OR of 6.8 (95% CI = 1.6-28.5) (Reif et al., 1995). This study is impressive because the exposure of the dogs reflects the environment in which exposure has been associated with elevated risk of human cancer in two independent investigations (Wertheimer and Leeper, 1979: Savitz et al., 1988).

It is curious that in many legal situations the courts are reluctant to accept only evidence that substance X causes cancer in animals without corresponding evidence in humans. In the case of EMFs we have strong evidence that EMFs cause cancer in human, but much less evidence from animal models. The US Supreme Court, in the case of Daubert vs. Merrell Dow Pharmaceuticals, effectively ruled that animal studies were not relevant to human health, and that the only admissible evidence must be from human epidemiological studies! While this is certainly not a justifiable conclusion, the situation with regards to EMF health effects is that we have strong evidence for human cancer from epidemiological studies, but do not have good evidence for cancer in experimental animals. But it is humans that we should be concerned about, not the laboratory rats.

E. "We do not know a mechanism."

We do not know the mechanism of cancer in general, although we know a lot about cancer. It came as a major surprise to most scientists when Lichtenstein et al., (2000) reported that genetic factors play a minor role in causing most types of cancer, since it was commonly assumed that genetics was the major cause. However Lichtenstein et al. concluded from their study of identical twins that environmental factors were the initiating event in the great majority of cancers. This does not, of course, mean that genetic susceptibility to environmental contaminants is unimportant, but only that genetic factors alone do not result in cancer. We know mechanisms of action for some carcinogenic substances, but for most cancers we know neither the environmental trigger nor the mechanism of action. So there is no reason to negate the evidence that EMFs cause cancer just because we do not know a single mechanism to explain it's mode of action.

We do not know the mechanism or cause for development of Alzheimer's Disease or ALS. We do know that both are more common in individuals in certain occupations, and that exposure to certain metals appears to be associated with increased risk (Kamel et al., 2002; Shcherbatykh and Carpenter, 2007). In the case of Alzheimer's Disease there are abnormalities of amyloid β and tau protein (Goedert and Spillantini, 2006), but very limited understanding of why or how they form. Neither the association with metals nor the presence of abnormal proteins constitutes a mechanism for cause of disease. So rather than discounting the relationship between EMF exposure and neurodegenerative diseases we should be using this information as a tool to better understand the etiology of these diseases.

There is clear evidence from animal and cell culture studies that ELF and RFR have biological effects. Furthermore, these effects occur at intensities commonly experienced by humans. We know a number of ways in which EMFs alter cell physiology and function, as detailed in various chapters in this report. EMFs affect gene transcription (Chapter 5 and 6), cause the synthesis of stress proteins (Chapter 7) and cause breakage of DNA, probably through generation of reactive oxygen species (Chapter 6 and 9 - Lai and Singh, 2004). Any one of these actions might be responsible for the carcinogenic and neurodegenerative actions of EMFs. However, as with many environmental agents, it would be a mistake to assume that there is only one target or mechanism of action. It is unlikely, for example, that the effects on the nervous system and behavior are secondary to exactly the same cellular targets and actions that lead to cancer. It is likely that there are multiple mechanisms of action leading to disease. But the lack of complete understanding of basic mechanisms does not alter the importance of the relationships.

F. Vested Interests: How They Shape the Public Health Debate

There is no question but that global implementation of the safety standards proposed in this report has the potential to not only be very expensive but also could be disruptive of life and economy as we know it if implemented abruptly and without careful planning. Action must be a balance of risk to cost to benefit. However, "deny and deploy" strategies by industry should not be rewarded in future risk assessment calculations. For example, if significant economic investments in the roll-out of risky technologies persist beyond the time that there is reasonable suspicion of risk available to all who look, then such costs should not be borne by ratepayers (in the case of new powerlines) or by compensating industry for bad corporate choices. Such investments in the deployment of new sources of exposure for ELF and RF should not count toward the balance sheet when regulatory agencies perform risk assessments. Mistakes may be made, but industry should make mid-course corrections to inform and protect the public, rather than deny effects pending "proof". Whether the costs of remedial action are worth the societal benefits is a formula that should reward precautionary behavior. Prudent corporate policies should be expected to address and avoid future risks and liabilities. Otherwise, there is no market incentive to produce safe (and safer) products.

The deployment of new technologies is running ahead of any reasonable estimation of possible health impacts and estimates of probabilities, let alone a solid assessment of risk. However what has been missing with regard to EMF has been an acknowledgement of the risk that is demonstrated by the scientific studies. As discussed in earlier sections, in this case there is clear evidence of risk, although the magnitude of the risk is uncertain, and the magnitude of doing nothing on the health effects cost to society is similarly uncertain. This situation is very similar to our history of dealing with the hazards of smoking decades ago, where the power of the industry to influence governments and even conflicts of interest within the public health community delayed action for more than a generation, with consequent loss of life and enormous extra health care costs to society.

Just because a problem is difficult to solve is not a reason to deny that a problem exists. In fact solutions to difficult issues usually can't be expected until the issues are known and creative thinking is brought to bear to find a solution.

The most contentious issue regarding public and occupational exposures to ELF and RF involves the resolute adherence to existing ICNIRP and IEEE standards by many countries, in the face of growing scientific evidence of health risks at far lower levels. Furthermore there is widespread belief that governments are ignoring this evidence. There are two obvious factors that work against governments taking action to set exposure guidelines based on current scientific evidence of risk. These are: 1) contemporary societies are very dependent upon electricity usage and RF communications, and anything that restricts current and future usage potentially has serious economic consequences and 2) the electric power and communications industries have enormous political clout and even provide support for a significant fraction of what research is done on EMF. This results in legislation that protects the status quo and scientific publications whose conclusions are not always based on only the observations of the research. It hinders wise public health policy actions and implementation of prevention strategies because of the huge financial investments already made in these technologies.

In 1989, in an editorial for Science Magazine, Philip H. Abelson called for more research into low-frequency electromagnetic fields. At that time, he confirmed that a US Office of Technology Assessment (OTA) study had determined that *"(o)verall, the evidence is too weak to allow firm conclusions either way*" but a policy of prudent avoidance strategy was suggested, Abelson defined this as "*to systematically look for strategies which can keep people out of 60 Hz fields*". Both policy actions were developed in the midst of scientific uncertainty, but rising concern for possible health impacts to the public. At that time, with high level of unknowns, the appropriate level of policy action was prudent avoidance or precautionary action. Nearly two decades later, the level of action warranted is higher – based on many new scientific publications confirming risks may exist – and justifying prevention or preventative action.

III. EMF EXPOSURE AND PRUDENT PUBLIC HEALTH PLANNING

• *The scientific evidence is sufficient to warrant regulatory action for ELF; and it is substantial enough to warrant preventative actions for RF.*

• *The standard of evidence for judging the emerging scientific evidence necessary to take action should be proportionate to the impacts on health and well-being*

• *The exposures are widespread.*

• *Widely accepted standards for judging the science are used in this assessment.*

Public exposure to electromagnetic radiation (power-line frequencies, radiofrequency and microwave) is growing exponentially worldwide. There is a rapid increase in electrification in developing countries, even in rural areas. Most members of society now have and use cordless phones, cellular phones, and pagers. In addition, most populations are also exposed to antennas in communities designed to transmit wireless RF signals. Some developing countries have even given up running land lines because of expense and the easy access to cell phones. Long-term and cumulative exposure to such massively increased RF has no precedent in human history. Furthermore, the most pronounced change is for children, who now routinely spend hours each day on the cell phone. Everyone is exposed to a greater or lesser extent. No one can avoid exposure, since even if they live on a mountain-top without electricity there will likely be exposure to communication-frequency RF exposure. Vulnerable populations (pregnant women, very young children, elderly persons, the poor) are exposed to the same degree as the general population. Therefore it is imperative to consider ways in which to evaluate risk and reduce exposure. Good public health policy requires preventative action proportionate to the potential risk of harm and the public health consequence of taking no action.

IV. RECOMMENDED ACTIONS

A. Defining new exposure standards for ELF

This chapter concludes that new ELF limits are warranted based on a public health analysis of the overall existing scientific evidence. The public health view is that new ELF limits are needed now. They should reflect environmental levels of ELF that have been demonstrated to increase risk for childhood leukemia, and possibly other cancers and neurological diseases. ELF limits should be set below those exposure levels that have been linked in childhood leukemia studies to increased risk of disease, plus an additional safety factor. It is no longer acceptable to build new power lines and electrical facilities that place people in ELF environments that have been determined to be risky. These levels are in the 2 to 4 milligauss* (mG) range (0.2 – 0.4 μT), not in the 10s of mG or 100s of mG. The existing ICNIRP limit is 1000 mG (100 μT) and 904 mG (90.4 μT) in the US for ELF is outdated and based on faulty assumptions. These limits are can no longer be said to be protective of public health and they should be replaced. A safety buffer or safety factor should also be applied to a new, biologically-based ELF limit, and the conventional approach is to add a safety factor lower than the risk level.

While new ELF limits are being developed and implemented, a reasonable approach would be a 1 mG (0.1 μT) planning limit for habitable space adjacent to all new or upgraded power lines and a 2 mG (0.2 μT) limit for all other new construction. It is also recommended for that a 1 mG (0.1 μT) limit be established for existing habitable space for children and/or women who are pregnant (because of the possible link between childhood leukemia and *in utero* exposure to ELF). This recommendation is based on the assumption that a higher burden of protection is required for children who cannot protect themselves, and who are at risk for childhood leukemia at rates that are traditionally high enough to trigger regulatory action. This situation in particular warrants extending the 1 mG (0.1 μT) limit to existing occupied space. "Establish" in this case probably means formal public advisories from relevant health agencies. While it is not realistic to reconstruct all existing electrical distribution systems, in the short term; steps to reduce exposure from these existing systems need to be initiated, especially in places where children spend time, and should be encouraged. These limits should reflect the exposures that are commonly associated with increased risk of child hood leukemia (in the 2 to 5 mG (0.2 to 0.5 μT) range for all children, and over 1.4 mG (0.14 μT) for children age 6 and younger). Nearly all of the occupational studies for adult cancers and neurological diseases report their highest exposure category is

4 mG (0.4 μT) and above, so that new ELF limits should target the exposure ranges of interest, and not necessarily higher ranges.

Avoiding chronic ELF exposure in schools, homes and the workplace above levels associated with increased risk of disease will also avoid most of the possible bioactive parameters of ELF discussed in the relevant literature.

It is not prudent public health policy to wait any longer to adopt new public safety limits for ELF. These limits should reflect the exposures that are commonly associated with increased risk of childhood leukemia (in the 2 to 5 mG (0.2-0.5 μT) range for all children, and over 1.4 mG (0.14 μT) for children age 6 and younger). Avoiding chronic ELF exposure in schools, homes and the workplace above levels associated with increased risk of disease will also avoid most of the possible bioactive parameters of ELF discussed in the relevant literature.

B. Defining preventative actions for reduction in RF exposures

Given the scientific evidence at hand, the rapid deployment of new wireless technologies that chronically expose people to pulsed RF at levels reported to cause bioeffects, whicih in turn, could reasonably be presumed to lead to serious health impacts, is a public health concern. A public health action level that implements preventative action now is warranted, based on the collective evidence. There is suggestive to strongly suggestive evidence that RF exposures may cause changes in cell membrane function, cell communication, metabolism, activation of proto-oncogenes and can trigger the production of stress proteins at exposure levels below current regulatory limits. Resulting effects can include DNA breaks and chromosome aberrations, cell death including death of brain neurons, increased free radical production, activation of the endogenous opioid system, cell stress and premature aging, changes in brain function including memory loss, retarded learning, performance impairment in children, headaches and fatigue, sleep disorders, neurodegenerative conditions, reduction in melatonin secretion and cancers (Chapters 5, 6, 7, 8, 9, 10, and 12).

As early as 2000, some experts in bioelectromagnetics promoted a 0.1 μW/cm2 limit (which is 0.614 Volts per meter) for ambient outdoor exposure to pulsed RF, so generally in cities, the public would have adequate protection against involuntary exposure to pulsed radiofrequency (e.g., from cell towers, and other wireless technologies). The Salzburg Resolution of 2000 set a target of 0.1 μW/cm2 (or 0.614 V/m) for public exposure to pulsed radiofrequency. Since then, there are many credible anecdotal reports of unwellness and illness in the vicinity of wireless transmitters (wireless voice and data communication antennas) at lower levels. Effects include sleep disruption, impairment of memory and concentration, fatigue, headache, skin disorders, visual symptoms (floaters), nausea, loss of appetite, tinnitus, and cardiac problems (racing heartbeat), There are some credible articles from researchers reporting that cell tower -level RF exposures (estimated to be between 0.01 and 0.5 μW/cm2) produce ill-effects in populations living up to several hundred meters from wireless antenna sites,

This information now argues for thresholds or guidelines that are substantially below current FCC and ICNIPR standards for whole body exposure. Uncertainty about how low such standards might have to go to be prudent from a public health standpoint should not prevent reasonable efforts to respond to the information at hand. No lower limit for bioeffects and adverse health effects from RF has been established, so the possible health risks of wireless WLAN and WI-FI systems, for example, will require further research and no assertion of safety at any level of wireless exposure (chronic exposure) can be made at this time. The lower limit for reported human health effects has dropped 100-fold below the safety standard (for mobile phones and PDAs); 1000- to 10,000-fold for other wireless (cell towers at distance; WI-FI and WLAN devices). The entire basis for safety standards is called into question, and it is not unreasonable to question the safety of RF at any level.

A cautionary target level for pulsed RF exposures for ambient wireless that could be applied to RF sources from cell tower antennas, WI-FI, WI-MAX and other similar sources is proposed. The recommended cautionary target level is 0.1 microwatts per centimeter squared (μW/cm2)** (or 0.614 Volts per meter or V/m)** for pulsed RF where these exposures affect the general public; this advisory is proportionate to the evidence and in accord with prudent public health policy. A precautionary limit of 0.1 μW/cm2 should be adopted for outdoor, cumulative RF exposure. This reflects the current RF science and prudent public health response that would reasonably be set for pulsed RF (ambient) exposures where

people live, work and go to school. This level of RF is experienced as whole-body exposure, and can be a chronic exposure where there is wireless coverage present for voice and data transmission for cell phones, pagers and PDAs and other sources of radiofrequency radiation. An outdoor precautionary limit of 0.1 μW/cm2 would mean an even lower exposure level inside buildings, perhaps as low as 0.01 μW/cm2. Some studies and many anecdotal reports on ill health have been reported at lower levels than this; however, for the present time, it could prevent some of the most disproportionate burdens placed on the public nearest to such installations. Although this RF target level does not preclude further rollout of WI-FI technologies, we also recommend that wired alternatives to WI-FI be implemented, particularly in schools and libraries so that children are not subjected to elevated RF levels until more is understood about possible health impacts. This recommendation should be seen as an interim precautionary limit that is intended to guide preventative actions; and more conservative limits may be needed in the future.

Broadcast facilities that chronically expose nearby residents to elevated RF levels from AM, FM and television antenna transmission are also of public health concern given the potential for very high RF exposures near these facilities (antenna farms). RF levels can be in the 10s to several 100's of μW/cm2 in residential areas within half a mile of some broadcast sites (for example, Lookout Mountain, Colorado and Awbrey Butte, Bend, Oregon). Like wireless communication facilities, RF emissions from broadcast facilities that are located in, or expose residential populations and schools to elevated levels of RF will very likely need to be re-evaluated for safety.

For emissions from wireless devices (cell phones, personal digital assistant or PDA devices, etc) there is enough evidence for increased risk of brain tumors and acoustic neuromas now to warrant intervention with respect to their use. Redesign of cell phones and PDAs could prevent direct head and eye exposure, for example, by designing new units so that they work only with a wired headset or on speakerphone mode.

These effects can reasonably be presumed to result in adverse health effects and disease with chronic and uncontrolled exposures, and children may be particularly vulnerable. The young are also largely unable to remove themselves from such environments. Second-hand radiation, like second-hand smoke is an issue of public health concern based on the evidence at hand.

V. CONCLUSIONS

• We cannot afford 'business as usual" any longer. It is time that planning for new power lines and for new homes, schools and other habitable spaces around them is done with routine provision for low-ELF environments . The business-as-usual deployment of new wireless technologies is likely to be risky and harder to change if society does not make some educated decisions about limits soon. Research must continue to define what levels of RF related to new wireless technologies are acceptable; but more research should not prevent or delay substantive changes today that might save money, lives and societal disruption tomorrow.

• New regulatory limits for ELF based on biologically relevant levels of ELF are warranted. ELF limits should be set below those exposure levels that have been linked in childhood leukemia studies to increased risk of disease, plus an additional safety factor. It is no longer acceptable to build new power lines and electrical facilities that place people in ELF environments that have been determined to be risky (at levels generally at 2 mG (0.2 μT) and above).

• While new ELF limits are being developed and implemented, a reasonable approach would be a 1 mG (0.1 μT) planning limit for habitable space adjacent to all new or upgraded power lines and a 2 mG (0.2 μT) limit for all other new construction, It is also recommended for that a 1 mG (0.1 μT) limit be established for existing habitable space for children and/or women who are pregnant . This recommendation is based on the assumption that a higher burden of protection is required for children who cannot protect themselves, and who are at risk for childhood leukemia at rates that are traditionally high enough to trigger regulatory action. This situation in particular warrants extending the 1 mG (0.1 μT) limit to existing occupied space. "Establish" in this case probably means formal public advisories from relevant health agencies.

• While it is not realistic to reconstruct all existing electrical distributions systems, in the short term; steps to reduce exposure from these existing systems need to be initiated, especially in places where children spend time, and should be encouraged.

• A precautionary limit of 0.1 (μW/cm2 (which is also 0.614 Volts per meter) should be adopted for outdoor, cumulative RF exposure. This reflects the current RF science and prudent public health response that would reasonably be set for pulsed RF (ambient) exposures where people live, work and go to school. This level of RF is experienced as whole-body exposure, and can be a chronic exposure where there is wireless coverage present for voice and data transmission for cell phones, pagers and PDAs and other sources of radiofrequency radiation. Some studies and many anecdotal reports on ill health have been reported at lower levels than this; however, for the present time, it could prevent some of the most disproportionate burdens placed on the public nearest to such installations. Although this RF target level does not preclude further rollout of WI-FI technologies, we also recommend that wired alternatives to WI-FI be implemented, particularly in schools and libraries so that children are not subjected to elevated RF levels until more is understood about possible health impacts. This recommendation should be seen as an interim precautionary limit that is intended to guide preventative actions; and more conservative limits may be needed in the future.

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SECTION 24

Key Scientific Evidence and Public Health Policy Recommendations

(Supplement 2012)

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I. INTRODUCTION

In public health and environmental policy-making, asking the right questions is a highly evolved art form. It is necessary to periodically look for '*not-so-early-now warnings'* from new science and medical information. At some point it becomes '*old news'* in the real-world process of commercializing new technologies* and is ignored. Precious time is lost if the '*evidence curve'* does not come quickly enough to '*change the rollout curve*' and result in early enough interventions. EMF may be a highly preventable source of disease but not without early enough translation of the science into action. The time for arguing whether EMF health effects exist is over. We know they exist and that they result in human disease.

Asking the right questions and looking for proportionate responses necessarily involves make mid-course corrections guided by new evidence. This is particularly true when the consequences of doing nothing are too great to ignore – because they will affect billions of people in societies around the world. "*While there are many unanswered questions, the cost of doing nothing will result in an increasing number of people, many of them young, developing cancer*." (Carpenter, 2010).

What questions should be asked now, to move forward on the body of evidence? How much evidence do we need to act? Do we have enough? What standard of evidence should be used to judge (purely scientific vs precautionary public health). What is a relevant biological 'dose'? How long does a biological effect last? Are we accounting for differences among individuals or different types of cells?

Which of the studies are truly measuring chronic exposures (is a one-month or a one-year study really revealing chronic effects; if mid-length studies show no effect, does this tell us anything useful)? Why is it still considered reasonable to base safety standards on time-averaged radiofrequency exposures when the technologies today use pulsed RFR?

*Electronics, the internet, cellular telecommunications, wireless medical technologies, and wireless sensors for energy conservation, electric utilities management, transportation, education, banking and national security.

For example, the collective behavior of neurons is established through synchrony. "*Individual neurons have a time window of tens of milliseconds range for single neurons, but oscillatory coalitions of neurons can expand the effect window of synchronization from hundreds of milliseconds to many seconds"* (Buzsaki, 2006). This means the time span a bioeffect can last long enough to overlap with the next environmental provocation (pulsed RFR in this case) so that repetitive exposures may induce an unending cascade of neurological firing that eventually disrupts normal homeostasis and causes chronically abnormal function in cooperative assemblies of cells like neurons. RFR is bioactive and already classified as a Possible Human Carcinogen but the relevant RFR bursts are camouflaged and their relevant metrics are diluted away by time averaging. Why is it reasonable to use safety standards that were developed to guard against induced currents in tissue (ELF-EMF) or that heat or burn tissue (RFR)?

Briefly stated, here is what we knew in 2007.

- Bioeffects and adverse health effects of chronic exposure to low-intensity (non-thermal) non-ionizing radiation are established.
- Existing FCC and ICNIRP public safety limits are not sufficiently protective of public health.
- The World Health Organization has classified ELF-EMF as a Group 2B Possible Human Carcinogen (2001).
- New, biologically-based public exposure standards are critically needed.
- It is not in the public interest to wait.

Here is what we know in 2012. There is more evidence, over a broader range of studies. The levels of biological responses are extraordinarily low (down to the nanowatt and picowatt power density level).

New studies address fertility and reproduction, fetal and neonatal effects, cognitive and behavioral problems in children and neurological damage. There are more mobile phone base station studies with longer testing periods, much more information on genetic damage and confirmation of increased risk of brain cancers from not one or two

studies, but from many studies and many authors including the World Health Organization's massive 13-country INTERPHONE STUDY (Interphone Study Group, 2010).

There are many studies reporting effects of cell phone radiation (even on standby-mode), wireless laptop exposure, cell phone use by mothers resulting in altered fetal brain development in the offspring, and more evidence that the blood-brain barrier and memory are at risk from cell phone use. There is evidence from human and animal studies that key areas of the brain are negatively affected by RFR at legal levels.

There is better understanding of the important physical and biological factors that make ELF-EMF and RFR potent disruptors of living tissues and basic metabolic processes. More and more, EMF devices are being used for medical treatments in cancer, bone and wound healing and re-tuning the nervous system. Increased depth of evidence in many threads is presented in this report by well-regarded scientists and researchers from around the world. The number of good studies has grown. The exposure levels causing effects are documented to be much lower than in the past. The epidemiological evidence is now showing risks for a variety of adverse health outcomes. All this should be taken seriously by governments, and translated quickly into more protective safety standards, and in the interim, into strong preventative actions, warnings and substitution of safer technologies and redesigned devices.

Bioeffects are clearly established and occur at very low levels of exposure to electromagnetic fields and radiofrequency radiation. Bioeffects can occur in the first few minutes at levels associated with cell and cordless phone use. Bioeffects can also occur from just minutes of exposure to mobile phone masts (cell towers), WI-FI, and wireless utility 'smart' meters that produce whole-body exposure. Chronic base station level exposures can result in illness.

Many of these bioeffects can reasonably be expected to result in adverse health effects if the exposures are prolonged or chronic. This is because they interfere with normal body processes (disrupt homeostasis), prevent the body from healing damaged DNA, produce immune system imbalances, metabolic disruption and lower resistance to disease across multiple pathways. Essential body processes can eventually be disabled by incessant external stresses (from system-wide electrophysiological interference) and lead to pervasive impairment of metabolic and reproductive functions.

What does the WHO IARC Classification of ELF-EMF and RFR as Group 2B Possible Human Carcinogens Mean?

The World Health Organization International Agency for Cancer Research (IARC) designated ELF-EMF as a Group 2B (Possible) Carcinogen in 2001. This is the kind of exposure from power lines, battery switching in cell phone devices, laptop computers and appliances. The World Health Organization specifically reaffirmed its finding that EMF is classifiable as a Group 2B Possible Human Carcinogen in 2006 in their Health Criteria Monograph #238 (WHO, 2007).

World Health Organization International Agency for Research on Cancer (IARC) Cancer Classifications

Group 1	Known Carcinogen
Group 2A	Probable Carcinogen
Group 2B	Possible Human Carcinogen
Group 3	Insufficient Information
Group 4	Not a Carcinogen

In 2011, IARC determined that scientific evidence is sufficient now to classify radiofrequency radiation as a Group 2B Possible Human Carcinogen (Baan et al, 2011). This is the kind of exposure coming from cell and cordless phones, cell towers, WI-FI, wireless laptops, electronic baby monitors and wireless 'smart' utility meters.

So, what does this mean? According to the classification categories, it is again clear IARC did NOT find so little clear and consistent evidence that it should support a finding of "Not A Carcinogen". That would be the valid test that RFR is safe, as best public health experts can judge the evidence. Nor did IARC find that the evidence sufficient so as to make a stronger classification (Probably or Known Carcinogen). Rather, IARC found the evidence supports classification as a "Possible" cancer-causing

agent. That is not a weak or reckless judgment made with few facts. It should be a strong warning to governments to reconsider their safety standards, particularly in light of the billions of people at potential health risk from new wireless technologies. Studies of cell and cordless phones and of wireless whole-body RFR exposures consistently show human health impacts that have become 'epidemiologically visible' (Sections 11 and 21).

ELF-EMF AND RFR ARE CLASSIFIED AS POSSIBLE CANCER-CAUSING AGENTS – WHY ARE GOVERNMENTS NOT ACTING?

The World Health Organization International Agency for Research on Cancer has classified wireless radiofrequency as a Possible Human Carcinogen (May, 2011). The designation applies to low-intensity RFR in general, covering all RFR-emitting devices and exposure sources (cell and cordless phones, WI-FI, wireless laptops, wireless hotspots, electronic baby monitors, wireless classroom access points, wireless antenna facilities, etc). The IARC Panel could have chosen to classify RFR as a Group 4 – Not A Carcinogen if the evidence was clear that RFR is not a cancer-causing agent. It could also have found a Group 3 designation was a good interim choice (Insufficient Evidence). IARC did neither.

II. KEY SCIENTIFIC EVIDENCE (2006- 2012)

Many thousand scientific studies over four decades have provided warnings of serious biological effects and potential health harm from EMF and RFR. About 1800 new, scientific papers published in the last five years report more bioeffects and adverse health effects of EMF and RFR, and are presented in great detail in the BioInitiative Report 2012.

These studies since 2006 give critical support to the argument that current safety standards are grossly inadequate. They cannot be protecting public health if they do not prevent harm to a variety of types of human cells, human sperm and the developing fetus *in-utero*. These are all effects reported today due to cell phone radiation exposures that are both legal and common in daily home, business and school environments. These effects are shown to occur at very low-intensity permissible levels that have become 'typical' for pregnant women, the fetus, the infant, the child, and for adults. Such effects are occurring at hundreds to thousands of times lower intensity exposure levels than the current FCC public safety limits allow. These exposure levels are common in the

environment, but worst in close proximity to wireless devices like cell and cordless phones, 'smart' wireless utility meters, wireless routers, wireless classroom access points and laptops, to baby surveillance devices, and in the first few hundred meters of cell towers. WI-FI levels of RFR and cell phones-on-standby mode are sufficient to cause effects that, if chronic, may be damaging to the health of cellular DNA, reproductive germ cells (sperm) and the male reproductive organs.

Overall, these new studies report abnormal gene transcription (Section 5); genotoxicity and single-and double-strand DNA damage (Section 6); stress proteins because of the fractal RF-antenna like nature of DNA (Section 7); chromatin condensation and loss of DNA repair capacity in human stem cells (Sections 6 and 15); reduction in free-radical scavengers - particularly melatonin (Sections 5, 9, 13, 14, 15, 16 and 17); neurotoxicity in humans and animals (Section 9), carcinogenicity in humans (Sections 11, 12, 13, 14, 15, 16 and 17); serious impacts on human and animal sperm morphology and function (Section 18); effects on offspring behavior (Section 18, 19 and 20); and effects on brain and cranial bone development in the offspring of animals that are exposed to cell phone radiation during pregnancy (Sections 5 and 18). This is only a snapshot of the evidence presented in the BioInitiative 2014 updated report.

Many of these bioeffects are associated with disruption of normal biological functioning in the genes, and in the physiology of the nervous and cardiac systems of the body (brain, blood-brain barrier, heart, vascular system). Sleep disruption (insomnia) is a hallmark bioeffect of RFR. Hypersensitivity disorders like allergies and asthma are reported from exposure to environmental chemicals and to EMF. A pregnant woman's exposure to EMF has been linked to increased asthma and behavioral problems in the human child after *in-utero* exposure. Pregnant mice exposed to cell phone radiation give birth to baby mice with attention disorders, hyperactivity and impaired memory function, similar to effects seen in human babies as reported by Divan et al (2008).

A. Stress, Stress Proteins and DNA as a Fractal Antenna: The word stress invokes different concepts for people, but needs to be understood as a physiological response. BioInitiative author Martin Blank has described how both ELF-EMF and RFR produce stress proteins at very low exposure levels, and why this is only adaptive in the short-

term. Chronic exposures that trigger stress responses (stress proteins) regardless of their environmental cause are mal-adaptive if they go on too long. Any agent (EMF, ionizing radiation, chemicals, heavy metals, etc) that continuously generates stress proteins is not adaptive, and is harmful, if it is a constant provocation.

The work of Martin Blank and Reba Goodman of Columbia University has established that stress proteins are produced by ELF-EMF and RFR at levels far below current safety standards allow. Further, they think DNA is actually a very good fractal RF-antenna which is very sensitive to low doses of EMF, and may induce the cellular processes that result in chronic 'unrelenting' stress. That daily environmental levels of ELF-EMF and RFR can and do throw the human body into stress protein response mode (out of homeostasis) is a fundamental and continuous insult. Chronic exposures can then result in chronic ill-health**.**

B. Fetal Effects and Fetal Development Studies: Effects on the developing fetus from *in-utero* exposure to cell phone radiation have been observed in both human and animal studies since 2006. Divan et al (2008) found that children born of mothers who used cell phones during pregnancy develop more behavioral problems by the time they have reached school age than children whose mothers did not use cell phones during pregnancy. The July 2008 issue of Epidemiology reports that children whose mothers used cell phones during pregnancy had 25% more emotional problems, 35% more hyperactivity, 49% more conduct problems and 34% more peer problems (Divan et al, 2008).

Aldad et al (2012) showed that cell phone radiation significantly altered fetal brain development and produced ADHD-like behavior in the offspring of pregnant mice. Exposed mice had a dose-dependent impaired glutamatergic synaptic transmission onto Layer V pyramidal neurons of the prefrontal cortex. The authors conclude the behavioral changes were the result of altered neuronal developmental programming *in utero*. Offspring mice were hyperactive and had impaired memory function and behavior problems, much like the human children in Divan et al (2008).

A new study from Greece reports altered development of the cranial bones of the mouse fetus from low intensity (0.6 to 0.9 W/kg) *in-utero* 900 MHz cell phone radiation (Fragopoulou et al, 2009). They report *"our results clearly show that even modest exposure (e.g., 6-min daily for 21 days) is sufficient to interfere with the normal mouse developmental process."*

Other new studies by Fragopoulou et al report that brain astrocyte development followed by proteomic studies is adversely affected by DECT (cordless phone radiation) and mobile phone radiation (Fragopoulou et al, 2012); and that whole body exposure with GSM 900MHz affects spatial memory in mice (Fragopoulou et al, 2010).

FETAL BRAIN DEVELOPMENT MAY BE ALTERED

There is increasing evidence that fetal (*in-utero*) and early childhood exposures to cell phone radiation and wireless technologies in general is a risk factor for hyperactivity, learning disorders and behavioral problems in school.

Neonatal physician Carlo Bellieni of Italy found that heart rate variability is adversely affected in infants hospitalized in isolettes or incubators where ELF-EMF levels are in the 0.8 to 0.9 μT range (8 to 9 mG) (Bellieni, 2008). Infants suffer adverse changes in heart rate variability, similar to adults. He also reported that newborns cared for in the high ELF-EMF environments of isolettes have disrupted melatonin levels (Bellieni et al, 2012a).

C. Studies of Sperm: Several international laboratories have replicated studies showing adverse effects on sperm quality, motility and pathology in men who use and particularly those who wear a cell phone, PDA or pager on their belt or in a pocket (Agarwal et al, 2008; Agarwal et al, 2009; Wdowiak et al, 2007; De Iuliis et al, 2009; Fejes et al, 2005; Aitken et al, 2005; Kumar, 2012). Other studies conclude that usage of cell phones, exposure to cell phone radiation, or storage of a mobile phone close to the testes of human males affect sperm counts, motility, viability and structure (Aitken et al, 2004; Agarwal et al, 2007; Erogul et al., 2006). Animal studies have demonstrated oxidative and DNA damage, pathological changes in the testes of animals, decreased sperm mobility and viability, and other measures of deleterious damage to the male germ line

(Dasdag et al, 1999; Yan et al, 2007; Otitoloju et al, 2010; Salama et al, 2008; Behari et al, 2006; Kumar et al, 2012). There are fewer animal studies that have studied effects of cell phone radiation on female fertility parameters. Panagopoulous et al. 2012 report decreased ovarian development and size of ovaries, and premature cell death of ovarian follicles and nurse cells in *Drosophila melanogaster.* Gul et al (2009) report rats exposed to stand-by level RFR (phones on but not transmitting calls) caused decrease in the number of ovarian follicles in pups born to these exposed dams. Magras and Xenos (1997) reported irreversible infertility in mice after five (5) generations of exposure to RFR at cell phone tower exposure levels of less than one microwatt per centimeter squared (μW/cm2).

Agarwal et al (2009) evaluated the effect of cell phone radiation during talk mode on human sperm samples. The authors found "*radiofrequency electromagnetic waves emitted from cell phones may lead to oxidative stress in human semen. We speculate that keeping the cell phone in a trouser pocket in talk mode may negatively affect spermatozoa and impair male fertility.*"

Aitken et al (2005) studied the effect of 900 MHz cell phone radiation on mice (7 days, 12-hr per day at 0.09 W/kg). The authors found statistically significant damage to the mitochondrial genome of epididymal spermatozoa ($p<0.05$).

Avendano et al, 2012 provided evidence that a 4-hr exposure to WI-FI at exceeding low levels (0.5-1.0 μW/cm2) near a laptop computer caused decreased sperm viability and DNA fragmentation in human sperm samples. Avendado says "(*T)o our knowledge, this is the first study to evaluate the direct impact of a laptop use on human spermatozoa. Ex vivo exposure of human spermatozoa to a wireless internet-connected laptop decreased motility and induced DNA fragmentation by a nonthermal effect. We speculate that keeping a laptop connected wirelessly to the internet on the lap near the testes may result in decreased male fertility.*"

De Iuliis et al (2009) reported that "*RF-EMR in both the power density and frequency range of mobile phones enhances mitochondrial reactive oxygen species generation by human spermatozoa, decreasing the motility and vitality of these cells*

while stimulating DNA base adduct formation, and ultimately DNA fragmentation." They warned their findings *"have clear implications for the safety of extensive mobile phone use by males of reproductive age, potentially affecting both their fertility and the health and wellbeing of their offspring"* based on damage from a 6-hr exposure to 1800 MHz cell phone radiation in human sperm cells. This 6-hr exposure caused reduced sperm motility and viability and caused a significant increase in reactive oxygen species (free radicals that are associated with oxidative damage to DNA), and the effects were worse with more exposure (a significant dose-response was observed). Atasoy (2012) also questioned the safety of 2400 MHz exposure to those of reproductive age. This study reports that WI-FI internet access devices can damage DNA and reduce DNA repair when the exposures are very low(exposure level of 0.091 W/kg) and chronic; damage can occur even at levels that comply with 802.11 g WI-FI public safety limits.

Behari et al (2006) reported that chronic exposure of rats to cell phone radiation caused double-strand DNA breaks in sperm cells (35 days, 2-hr per day). This study also showed that the mobile radiation exposure at 900 MHz (at 0.9 W/kg) and at 2.45 GHz (at 0.1 W/kg) caused a statistically significant decrease in sperm count and the weight of testes.

Otitoloju et al., (2010) graphically describe sperm head abnormalities in mice exposed for six months to base-station level RF/MW at 70 to 100 nanowatts/cm2 (0.07 – 0.1 μW/cm2). Only 2% of controls but a stunning 39% to 46% of exposed mice had damaged sperm.

> *"The major abnormalities observed were knobbed hook, pin-head and banana-shaped sperm head. The occurrence of sperm head abnormalities was also found to be dose dependent. The implications of the observed increased occurrence of sperm head abnormalities on the reproductive health of humans living in close proximity to GSM base stations were discussed.*"

These studies taken together should provide a strong warning that 'normal' use of a cell phone presents risks that warrant strong preventative actions to protect the integrity of the human genome from de novo mutations and loss of fertility across entire male populations of cell phone users. Further, even the much lower exposure levels associated with mobile phone base station (cell tower) RFR levels are deleterious over time.

HUMAN SPERM AND THEIR DNA ARE DAMAGED

Human sperm are damaged by cell phone radiation at very low intensities (0.00034 – 0.07 μW/cm2). There is a veritable flood of new studies reporting sperm damage in humans and animals, leading to substantial concerns for fertility, reproduction and health of the offspring (unrepaired de novo mutations in sperm). Exposure levels are similar to those resulting from wearing a cell phone on the belt, or in the pants pocket, or using a wireless laptop computer on the lap. Sperm lack the ability to repair DNA damage.

D. Human Stem Cell Studies: Markova et al (2010) reported that 915 MHz microwave exposure significantly affects human stem cells. They found that very low-intensity microwave radiation from mobile phones can inhibit DNA repair processes in human stem cells. By placing a mobile phone at one meter distance from human stem cells in petri dishes (SAR = 0.037 W/Kg), they found a significant reduction in 53BP1 foci. These foci are a measure of DNA repair in cells with double strand DNA damage. The damage was greater to stem cells (derived from adipose tissue in humans) than in fibroblasts. Stem cells did not repair over time - and the damage was done within one hour of microwave exposure. Fibroblasts were similarly affected (inhibited 53BP1 foci) but repaired over time. The effects are carrier-frequency dependent. The effects occurred with GSM exposure at 915 MHz, but not at 905 MHz. The failure of DNA repair also occurred at the mobile phone UTMS carrier frequency of 1947 MHz. Analysis of the 53BP1 foci is a sensitive technique to measure double-strand DNA breaks in both unexposed cells and in cells exposed to cytotoxic agents. In the authors' words, *"this represents a direct mechanistic link to epidemiological data showing an association of MW exposure with increased cancer risk*." The data obtained from human stem cells is of "*utmost relevance for assessment of possible health risks of MW exposure from mobile phones."* Most, if not all adult tissues and organs including blood, skin and brain contain stem cells. Therefore, "*stem cells like blood cells and fibroblasts are always subjected to exposure from mobile phones*." With respect to children, because "*almost all organs and tissues possess stem cells and stem cells are more active in children, the possible relationship of chronic MW exposure and various types of tumors and leukemia especially in children should be investigated."*

Czyz et al (2004) reported that GSM cell phone exposure affected gene expression levels in embryonic stem cells (p53-deficient); and significantly increased heat shock protein HSP 70 production.

HUMAN STEM CELL DNA DOES NOT ADAPT OR REPAIR

Human adipose tissue stem cells lack the ability to repair DNA damage caused by chronic exposure to non-thermal microwaves. Damage to DNA in some other cells may be incompletely repaired.

E. Mobile Phone Base Station (Cell Tower) Studies

Human Studies: Hutter et al (2006) reported that short-term exposure to GSM cell phone radiation resulted in complaints of headache, neurological problems, sleep and concentration problems in adults with 0.01 - 0.05 μW/cm2 exposure levels. Kundi and Hutter (2009) reviewed human effects in fourteen (14) mobile phone base station studies and reported *"(F)rom available evidence it is impossible to delineate a threshold below which no effect occurs, however, given the fact that studies reporting low exposure were invariably negative it is suggested that power densities around 0.5–1 mW/m2 [*0.05 – 0.1 uW/cm2*] must be exceeded in order to observe an effect."*

Buchner and Eger (2012) conducted an eighteen (18) month study to assess changes in stress hormones in 60 persons exposed before and after a mobile phone base station went into operation in the Rimbach village in Germany. The study showed that chronic exposure to base station RF (whole-body) at 0.006 - 0.01 μW/cm2 in humans had significant impacts on stress hormones over time. In the beginning months, adrenaline levels first increased in a dose-dependent fashion according to exposure level ($p < 0.002$) and then decreased below normal levels ($p < 0.005$). Both the average as well as the median adrenaline values increased after the activation of the transmitter and decreased again after one year with exposure levels >0.006 μW/cm2. Chronically ill subjects and children showed especially strong responses; except for some "outliers," no effect was observed in healthy adults (Buchner and Eger, 2012). For dopamine, inverse effects to

those for adrenaline and noradrenaline were observed. The median dopamine levels decreased from 199 to 115 μg/g creatinine between January and July 2004. The fact that the dopamine levels of the study subjects decreased during this period is highly significant ($p<0.0002$). Thereafter, the median increased again: In January 2005, it was at 131 μg/g creatinine, in July of 2005. This increase is also significant between July 2004 and July 2005 ($p<0.05$).

Buchner (2012) indicates that the RFR transmitter induced changes in stress hormones that follow the classic stress syndrome of adaptation, then exhaustion established by Hans Seyle in the 1950's. *"After the stages of alarm and resistance, the last stage of exhaustion sets in. The parameters investigated in the Rimbach study follow this pattern"*.

A long-term 6-yr study assessed the role of exposure to radio frequency radiation (RFR) emitted either from mobiles or base stations and its relations with human's hormone profiles. The study revealed significant RFR effects on pituitary–adrenal axis, resulting in reduction of ACTH, cortisol, thyroid hormones, prolactin in young females, and testosterone levels in males (Eskander et al, 2012). But no direct measurements of RFR power density levels were made, only categories of distance from transmitter.

Oberfeld et al (2004) reported that populations exposed to base stations transmitting cell phone frequencies had more fatigue, depressive tendency, sleeping disorders, concentration difficulties, and cardio-vascular problems reported with exposure to GSM 900/1800 MHz cell phone signal.

Navarro et al (2003) reported that exposure levels of 0.01 - 0.11 μW/cm2 resulted in fatigue, headaches, sleeping problems in populations around mobile phone base stations.

Thomas et al (2008) reported an increase in adult complaints of headaches and concentration difficulties with short-term cell phone use at 0.005 to 0.04 μW/cm2 exposure levels.

Heinrich et al (2010) reported that children and adolescents (8-17 years old) with short-term exposure to base-station level RFR experienced headache, irritation, and concentration difficulties in school. RFR levels were 0.003 - 0.02 μW/cm2.

Thomas et al (2010) reported that RFR levels of 0.003 - 0.02 μW/cm2 resulted in conduct and behavioral problems in children and adolescents (8-17 years old) exposed to short-term cell phone radiation in school.

Mohler et al (2010) reported that adults exposed to 0.005 μW/cm2 cell phone radiation (base-station exposure levels) had sleep disturbances with chronic exposure, but this effect was not significantly increased across the entire population.

Human Studies at Base Station Exposure Levels (Cell Towers)

At least five new cell tower studies with base-station level RFR at levels ranging from 0.003 μW/cm2 to 0.05 uW/cm2 published since 2007 report headaches, concentration difficulties and behavioral problems in children and adolescents; and sleep disturbances, headaches and concentration problems in adults. This is highly consistent with studies done prior to 2007, but the 'effect levels' are significantly lower (dropping from the microwatt to the nanowatt range per square centimeter).

Public safety standards are 1,000 – 10,000 or more times higher than levels now commonly reported in mobile phone base station studies to cause bioeffects.

Sperm studies are showing DNA damage, impaired sperm quality, motility and viability from cell phones on standby mode and wireless laptop use at exposures of 0.00034 μW/cm2 to 0.07 μW/cm2. Several studies report sperm damage effects at 'standby model' cell phone emission levels, which are in the low nanowatt to picowatt per square centimeter range.

F. Electrohypersensitivity (EHS) Studies: McCarty et al (2011) studied electrohypersensitivity in a patient (a female physician). The patient was unable to detect the presence or absence of EMF exposure, largely ruling out the possibility of bias. In multiple trials with the fields either on or not on, the subject experienced and reported temporal pain, feeling of usease, skipped heartbeats, muscle twitches and/or strong headache when the pulsed field (100 ms, duration at 10 Hz) was on, but no or mild symptoms when it was off. Symptoms from continuous fields were less severe than with pulsed fields. The differences between field on and sham exposure were significant at the $p < 0.05$ level. The authors conclude that electromagnetic hypersensitivity is a neurological syndrome, and statistically reliable somatic reactions could be provoked in this patient by exposure to 60-Hz electric fields at 300 volts per meter (V/m). They

conclude *"EMF hypersensitivity can occur as a bona fide environmentally inducible neurological syndrome*." In their response to a letter to the editor of the journal, the authors say: *"(W)e followed an empirical approach and demonstrated a cause-and-effect relationship ($p < 0.05$) under conditions that permitted us to infer the existence of electromagnetic hypersensitivity (EHS), a novel neurological syndrome*." (Marino et al., 2012)

Further, the authors explain the significance of detecting EHS effects by non-linear methods.

> *"The important issue at this point is not whether EMF can produce symptoms (we empirically demonstrated that it can) but rather why this effect historically has been difficult to detect. It occurred to us that EHS has remained elusive because of the way it was studied. The experiments designed to detect EHS had been based on the assumption that if it existed, it was a linear phenomenon, whereas EHS is actually a nonlinear phenomenon." "Our study was designed to detect whether EHS was a linear or nonlinear phenomenon, and we were successful in showing a link between acute EMF exposure and somatic responses ($p < 0.05$). This finding – taken together with the unfailingly negative results of the linear studies – is good evidence that EHS is a nonlinear phenomenon, as we suspected."*

With the exception of the McCarty study there have not been clear demonstrations in controlled circumstances showing that persons reporting to be electrophypersensitive can distinguish whether or not RFR is being applied. There are, however, multiple reports of symptoms experienced by individuals exposed to EMFs in uncontrolled circumstances.

A. Johansson et al (2010) studied symptoms, personality traits and stress in people with mobile phone-related symptoms and electromagnetic hypersensitivity. They reported there is support for a difference between people with symptoms related to specific EMF sources and people with general EHS. The symptoms are anxiety, depression, somatization, exhaustion and stress. The EHS group reported more neurasthenic symptoms.

Two publications on electrohypersensitivity by O. Johansson (2007, 2009) provide an extensive overview of the relevant literature on electrohypersensitivity. Both

publications document symptoms and conditions giving rise to increased sensitivity to ELF-EMF and RFR. The need for new, biologically-based public exposure standards is recommended in both publications, in order to address electrohypersensitivity.

Landgrebe et al (2007) reported that their study of electrosensitive patients showed participants had a reduced intracortical facilitation as compared to two control groups. The EHS group of patients showed altered central nervous system function. In a follow-up study, the authors reported that EHS patients but not controls "*demonstrated significant cognitive and neurobiological alterations pointing to a higher genuine individual vulnerability of electromagnetic hypersensitive patients." (Landgrebe et al, 2008).*

The team of Sandstrom, Hansson Mild and Lyskov produced numerous papers between 1994 and 2003 involving people who are electrosensitive (Lyskov et al, 1995; Lyskov et al, 1998; Sandstrom et al, 1994; Sandstrom et al, 1995; Sandstrom et al, 1997; Sandstrom et al, 2003). Sandstrom et al (2003) presented evidence that heart rate variability is impaired in people with electrical hypersensitivity and showed a dysbalance of the autonomic nervous system. *"EHS patients had a disturbed pattern of circadian rhythms of HRF and showed a relatively 'flat' representation of hourly-recorded spectral power of the HF component of HRV"*. This research team also found that *"EHS patients have a dysbalance of the autonomic nervous system (ANS) regulation with a trend to hyper-sympathotonia, as measured by heart rate (HR) and electrodermal activity, and a hyperreactivity to different external physical factors, as measured by brain evoked potentials and sympathetic skin responses to visual and audio stimulation*." (Lyskov et al, 2001 a,b; Sandstrom et al, 1997). The reports referenced above provide evidence that persons who report being electrosensitive differ from others in having some abnormalities in the autonomic nervous system, reflected in measures such as heart rate variability. At present it remains unclear whether EHS is actually caused by RF/EMF exposure, or rather is a self-identifying syndrome of excessive responsiveness to a variety of stimuli. But given the relatively high percentage of persons reported to be electrosensitive (5% of the general population of Switzerland according to Schreier et al,

2006), with some being severely disabled as a consequence, it is critical that there be more study of this syndrome.

Tuengler and von Klitzing et al (2012) reported EHS people that were tested showed significant changes in regulation of the autonomic nervous system, including changes in capillary blood flow (microcirculation), heart rate variability, and electric skin potentials. The continuous detection of capillary blood flow is an important tool in analyzing the capacity of the autonomic nervous system. In EHS patients, von Klitzing finds that intestinal motility may also be disregulated and show no activity at all for some time after exposure.

G. Effects on the Blood-brain Barrier (BBB): The Lund University (Sweden) team of Leif Salford, Bertil Persson and Henrietta Nittby has done pioneering work on effects of very low level RFR on the human brain's protective lining – the barrier that protects the brain from large molecules and toxins that are in the blood.

THE BLOOD-BRAIN BARRIER IS AT RISK

The BBB is a protective barrier that prevents the flow of toxins into sensitive brain tissue. Increased permeability of the BBB caused by cell phone RFR may result in neuronal damage. Many research studies show that very low intensity exposures to RFR can affect the blood-brain barrier (BBB) (mostly animal studies). Summing up the research, it is more probable than unlikely that non-thermal EMF from cell phones and base stations do have effects upon biology. A single 2-hr exposure to cell phone radiation can result in increased leakage of the BBB, and 50 days after exposure, neuronal damage can be seen, and at the later time point also albumin leakage is demonstrated. *The levels of RFR needed to affect the BBB have been shown to be as low as 0.001 W/kg, or less than holding a mobile phone at arm's length. The US FCC standard is 1.6 W/kg; the ICNIRP standard is 2 W/kg of energy (SAR) into brain tissue from cell/cordless phone use. Thus, BBB effects occur at about 1000 times lower RFR exposure levels than the US and ICNIRP limits allow.* *(Salford, 2012)*

The consequence to modern life is that cell and cordless phone use may cause a pathological leakage of the BBB with very short use periods, and the damage may be long-lasting. Harmful substances may enter the brain. If the damage is ongoing (if cell and cordless phone use continues to occur over months and years), the potential for

harmful effects increases. There is already 'epidemiologically visible' evidence of increased brain cancer risk in humans (Section 11).

Volkow et al (2011a, b) reported increased glucose metabolism in the brain with cell phone use in humans. This important investigation of 47 human subjects used a randomized crossover design and labeled fluorodeoxyglucose to measure the metabolisms of the brain when the cell phone was activated but muted for 50 minutes as compared to not being activated. "*Our study showed that cell phone activation was associated with metabolic increases in brain regions closest to the antenna and that the increases showed a negative linear correlation with distance from the antenna. While the effect was small, the negative correlation of the effect with distance was statistically significant (R = −0.91; P <.001).* This study is particularly important in that it demonstrates definitively that an active cell phone, placed on the ear as one would normally be used, alters brain metabolic activity, but only in the region close to the cell phone.

H. Brain Cancer Studies: The Orebro University (Sweden) team led by Lennart Hardell, MD, an oncologist and medical researcher, has produced an extraordinary body of work on environmental toxins of several kinds, including the effects of radiofrequency/microwave radiation and cancer. Their 2012 work concludes:

> *"Based on epidemiological studies there is a consistent pattern of increased risk for glioma and acoustic neuroma associated with use of mobile phones and cordless phones. The evidence comes mainly from two study centres, the Hardell group in Sweden and the Interphone Study Group. No consistent pattern of an increased risk is seen for meningioma. A systematic bias in the studies that explains the results would also have been the case for meningioma. The different risk pattern for tumor type strengthens the findings regarding glioma and acoustic neuroma. Meta-analyses of the Hardell group and Interphone studies show an increased risk for glioma and acoustic neuroma. Supportive evidence comes also from anatomical localisation of the tumor to the most exposed area of the brain, cumulative exposure in hours and latency time that all add to the biological relevance of an increased risk. In addition risk calculations based on estimated absorbed dose give strength to the findings.*

In summary:

- *There is reasonable basis to conclude that RF-EMFs are bioactive and have a potential to cause health impacts.*

- *There is a consistent pattern of increased risk for glioma and acoustic neuroma associated with use of wireless phones (mobile phones and cordless phones) mainly based on results from case-control studies from the Hardell group and Interphone Final Study results.*
- *Epidemiological evidence gives that RF-EMF should be classified as a human carcinogen.*
- *Based on our own research and review of other evidence the existing FCC/IEE and ICNIRP public safety limits and reference levels are not adequate to protect public health.*
- *New public health standards and limits are needed.* (Hardell et al, 2012)

I**. Genetic Damage (Genotoxicity Studies):** There are at least several hundred published papers that report EMF affects cellular oxidative processes (oxidative damage). Increased free radical activity and changes in enzymes involved in cellular oxidative processes are the most consistent effects observed in cells and animals after EMF exposure. Aging may make an individual more susceptible to the detrimental effects of ELF EMF from oxidative damage, since anti-oxidants may decline with age. Clearly, the preponderance of genetic studies report DNA damage and failure to repair DNA damage.

Eighty six (86) new papers on genotoxic effects of RFR published between 2007 and mid-2012 are profiled. Of these, 54 (63%) showed effects and 32 (37%) showed no effects (Lai, 2012)

Forty three (43) new ELF-EMF papers and two static magnetic field papers that report on genotoxic effects of ELF-EMF published between 2007 and mid-2012 are profiled. Of these, 35 (81%) show effects and 8 (19%) show no effect (Lai, 2012).

J. Nervous System Damage: Factors that act directly or indirectly on the nervous system can cause morphological, chemical, or electrical changes in the nervous system that can lead to neurological effects. Both RF and ELF EMF affect neurological functions and behavior in animals and humans.

One hundred fifty five (155) new papers that report on neurological effects of RFR published between 2007 and mid-2012 are profiled. Of these, 98 (63%) showed effects and 57 (37%) showed no effects.

Sixty nine (69) new ELF-EMF papers (including two static field papers) that report on genotoxic effects of ELF-EMF published between 2007 and mid-2012 are profiled. Of these, 64 (93%) show effects and 5 (7%) show no effect. (Lai, 2012)

L. Children are More Vulnerable: Many studies demonstrate that children are more sensitive to environmental toxins of various kinds (Barouki et al, 2012; Preston, 2004; WHO, 2002; Gee, 2009; Sly and Carpenter, 2012).

> The Presidential Cancer Panel (2010) found that children '*are at special risk due to their smaller body mass and rapid physical development, both of which magnify their vulnerability to known carcinogens, including radiation.*'

> The American Academy of Pediatrics, in a letter to Congressman Dennis Kucinich dated 12 December 2012 states "*Children are disproportionately affected by environmental exposures, including cell phone radiation. The differences in bone density and the amount of fluid in a child's brain compared to an adult's brain could allow children to absorb greater quantities of RF energy deeper into their brains than adults. It is essential that any new standards for cell phones or other wireless devices be based on protecting the youngest and most vulnerable populations to ensure thay are safeguarded through their lifetimes."*

II. ISSUES AND ANSWERS IN THE EMF DEBATE

Much of the emphasis in the 2007 Bioinititative Report focused on cancer, which is still the best documented disease of concern from exposure to EMF/RF. The evidence that exposure to EMF/RF increases the risk of cancer has only gotten significantly stronger since then, and we have a better, albeit still incomplete, understanding of the mechanisms involved. However, in terms of threshold exposures that result in human disease, new research on male reproduction and neurobehavioral alterations provide evidence for harm at even lower exposure levels. RFR has been shown in this Report to act as an external synchronizer of neural activity, capable of disrupting sleep, circadian rhythms, diurnal hormone fluctuations, brain wave activity and heart rate variability by exposure to artificial electromagnetic signals (as opposed to natural evolutionary frequencies) and to do so at exceedingly low intensities.

Much of the debate over the body of EMF science ignores simple questions that would help to discriminate among studies with apparently conflicting results. Section 15 by Dr. Belyaev is helpful in identifying key factors which must be known and controlled for in experiments (biological variables and physical parameters include bandwidth, frequency, modulation, polarization, intermittence and coherence time of exposure, static

magnetic field, electromagnetic stray fields, sex, age, individual traits, and cell density during exposure). Dr. Andrew Marino emphasizes that detection of EMF/RFR effects require investigation of non-linear phenomena, a critical difference that if ignored, may miss important biological effects (Marino, 2012).

A unifying hypothesis for a plausible biological mechanism to account for very weak field EMF bioeffects other than cancer may lie with weak field interactions of pulsed RFR and ELF-modulated RFR as disrupters of synchronized neural activity. Electrical rhythms in our brains can be influenced by external signals. This is consistent with established weak field effects on coupled biological oscillators in living tissues. Biological systems of the heart, brain and gut are dependent on the cooperative actions of cells that function according to principles of non-linear, coupled biological oscillations for their synchrony, and are dependent on exquisitely timed cues from the environment at vanishingly small levels (Buzsaki, 2006; Strogatz, 2003). The key to synchronization is the joint actions of cells that co-operate electrically - linking populations of biological oscillators that couple together in large arrays and synchronize spontaneously according to the mathematics described for Josephson junctions (Brian Josephson, the 1993 Nobel prize winner for this concept). This concept has been professionally presented in journal articles and also popularized in print by Prof. Steven Strogatz, a mathematician at Cornell University who has written about 'sync' as a fundamental organizing principle for biological systems (Strogatz, 2001; 2003).

> *"Organisms are biochemically dynamic. They are continuously subjected to time-varying conditions in the form of both extrinsic driving from the environment and intrinsic rhythms generated by specialized cellular clocks within the organism itself. Relevant examples of the latter are the cardiac pacemaker located at the sinoatrial node in mammalian hearts and the circadian clock residing at the suprachiasmatic nuclei in mammalian brains. These rhythm generators are composed of thousands of clock cells that are intrinsically diverse but nevertheless manage to function in a coherent oscillatory state. This is the case, for instance, of the circadian oscillations exhibited by the suprachiasmatic nuclei, the period of which is known to be determined by the mean period of the individual neurons making up the circadian clock. The mechanisms by which this collective behavior arises remain to be understood."(Strogatz, 2003)*

Synchronous biological oscillations in cells (pacemaker cells) can be disrupted by artificial, exogenous environmental signals, resulting in desynchronization of neural

activity that regulates critical functions (including metabolism) in the brain, gut and heart and circadian rhythms governing sleep and hormone cycles (Strogatz, 1987). The brain contains a population of oscillators with distributed natural frequencies, which pull one another into synchrony (the circadian pacemaker cells). Strogatz has addressed the unifying mathematics of biological cycles and external factors disrupt these cycles. Buzsaki (2006) says "*rhythms can be altered by a wide variety of agents and that these perturbations must seriously alter brain performance. Rhythms are a robust phenomenon.*"

The heart's natural pacemaker center is the sinoatrial node, a cluster of about 10,000 cells that generate electrical rhythm that commands the rest of the heart to beat. Diseases related to disruption of that synchronization include epilepsy, chronic insomnia, and cardiac arrhythmias (Strogatz, 2003). Some EMF diseases are those where desynchronization of neural activity results in physiological changes that, if chronic, result in chronically disrupted homeostasis, and eventually ill-health and chronic diseases. Such a future burdens health care systems in an irreversible way.

The late Dr. Ross Adey in his last publication in Bioelectromagnetic Medicine (P. Roche and M. Markov, eds. 2004) concluded:

> "*There are major unanswered questions about possible health risks that may arise from exposures to various man-made electromagnetic fields where these human exposures are intermittent, recurrent, and may extend over a significant portion of the lifetime of the individual."*
>
> *"Epidemiological studies have evaluated ELF and radiofrequency fields as possible risk factors for human health, with historical evidence relating rising risks of such factors as progressive rural electrification, and more recently, to methods of electrical power distribution and utilization in commercial buildings. Appropriate models describing these bioeffects are based in nonequilibrium thermodynamics, with nonlinear electrodynamics as an integral feature. Heating models, based in equilibrium thermodynamics, fail to explain an impressive new frontier of much greater significance. Though incompletely understood, tissue free radical interactions with magnetic fields may extend to zero field levels."*

Our society appears determined to make everything wireless, and the consequence is to increase cumulative exposure to RFR. Many homes and almost every Starbucks or McDonalds has WiFi. Smart phones, tablets, video iPods and other wireless devices are even given to children as playthings. The result is a significant increase in cumulative RFR exposure of the whole population, but particularly of those who have and use wireless devices for prolonged periods of time. No national or international standard of RFR exposure considers cumulative effects, all being developed to avoid local tissue heating from acute exposures.

The issues around exposure of children to RFR is of critical importance. There is overwhelming evidence that children are more vulnerable than adults to many different exposures (Sly and Carpenter, 2012), including RFR, and that the diseases of greatest concern are cancer and effects on neurodevelopment. Yet parents place RFR baby monitors in cribs, provide very young children with wireless toys, and give cell phones to young children, usually without any knowledge of the potential dangers. A growing concern is the movement to make all student computer laboratories in schools wireless. A wired computer laboratory will not increase RFR exposure, and will provide safe access to the internet.

An urgent example for the need to address the lack of adequate public protection from inadequate safety standards for pulsed RFR exposures is the rapid, global rollout of wireless utility meters (‘smart’ meters for electricity, gas and water meters). Current safety standard calculations that rely on time-averaging of RFR almost entirely dilute out the power density of RFR levels that are delivered in millisecond bursts, but occur at intervals of every second, or multiple times per second when in use within a wireless mesh network. Said differently, the RFR power density levels are usually legal. While there have been no long term studies of adverse effects of smart meters on human health (primarily because they are so new), there are increasing reports from electrosensitive individuals of harm. Added together, these RFR pulses that now appear to be a highly bioactive agent but are essentially erased or made energetically invisible by time-averaging the pulses as current FCC safety rules mandate.

The wireless meters transmit RF signals like a mini-cell tower antennas in the cell phone radiation frequencies. Currently, they are being deployed in the US and are on the drawing boards around the world including many European countries. The 'smart meter' infrastructure represents the largest single commercial saturation of living space with pulsed RFR yet rolled out by industry. This program places a wireless device (like a mini-mobile phone base station) on the wall, replacing the electromechanical (spinning dial) meter. They will be installed on every home and classroom (every building with an electric meter). Utilities from California to Maine have installed tens of millions already, despite health concerns of experts who already are seeing thousands of health complaints. The wireless meters produce spikes of pulsed radiofrequency radiation on a continuous basis (24/7), and in typical operation, will saturate living space at levels that can be much higher than already reported to cause bioeffects and adverse health effects for some people. These meters, depending on where they are placed relative to occupied space in the home or classroom, can produce RFR exposure levels similar to that within the first 100 feet to 600 feet of a mobile phone base station (cell tower). In the not-so-distant future the plan is to have a wireless device implanted in every household appliance, which will communicate with the smart meter whenever electricity is being used. This will likely make the kitchen a major source of exposure to RFR.

The cumulative RFR burden within any community is largely unknown. Both involuntary sources (like cell towers, smart meters and second-hand radiation from the use of wireless devices by others) plus voluntary exposures from ones' personal use of cell and cordless phones, wireless routers, electronic baby surveillance monitors, wireless security systems, wireless hearing aids, and wireless medical devices like implanted insulin pumps all add up. No one is tallying up the combined exposure levels. Billions of new RFR transmitters from a global smart meter rollout will significantly add to the existing RFR body-burden of pulsed RFR for millions of people. The health concerns are the same as with all other sources of EMF/RFR. Cancer is a serious adverse effect, but damage to male reproduction and central nervous system effects may results from even lower levels of exposure. The work by Strogatz (2001, 2003) and Buzsaki (2006) on weak-field effects on non-linear biological oscillators (brain waves and synchronization of neural activities that regulate body processes) is directly relevant to an understanding

of the profound biological disruptions and health symptoms that continued exposures of pulsed RFR may produce.

The Commons of the Air

Turning to questions of social equity and the individuals' choice not to be exposed to harmful levels of environmental toxins, there has been little inclusion of the public in discussions of wireless radiofrequency exposure. Wireless technologies have become infused in daily habits of billions of people; often choices for wired equivalents are lacking (or those that exist are disappearing). Involuntary exposure to EMF and RFR is becoming more the norm, even where it runs counter to individual choice (second-hand radiation, like second-hand smoke is difficult to avoid).

> *"Wireless technologies drive electromagnetic energy through our air, into and through virtually all indoor and outdoor living environments. The protective air cushion around our planet holds breathable air, buffers us from space radiation, and supports and sustains life in tandem with the natural electromagnetic signature of the earth itself. We are changing this 'commons of the air' in major ways. Wireless signals from broadcast and communications technologies are crowding out and overpowering the natural background. The 'commons of the air' is being altered in unprecedented ways that have enormous consequences for life on earth."(Sage, 2010).*

The rush to 'buy the airwaves' and to market them for commercial purposes is loading '*the commons of the air*' with unsustainable levels of exposure (Sage, 2010). Commercial markets for wireless spectrum successfully lobby government regulators to allocate even more spectrum, once the existing frequencies are allocated. Sage (2010) asks:

> *"Who owns the 'commons of the air'? Who should be allowed to pollute it? What are the limits? On what basis should carrying capacity be defined? Who defines the limits? Do these limits conserve the resource for the future? Do they protect public health and welfare, and the health and well-being of other living things on earth? Who bears the burden of proof of safety or of harm? How should the 'new commons' be managed for the greater good? Do we know enough to act responsibly? Who decides? When should limits be placed on utilization?"*

With no regard to cumulative harm, this commercial rush to buy up wireless spectrum territorial rights has vast implications for public health and well-being. Environmental protections afforded to other natural resources under the National Environmental Policy Act have been ignored. The cumulative impacts and irretrievable commitments on humans, wildlife, and natural resources have never been assessed.

> *"Societies must now define carrying capacity for chronic electromagnetic and wireless exposures. Taking into account the large individual variability to withstand it, new limits must conserve and sustain the 'commons of the air' so that is sustainable for all—and this includes sensitive populations, the young, the elderly, and those with existing sensitivity. Some countries of the world already have surpassed sustainable wireless exposure levels as demonstrated by significant percentages that have already become electrosensitive." (Sage, 2010)*

Homeostasis and Human Health Rights

Chronic exposure to low-intensity RFR and to ELF-modulated RFR at today's environmental levels in many cities will exceed thresholds for increased risk of many diseases and causes of death (Sage and Huttunen, 2012). RFR exposures in daily life alter homeostasis in human beings. These exposures can alter and damage genes, trigger epigenetic changes to gene expression and cause de novo mutations that prevent genetic recovery and healing mechanisms. These exposures may interfere with normal cardiac and brain function; alter circadian rhythms that regulate sleep, healing, and hormone balance ; impair short-term memory, concentration, learning and behavior; provoke aberrant immune, allergic and inflammatory responses in tissues; alter brain metabolism; increase risks for reproductive failure (damage sperm and increase miscarriage risk); and cause cells to produce stress proteins. Exposures now common in home and school environments are likely to be physiologically addictive and the effects are particularly serious in the young (Sage and Huttunen, 2012). This declaration of human health rights below (Sage and Huttunen, 2012) is based on specific reference to health impacts of EMF and RFR that are reasonably well established to occur (Sage and Carpenter, 2009).

Human Health Rights Declaration
Fundamental Human Health Rights (Sage and Huttunen, 2012)

The right to homeostasis in our own bodies.
The right to normal central nervous system function.
The right to natural environmental cues that synchronize our circadian rhythms.
The right to sleep.
The right to heal.
The right to hear.
The right to reproduce.
The right to learn and retain memories.
The right to an intact genome.

If even one of these rights is compromised – placed at risk from involuntary wireless exposures in daily life, it is a breach of human health rights. When many of these human health rights are compromised without the consent of the individual, then the deployment of wireless technologies should be halted and existing exposures reduced or eliminated, in accord with the scientific and public health findings on chronic exposure to low-intensity radiofrequency radiation, and other forms of potentially harmful electromagnetic fields (Sage and Huttunen, 2012)

V. CONCLUSIONS FOR PRUDENT PUBLIC HEALTH PLANNING

Methodology and Approach for Precautionary Action Limits

In 2007, the BioInititive Report chapter on Key Scientific Evidence and Public Health Policy Implications, proposed a specific, interim radiofrequency radiation target level of 0.1 μW/cm2 for cumulative, outdoor RFR exposure (for AM, FM, TV and wireless). It was based on best-available scientific studies to that date. There were few studies prior to 2006 that reported effects at less than 0.1 to 1 μW/cm2 chronic RFR exposures.

In 2009, the journal Pathophysiology produced many peer-reviewed articles in a special two-volume edition on EMF (both ELF-EMF and RFR) essentially publishing the contents of the BioInitiative Report and updating some information. One of these 2009 Pathophysiology papers presented a review of mobile phone base station studies (Kundi and Hutter, 2009). It concluded that the overall studies did not detect effects (headache,

fatigue, tinnitus, concentration difficulties, sleep disruption, etc) at levels of RFR exposure below 0.05 to 0.1 μW/cm2.

New base station-level RFR studies are available in 2012 that can be analyzed to determine if new (and lower) RFR recommendations are warranted. The approach in this chapter relies on "lowest levels at which effects are not seen" akin to the “no observed effect level (NOEL)” used for chemical exposures, as a sufficient basis to establish scientific benchmarks for harm (or alternately, the lowest observed effects level of exposure). It is the province of the science and public health evaluation we do here to report the evidence regardless of what political or strategic complications it may create. An objective presentation of what the studies reveal for ‘effects levels’ is our goal; not to pre-judge or dilute the evidence because it may present strategic or political hurdles to achieve consensus on policy and regulatory changes. What this report does not intend to do is take into account“how could we do this” or “what would it mean”. The purpose is to lay out the science, and make some defensible reductions for factors that studies cannot or do not yet test for, and compensate with deductions for them (safety margins). As interim targets for precautionary action, they will serve as guides for decision-makers who will take up the issues of health, the quality of the future gene pool, social equity and cost.

There is no one study alone that meets impeccable standards for exposure assessment or totally eliminates all possibility for bias, but the constellation of studies together gives adequate support to delineate a ‘lowest observed effects level’, that in turn, with added safety margins, can serve as a guideline for precautionary action.

A reduction from the BioInitiative 2007 recommendation of 0.1 uW/cm2 (or one-tenth of a microwatt per square centimeter which is the same as 100 nanowatts/cm2) for cumulative outdoor RFR down to something three orders of magnitude lower (in the low nanowatt per square centimeter range) is justified on a public health basis. We use the new scientific evidence documented in this Report to identify ‘effect levels’ and then apply one or more reduction factors to provide a safety margin. We do note however, even a precautionary action level of several tenths of a nanowatt per square centimeter (or

several hundred picowatts per square centimeter) would still allow for cell phone transmissions (that can operate down to about 0.00003 V/m).

Even so, these levels may need to go lower in the future, as new and better studies are completed. This is what the authors said in 2007 (Carpenter and Sage, 2007, BioInitiative Report) and it remains true today in 2012. We leave room for future studies that may lower today's observed 'effects levels' and should be prepared to accept new information as a guide for new precautionary actions.

Establishing A Scientific Benchmark for 'Lowest Observed Effect Levels'

Studies that provide information at 'new levels of observed effect' have been identified. These serve as scientific benchmarks for possible risk to health and well-being. Next, we indentify reduction factors to compensate for sensitive subpopulations and apply them to the scientific benchmarks (lowest observed effect levels).

A ten-fold reduction factor is warranted (or higher) for studies that report effects from only short-term (i.e., acute) rather than chronic (i.e., long-term) exposures. Longer duration of exposure can cause bioeffects at lower exposures where these effects are NOT seen with shorter (acute) exposures (Belyaev, 1997; Belyaev, 2012). Chronic exposures with longer durations of weeks, months or years is what most populations face with respect to wireless classrooms, wireless offices and locations near base stations.

A second ten-fold reduction (or higher) is justified as a buffer for sensitive populations including children, the elderly and other adult groups that may be ill, already sensitized, in remission or suffer from ailments made worse by physiological stress and insomnia.

Studies which contribute together can reasonably contribute to delineating a new RFR lower effects level are primarily mobile phone (cell phone) base station studies of healthy human populations and studies of sperm damage in men who use and/or wear their wireless devices on or around the belt or pants pocket.

Power Density Studies (Mobile Phone Base Stations and Sperm/Fertility Studies)

A scientific benchmark of 0.003 uW/cm2 or three nanowatts per centimeter squared for 'lowest observed effect level' for RFR is based on mobile phone base station-level studies. The Thomas et al, (2008) study shows effects at a LOEL of 0.005 uW/cm2 on adults exposed to short-term cell phone radiation only (it is not a chronic exposure study). Other studies that are relevant are Thomas et al (2010) with a LOEL of 0.003 uW/cm2 and Heinrich et al (2010) with a LOEL of 0.003 uW/cm2. Both studied mixed child/adolescent populations of students, but have short-term test periods (are not chronic exposure studies) and have LOELs of 0.003 uW/cm2. Buchner et al (2012) shows a 0.006 uW/cm2 'effect level' and tests adult populations, but achieves 'chronic' exposure testing criterion (over 18 months). Applying a ten-fold reduction to compensate for the lack of long-term exposure (to provide a safety buffer for chronic exposure) or for children as a sensitive subpopulation yields a 300 to 600 picowatts per square centimeter precautionary action level. This is also equal to a 0.3 nanowatts to 0.6 nanowatts per square centimeter as a reasonable, precautionary action level.

Of the studies that deal with children and base-station level RFR exposures, none studied children exclusively, so the results may dilute out any apparent effects accruing to the younger test subjects. Thomas et al (2010) is a short-term exposure study of children and adolescents 8 to 17 years in age. Heinrich et al (2010) is a further study of the same population of 8 to 17 year olds over the short-term. A 100-fold reduction could be defended as reasonably conservative in this instance.

Behari et al (2006) provides the one sperm study expressed in power density units with a LOEL of 0.00034 uW/cm2. It is a chronic exposure study. The majority of sperm studies with good exposure information are expressed in SARs (W/kg). These range from LOELs of 0.014 (Kumar et al, 2012) to 0.091 W/kg (Atasoy et al, 2012) to 0.43 W/kg (Salama et al, 2008) to 0.795 W/kg (Panagopoulous et al, 2012) to 0.9 W/kg (Kesari et al, 2012). All the other sperm damage or ovarian damage studies have SARs

of greater than 1.0 W/kg (7 more studies). All are short-term studies. There are more sperm damage studies but without any measurements or other specific exposure information. These are studies that place sperm, or mice, or give prenatal exposures to animals close to sources of cell phone radiation. Such studies give weight to the argument that low-intensity RFR exposures can cause damage, but do not help in delineating LOELs because they have no specific exposure numbers, just distances.

Most of the sperm studies and base station studies which have exposures expressed power density (microwatts per square centimeter) have 'effect' levels in the nanowatt range (0.34 nanowatt/cm2 to 100 nanowatt/cm2)*. They include Behari and Kesari, 2006; Buchner and Eger, 2012; Oberfeld et al, 2004; Thomas et al, 2008, 2010; Heinrich et al, 2010; Navarro et al, 2003; and Otitoloju et al 2010. Avendano et al (2012) report that WI-FI exposure from a 4-hr laptop exposure decreased sperm viability and caused DNA fragmentation in human sperm samples (exposure in petri dishes) at 0.5 to 1.0 uW/cm2. The Kundi-Hutter 2009 Pathophysiology Journal review paper of base station studies through 2006 reports an overall NOEL below 0.05 to 0.1 uW/cm2. Overall, the new 2007-2012 power density studies are reporting 'lowest effects levels' two or three orders of magnitude lower than in 2006, down from the microwatt/cm2 range to the nanowatt/cm2 range.

SAR Studies (Sperm Studies and Ovarian Damage with Cell Phone Radiation Exposures)

Studies on male fertility (adverse effects on sperm, on the testes size and morphology, etc) coming from cell phone-in-the-pocket-on-stand-by-mode and wireless laptop studies provide us with a flood of new data showing very low-intensity effects to guide precautionary actions and to educate the public about potential risks to health, fertility and reproduction.

*The RF Color Charts in this Report are a guide to reported biological effects and those RFR levels reported to cause them.

Sperm and fertility studies with 'effects levels' in the 9 microwatt/kg to 80 milliwatt/kg range are Kumar et al (2012) (male infertility) and Aitken et al (2005) (sperm DNA damage). Sperm studies with 'effect levels' in the 90 to 900 milliwatt/kg range are De Iuliis et al (2009) (human sperm cell damage), Salama et al (2008) (decrease in sperm mobility and concentration), Panagopoulous et al (2012) (ovarian damage) and Kesari et al (2012) (sperm damage). Studies from 1 W/kg to 1.8 W/kg that report sperm or reproductive damage are Gul et al (2009) (toxic effect on ovaries), Agarwal et al (2008) (sperm damage), Agarwal et al (2009) (sperm damage) and Yan et al (2007) (deformed sperm cells, disabled for swimming).

The WI-FI laptop study by Atasoy et al (2012) reports that exposures to laptops estimated at 0.091 W/kg increase DNA damage and reduce DNA repair in damaged sperm, and "*raise questions about safety of radiofrequency exposure from WI-FI internet access dvices for growing organisms of reproductive age, with a potential effect on fertility and integrity of germ lines*."

Altered fetal development in mice exposed to RFR at SARs of 0.3 to 60 milliwatt/kg is reported to result in consequent adverse effects on learning and behavior (Aldad et al, 2012). Fragopoulou et al (2009) reported changes at 600 to 900 milliwatts/kg in mouse embryos.

General Approach to Delineating a Precautionary Action Level

As a methodology, is not necessary or wise to use an averaging approach among studies. The technique itself is too vulnerable to weighting problems by the older studies that did not test for effects at the lowest range of exposures to RFR (or did not have the power to assess effects). Averaging also is insensitive in giving proper visibility to important NEW results at the very low-intensity (nanowatt, picowatt and femtowatt/cm2 range). Even when they are averaged together, these studies contribute vanishingly small influence when averaged together with studies of much higher power density to determine a scientific benchmark for harm.

One limitation of the sperm studies using base station-level RFR exposures is that good estimates of exposure are available if sperm are tested outside the body (in petri dishes), but that does not reflect the more realistic situation of sperm exposed in humans themselves (using or carrying a mobile phone near the testes) where exposure estimates are more difficult to determine. So, it is useful and informative to observe the combined results of both in-vivo and ex-vivo studies as a guide. For base station studies on human populations, the quality of exposure assessments is variable, and in some cases inadequate. Further, very few base station studies are conducted so that test subjects do not know if/when they are subjected to elevated RFR (blinded studies), so that some bias may influence results. People often report more ill effects because they are aware of the exposure (from a nearby base station, for example). These variations in quality across the studies, however, do not offset their usefulness in the aggregate for delineating what the lowest observable effect exposures are, and helping to guide decision-making for public health and precautionary actions.

A further concern is that time-averaging of RFR to give a single numeric recommendation for a precautionary action guideline does not address the critical difference between peak power levels (RFR spikes that occur intermittently) and measurements that hide how high peak power spikes are by dilution. Biological responses can last over seconds of time, or have even longer effects on proteins and enzymes, while the RFR pulses may be in microseconds or milliseconds in duration. It is entirely possible that what causes bioeffects is the high, intermittent RFR spikes that the body perceives and responds to as one continuous, high-power assault. For example, the DECT phone peak power is about 100 times larger than what RFR is measured with time-averaging. A person near a cell tower that produces an RFR measurement of 0.1 microwatts/cm2 is probably getting RFR power density spikes of eight times higher, if one could measure the spikes individually. None of the studies profiled in this section deal with peak power pulses and biological response times that are longer than the 'intermission' between RFR spikes. Thus, precautionary action levels should err on the side of being conservative.

The planning of base stations, and other site evaluations needs to have a scientific benchmark below which effects have not (not yet) been characterized, published or vetted. Then, a reasonable safety buffer should be added - remembering that the design life of such facilities may be 30-50 years long. This is standard procedure for environmental planning constraints.

Health Agencies Should Act Now

Health agencies and regulatory agencies that set public safety standards for ELF-EMF and RFR should act now to adopt new, biologically-relevant safety limits that key to the lowest scientific benchmarks for harm coming from the recent studies, plus a lower safety margin. Existing public safety limits are too high by several orders of magnitude, if prevention of bioeffects and resulting adverse health effects are to be minimized or eliminated. Most safety standards are a thousand times or more too high for healthy populations, and even less effective in protecting sensitive subpopulations.

New, biologically-based public exposure standards are critically needed now and should key to scientific benchmarks for harm, plus a safety margin below that level.

Standard of Evidence for Judging the Science

The standard of evidence for judging the scientific evidence should be based on good public health principles rather than demanding scientific certainty before actions are taken.

Sensitive Populations Require Special Protections

Safety standards for sensitive populations will need to be set at lower levels than for healthy adult populations to protect the developing fetus, the infant and young child, school-age children, the elderly, those with pre-existing chronic diseases, and those with

developed electrical sensitivity (EHS). Men of child-bearing age should not wear wireless devices on their body in order to protect the integrity of sperm DNA. Sperm should be considered a 'sensitive population'. Scientific benchmarks for lowest effect levels should be identified, and applied with additional safety margin reductions to safeguard populations against excessively high exposure to chronic ELF-EMF and RFR.

Protect Children Against Chronic Exposure to Wireless Devices

Strong precautionary action and clear public health warnings are universally warranted for use of cordless and cell phones to help prevent a global epidemic of brain tumors. This is especially important for children, adolescents and young adults, while new safety standards are established and implemented. Children should not use wireless devices except in the case of emergencies, or be exposed on an involuntary and chronic basis to wireless in their living, sleeping or learning environments.

Common Sense Precautionary Measurees are Warranted Now

Common sense measures to limit both ELF-EMF and RFR in the fetus and newborn infant are needed, especially with respect to avoidable exposures like baby monitors in the crib and baby isolettes (incubators) in hospitals that can be modified; and where education of the pregnant mother with respect to laptop computers, mobile phones and other sources of ELF-EMF and RFR are easily instituted.

Wireless laptops and other wireless devices should be strongly discouraged in schools for children of all ages, and wireless systems already installed should be replaced with wired (cable) alternatives. While without question it is important for children to have access to the internet, wired computer laboratories will have no elevated exposure to RFR. What might be lost in flexibility of moving rooms arounds will be more than gained by reducing exposure to RFR if wired connections, rather than wireless, are used. Pregnant women should be strongly cautioned not to use wireless devices during pregnancy. If a school already has wireless facilities, classrooms without wireless should

be made available to students, teachers and staff during the transition if sensitivities to EMF are reported by the individual. Special education classroom teaching environments should offer wired teaching environments (not wireless), nor should they be exposed to off-site wireless radiofrequency radiation from other sources that elevate interior levels for children.

Special Protections for the Integrity of the Genome and Reproduction

Reducing life-long health risks should begin in the earliest stages of embryonic and fetal development. Development pace is accelerated for the infant and very young child compared to adults, and is not complete in young people (as far as brain and nervous system maturation) until the early 20's. Windows of critical development mean that risk factors once laid down in the cells, or in epigenetic changes in the genome may have grave and life-long consequences for health or illness for every individual, and furthermore these genetic and epigenetic changes may be passed to the next generation. All relevant environmental conditions, including biologically active exposures to EMF and RFR that can degrade the human genome, and impair normal health and development of all species including humans - should be given weight in defining and implementing strong precautionary actions now to protect public health. The consequence of ignoring clear evidence of large-scale health risks to global populations, when the risk factors are largely avoidable or preventable is too high a risk to take.

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SECTION 25

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SECTION 26

Glossary of Terms and Abbreviations

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Absorption. In radio wave propagation, attenuation of a radio wave due to dissipation of its energy, i.e., conversion of its energy into another form, such as heat.

Athermal effect. Any effect of electromagnetic energy on a body that is not a heat-related effect.

Blood–brain barrier. A functional concept developed to explain why many substances that are transported by blood readily enter other tissues but do not enter the brain; the "barrier" functions as if it were a continuous membrane lining the vasculature of the brain. These brain capillary endothelial cells form a nearly continuous barrier to entry of substances into the brain from the vasculature.

Conductance. The reciprocal of resistance. Expressed in siemens (S).

Conductivity: A property of materials that determines the magnitude of the electric current density when an electric field is impressed on the material.

Continuous wave. A wave whose successive oscillations are identical under steady-state conditions.

Current density. A vector of which the integral over a given surface is equal to the current flowing through the surface; the mean density in a linear conductor is equal to the current divided by the cross-sectional area of the conductor. Expressed in ampere per square metre (A $m^{!2}$).

Depth of penetration. For a plane wave electromagnetic field (EMF), incident on the boundary of a good conductor, depth of penetration of the wave is the depth at which the field strength of the wave has been reduced to 1/e, or to approximately 37% of its original value.

Dielectric properties: In the context of this document the properties of materials conductivity and permeability.

Dosimetry. Measurement, or determination by calculation, of internal electric field strength or induced current density, of the specific energy absorption, or specific energy absorption rate distribution, in humans or animals exposed to electromagnetic fields.

Electric field strength. The force (**E**) on a stationary unit positive charge at a point in an electric field; measured in volt per metre (V $m^{!1}$).

Electrosensitivity (Electrohypersensitivity): A working definition of EHS from Bergqvist et al. (1997) is "a phenomenon where individuals experience adverse health effects while using or being in the vicinity of devices emanating electric, magnetic or electromagnetic fields (EMFs)".

Electromagnetic energy. The energy stored in an electromagnetic field. Expressed in joule (J).

Electric field strength (E): The magnitude of a field vector at a point that represents the force (F) on a charge (q). E is defined as E = F/q and is expressed in units of Volt per meter (V/m).

Electromagnetic field: Electromagnetic phenomena expressed in vector functions of space and time.

Electromagnetic radiation: The propagation of energy in the form of electromagnetic waves through space.

EMF. Electric, magnetic, and electromagnetic fields.

Exposure: Exposure occurs wherever a person is subjected to electric, magnetic or electromagnetic fields or contact currents other than those originating from physiological processes in the body.

Extra low frequency (ELF): Extra low frequency fields include, in this document, electromagnetic fields from 1 to 300 Hz. Alternately, **ELF-** Extremely low frequency where the European convention is extremely low frequncy, US is extra-low frequency.

Frequency modulation (FM): Frequency Modulation is a type of modulation representing information as variations in the frequency of a carrier wave. FM is often used at VHF frequencies (30 to 300 MHz) for broadcasting music and speech.

Far field. The region where the distance from a radiating antenna exceeds the wavelength of the radiated EMF; in the far-field, field components (**E** and **H**) and the direction of propagation are mutually perpendicular, and the shape of the field pattern is independent of the distance from the source at which it is taken.

Frequency. The number of sinusoidal cycles completed by electromagnetic waves in 1 second; usually expressed in hertz (Hz).

Impedance, wave. The ratio of the complex number (vector) representing the transverse electric field at a point to that representing the transverse magnetic field at that point. Expressed in ohm (S).

Magnetic flux density (B): The magnitude of a field vector at a point that results in a force (F) on a charge (q) moving with the velocity (v). The force F is defined by F = q*(v x B) and is expressed in units of Tesla (T).

Magnetic field strength (H): The magnitude of a field vector that is equal to the magnetic flux density (B) divided by the permeability (μ) of the medium. H is defined as H = B/μ and is expressed in units of Ampere per metre (A/m).

Magnetic permeability. The scalar or vector quantity which, when multiplied by the magnetic field strength, yields magnetic flux density; expressed in henry per metre ($H\ m^{-1}$). *Note:* For isotropic media, magnetic permeability is a scalar; for anisotropic media, it is a tensor quantity.

Microwaves: Microwaves are defined in the frame of this expertise as electromagnetic waves with wavelengths of approximately 30 cm (1 GHz) to 1 mm (300 GHz).

Milligauss (mG): A milligauss is a measure of ELF intensity and is abbreviated mG. This is used to describe electromagnetic fields from appliances, power lines, interior electrical wiring.

Milliwatt (mW): A unit of power equal to 10^{-3}.

Microwatt (uW): A unit of power equal to 10^{-6}

Microwatts per centimeter squared (µW/cm2)

Radiofrequency radiation in terms of power density is measured in microwatts per centimeter squared and abbreviated (µW/cm2). It is used when talking about emissions from wireless facilities, and when describing ambient RF in the environment. The amount of allowable RF near a cell tower is 1000 µW/cm2 for some cell phone frequencies, for example.

Nanowatt (nW): A unit of power equal to 10^{-9} Watt.

Non – thermal effects (or athermal effects): An effect which can only be explained in terms of mechanisms other than increased molecular motion (i.e. heating), or occurs at absorbed power levels so low, that a thermal mechanism seems unlikely, or displays so unexpected a dependence upon some experimental variable that it is difficult to see how heating could be the cause.

Near field. The region where the distance from a radiating antenna is less than the wavelength of the radiated EMF. *Note:* The magnetic field strength (multiplied by the impedance of space) and the electric field strength are unequal and, at distances less than one-tenth of a wavelength from an antenna, vary inversely as the square or cube of the distance if the antenna is small compared with this distance. Near field exposures are unreliable for estimation of exposures by calculation. The can zero out or be additive and nearly infinite, thus creating problems for exposure assessment.

Non-ionizing electromagnetic radiation (NIER). Includes all radiations and fields of the electromagnetic spectrum that do not normally have sufficient energy to produce ionization in matter; characterized by energy per photon less than about 12 eV, wavelengths greater than 100 nm, and frequencies lower than 3×10^{15} Hz.

Occupational exposure. All exposure to EMF experienced by individuals in the course of performing their work. Safety limits are five times higher for allowable occupational exposures than for general public exposures in the US.

Permeability (µ): A property of materials that indicates how much polarisation occurs when an electric field is applied.

Permittivity. A constant defining the influence of an isotropic medium on the forces of attraction or repulsion between electrified bodies, and expressed in farad per metre ($F\ m^{!1}$); *relative permittivity* is the permittivity of a material or medium divided by the permittivity of vacuum.

Public Exposure. All exposure to EMF experienced by the general public excluding exposure during medical procedures and occupational work environments. Public exposure limits in the US are five times lower than for occupational exposures, where informed consent by employees is required.

Power Density. The power as measured in free space (ambient) as opposed to measured by SAR or specific absorption rate (within tissues or the body). The unit of measurement can be watts per square meter, milliwatts per square meter or microwatts per centimeter squared. Radiofrequency (RF). Any frequency at which electromagnetic radiation is useful for telecommunications, or broadcasting for radio and television. Frequency range is usually defined as 300 Hz (300 hertz) to 300 GHz (300 gigahertz).

Radiofrequency (RF): The frequencies between 100 kHz and 300 GHz of the electromagnetic spectrum.

Reasonance. The change in amplitude occurring as the frequency of the wave approaches or coincides with a natural frequency of the medium; whole body absorption of electromagnetic waves presents its highest value, i.e., the reasonance. for frequencies (in MHz or megahertz) corresponding to approximately 114/L where L is the height of the individual in meters. Reasonance can also be applicable to organs, tissues, or other body parts.

Specific Absorption Rate (SAR is measured in watts per kilogram or W/Kg)
SAR stands for specific absorption rate. It is a calculation of how much RF energy is absorbed into the body, for example when a cell phone or cordless phone is pressed to the head. SAR is expressed in watts per kilogram of tissue (W/Kg). The amount of allowable energy into 1 gram of brain tissue from a cell phone is 1.6 W/Kg in the US. For whole body exposure, the exposure is 0.8 W/Kg averaged over 30 minutes for the general public. International standards in most countries are similar, but not exactly the same.

Static electric field: Static fields produced by fixed potential differences.

Static magnetic fields: Static fields established by permanent magnets and by steady currents.

VDU: Video display units for computers, videos, TV and some measurement devices using cathode ray tubes

WI-FI: Stands for wireless fidelity. WI-FI systems create zones of wireless RF that allow access to wireless internet for computers, internet phone access and other wireless services. Access points that provide WI-FI to access Land Area Networks (LANs) can be installed on streets (for city-wide coverage) or indoors in buildings, Restaurants, hotels, coffee shops, airports, malls and other commercial enterprises are widely installing WI-FI. The range of typical WI-FI systems is about 300 feet.

WI-MAX: Stands for "Wireless interoperability for Microwave Access" and is a telecommunications technology aimed at providing wireless data over long distances. Like WI-FI, WI-MAX systems are designed to provide wireless access but over much broader geographic areas, with some systems transmitting signal up to 10 miles. Higher levels of RF are produced at the wireless transmission facilities than for WI-FI.s

Section 20 LIST OF ABBREVIATIONS

µT	microtesla
µW	microwatt
AC	Alternating current
ALS	Amyotrophic Lateral Sclerosis
AM	Amplitude modulation
B	Magnetic flux density
BBB	Blood-Brain-Barrier
CENELEC	European Committee for Electrotechnical Standardization
CI	Confidence Interval
CNS	Central Nervous System
CW	Continuous wave
DC	Direct current
DECT	Digital Enhanced Cordless Telephone
DMBA	7,12-dimethylbenz[a]anthracene
DNA	Deoxyribonucleic acid
EEG	Electroencephalogram
EHS	Electromagnetic hypersensitivity
ELF	Extra low frequency (also ELF-EMF)
EMF	Electromagnetic field
FM	Frequency Modulation
GSM	Global System for Mobile Communication
H	Magnetic field strength
HSP	Heat-shock proteins (stress proteins)
Hz	Frequency in Hertz
IARC	International Agency for Research on Cancer
IL	Interleukin
kg	Kilogram
kHz	Kilohertz
kV	Kilovolt
MF	Magnetic Field (sometimes MF-ELF)
MHz	Megahertz
ms	Milliseconds
mT	Millitesla
mG	Milligauss
mW	Milliwatt
nT	Nanotesla

nW Nanowatt

NRPB National Radiation Protection Board (HPA)

OR Odds Ratio (measure of increased risk of disease)

REFLEX European Research Program for Radiofrequency Hazards

RF Radiofrequency Radiation (also written as RFR or RF-EMF)

SCENIHR Scientific Committee on Emerging and Newly Identified Health Risks

TNO Nederlandse Onderzoek (Netherlands Organisation Applied Scientific Research

UMTS Universal Mobile Telephony System **UNEP** United Nations Environmental

VDT Video display terminal (VDU – for computers, videos, TV, that use cathode ray tubes).

Wi-Fi Short for wireless fidelity – wireless internet access - works for short- distances for cell phone and laptop computer access without wires.

WLAN Wireless Local Area Network (wireless internet coverage usually up to 300' provided by access points that create elevated radiofrequency radiation for that service zone

WiMAX Worldwide Interoperability for Microwave Access (wireless service up to 10 miles in comparison to Wi-Fi that may serve 300' area)

WHO World Health Organisation

FCC The Federal Communications Commission (FCC) is an independent United States government agency, created, directed, and empowered by Congressional statute to oversee the regulation of radio and TV broadcasting and wireless technologies. It is not a health agency.

HPA Health Protection Agency (UK) that was formerly the National Radiation Protection Division Board). The Health Protection Agency (HPA) is an independent body that protects the health and well-being of the population. The Agency plays a critical role in protecting people from infectious diseases and in preventing harm when hazards involving chemicals, poisons or radiation occur.

DNA Deoxyribonucleic acid, or DNA is a nucleic acid molecule that contains the genetic instructions used in the development and functioning of all living things.

Melatonin Melatonin is a hormone produced in the brain by the pineal gland, It is a potent anti-oxidant that protects against oxidative damage from free radicals that can cause DNA damage.

Alzheimer's Alzheimer's disease is a progressive brain disorder that gradually destroys a person's memory and ability to learn, reason, make judgments, communicate and carry out daily activities. As Alzheimer's progresses, individuals may also experience changes in personality and behavior, such as anxiety, suspiciousness or agitation, as well as delusions or hallucinations.

RFIAWG Radiofrequency Interagency Working Group (US) composed of members from federal agencies with some interest in radiofrequency radiation issues. This Working Group was made up of representatives from the US government's National Institute for Occupational Safety and Health (NIOSH), the Federal Communications Commission (FCC), Occupational Health and Safety Administration (OSHA), the Environmental Protection Agency (US EPA), the National Telecommunication and Information Administration, and the US Food and Drug Administration (FDA).

ICNIRP International Commission on Non-Ionizing Radiation. It is a body of independent scientific experts consisting of a main Commission of 14 members, 4 Scientific Standing Committees covering Epidemiology, Biology, Dosimetry and Optical Radiation and a number of consulting experts. This expertise is brought to bear on addressing the important issues of possible adverse effects on human health of exposure to non-ionising radiation.

SECTION 27

Appendix 20-A Average Residential Exposures to ELF (Power Frequency Fields)

Prepared for the BioInitiative Working Group

July 2007

What are Ambient ELF and RF Levels?

A nation-wide survey in the United States by Zaffanella et al (1993) collected engineering data on sources and levels of 60 Hz electric power magnetic fields that exist inside residences in the United States.

Approximately 1000 residences were randomly selected for the survey. The goals were to 1) identify all significant sources of magnetic field, 2) estimate for each source the percentage of residences where magnetic fields exceeded specified levels, 3) to determine the relation between magnetic field and sources and 4) to characterize the field varations in time.

The median field was identified as 0.5 mG and the average field was 0.9 mG. Thus, this confirms that average residential magnetic fields based on the 1000-home study is less than 1 mG.

Appliances produce magnetic fields but these diminish rapidly with distance (at $1/R^3$),

Power lines generally produce the largest average residential magnetic field when the entire living space of a residence and a 24-hour period are considered. Power line magnetic field exceeds 1 mG in 17%, exceed 2.5 mG in 9.5% and exceed 5 mG in 0.3% of all the residences surveyed.

Zaffanella (1998) conducted measurements to characterize typical EMF exposure levels in persons living in the United States - a study called the 1000-Person Study. Table A-S.2 shows that about half of all people in the US have EMF exposures at home under 0.75 mG; in bed are 0.48 mg; at school 0.60 mG; at work 0.99 mG; and 0.87 mG is the median EMF exposure for an average 24-hour day.

Table A-S.2

Table S.2 Descriptive Statistics for Different Activity Periods

Parameter	Home not in Bed	In Bed	Work	School	Travel	24-Hour
Number of Valid Data Sets	1011	996	525	139	765	1012
1st Percentile	0.10 mG	0.01 mG	0.14 mG	0.13 mG	0.13 mG	0.18 mG
5th Percentile	0.20 mG	0.08 mG	0.24 mG	0.18 mG	0.29 mG	0.27 mG
10th Percentile	0.27 mG	0.12 mG	0.30 mG	0.29 mG	0.41 mG	0.35 mG
25th Percentile	0.44 mG	0.24 mG	0.60 mG	0.35 mG	0.66 mG	0.51 mG
50th Percentile	0.75 mG	0.48 mG	0.99 mG	0.60 mG	0.98 mG	0.87 mG
75th Percentile	1.39 mG	1.24 mG	1.78 mG	1.01 mG	1.46 mG	1.41 mG
90th Percentile	2.49 mG	2.44 mG	3.32 mG	1.64 mG	2.18 mG	2.38 mG
95th Percentile	3.89 mG	3.63 mG	5.00 mG	1.77 mG	2.73 mG	3.38 mG
99th Percentile	9.50 mG	9.19 mG	13.5 mG	3.55 mG	5.43 mG	6.16 mG
Mean	1.29 mG	1.11 mG	1.73 mG	0.82 mG	1.22 mG	1.25 mG
Standard Deviation	2.54 mG	2.06 mG	3.09 mG	0.70 mG	0.99 mG	1.51 mG
Geometric Mean	0.80 mG	0.52 mG	1.03 mG	0.64 mG	0.96 mG	0.89 mG
Geometric Standard Deviation	2.50	3.52	2.57	2.06	2.03	2.18

In Sweden, Mild et al (1996) report that overall mean residential ELF exposures are 0.4 mG, and in Norway are 0.13 mG.

Average Occupational Exposures to ELF

Average occupational exposures in commercial office buildings are 1-2 mG or less and have been reported fairly consistently across numerous studies of exposure assessment (Table 1). Powerline and electrical workers have higher average occupational exposures from 10 mG to 16.6 mG.

Table A-2: Average Occupational Exposures to ELF

EMF RAPID Program – Questions and Answers, NIEHS, June 2002	
Office buildings (median)	0.6 mG
Support staff	0.5 mG
Professional staff	0.6 mG
Maintenance staff	0.6 mG
Visitors	0.6 mG
EMF RAPID Program Engineering Project #3 Executive Summary, May 1996	
Office building (average)	0.7 mG
Office building (median)	0.4 mG
Electric and Magnetic Field Fundamentals (EPRI Resource Paper, March 1994)	
Typical magnetic fields in offices	1 – 2 mG
Power line workers	10 mG
Occupational EMF Exposure Assessment (EPRI Resource Paper, February 1994)	
Office Worker Comparison Group	1.6 mG
All Occupationally Exposed Utility Workers	16.6 mG
Table 7 – Other Studies Cited	
Bracken Study (1990)	1.0 mG
Deadman Study (1988)	1.6 mG
Bowman Study (1992)	0.9 – 1.8 mG

Limits on Operation of Sensitive Electronic Equipment

Companies that manufacture or use equipment in nanotechnology and biotechnology and found 1.0 mG is generally the limit for proper operation of electron beam devices (mass spectrometers, scanning electron microscopes, lithography, etc) used in these technologies. Ten (10) milligauss (mG) is the EMF limit for normal computers – above 10 mG can introduce "computer jitter" and other problems.

What are Ambient Radiofrequency Radiation/Microwave Levels?

Prior to the rapid development of wireless communications for personal and business usage, RF power density levels were primarily related to AM, FM and television broadcasting signal in both urban and rural areas of the United States. Microwave frequencies used for wireless communications were negligible.

Original extra-planetary sources of microwave radiation were infinitesimally small, on the order of a billionth of a microwatt per centimeter squared (10^{-12} uW/cm^2). Human evolution took place without any appreciable exposure to microwave radiation from background sources. The human body has no evolutionary protection against microwave radiation, as it does for ultraviolet radiation from the sun (Johannson, 2000). Wireless voice and communications have introduced unprecedented levels of public exposure in the last decade.

Mantiply (1997) measured and reported common sources and levels of RF in the environment. He identified areas near cellular base stations on the ground near towers to be from 0.003 to 0.3 μW/cm2. Background level ambient RF exposures in cities and suburbs in the 1990's were generally reported to be below 0.003 μW/cm2.

Hamnerius (2000) reported that ambient RF power density measurements in twelve (12) large cities in Sweden were roughly ten times higher than in the United States for equivalent measurement locations by Mantiply in 1978 (when no cellular phone service existed in the US). He reported a total mean value of 26 measured sites in the study was 0.05 μW/cm2 and the median value was 40 μW/cm2. An office location with a base station nearby at about 300 feet distance tested 150 μW/cm2. A train station with antennas mounted indoors tested at about 3 μW/cm2. Both indoor and outdoor ambient RF power density measurements showed high variability depending on proximity to transmitting antennas.

Sage Associates reported on microwave frequency RF power density levels at outdoor locations both near and far from wireless antenna sites in the United States (Sage, 2000). Within the first 100-300 feet, power density levels have been measured at 0.01 to 3.0 μW/cm2. Elevated RF power density levels from a major wireless antenna site can often be detected at 1000 feet or more. Power density levels away from wireless antenna sites measure between 0.001 μW/cm2 to 0.000001 μW/cm2. Vegetation often reduces signal (and therefore the reach of elevated RF exposures) but dry building materials used to visually screen wireless sites do not appreciably diminish signal transmission. Therefore, many sites that are "out-of-sight" because of stealth design can still produce elevated RF levels in nearby areas where people live, work and go to

school. For purposes of this evaluation, a 10 dB attenuation has been incorporated to take building material shielding effects into account.

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APPENDIX 20-B

STANDARDS OF EVIDENCE FOR DECISIONMAKING DIFFERS AMONG PROFESSIONS

There is a large difference between what constitutes causal evidence for purposes of achieving scientific consensus, what constitutes sufficient evidence for purposes of interim public health policy, and what constitutes "a more likely than not" case. A central confusion in this debate is whether prudent policy and public health decisions necessarily require conclusive scientific evidence first. This is not the case. The state of the science needs to be presented in an understandable and scientifically accurate manner, but prudent public health actions do not and should not require 100% proof of harm. In fact, precautionary and preventative actions are specifically justified at a point in time before scientific proof is established. If the growing weight of evidence is positive (although all studies need not report positive effects) then it may be essential to take preventative actions and implement policies that are protective of public health, safety and welfare rather than wait for absolute certainty. The following discussion is presented to highlight some of the main differences in professional approach and traditional ways of viewing and interpreting scientific evidence. In reality, the basis for taking action (preventative or precautionary action) is a continuum – there are no hard and fast rules. The bar for Public Health Policy may be higher or lower than shown in Figure 2; based on many factors, including how widespread the risk, how dread the disease, the cost of inaction (doing nothing until there is proof, but many may be harmed), etc.

A. Scientific Standard of Evidence

There are several levels of proof for adverse effects of environmental exposures. The most rigorous is a scientific standard, where virtual proof of causation is typically required by scientists to arrive at consensus about an effect. This approach works best in physics and chemistry. In biological systems this is rarely possible.

In this case, the 'scientific standard' refers to the overall evidence that the science community typically requires before rendering opinions on the strength of evidence, and what evidence they believe is necessary to establish a causal link (proof).

Figure 1 shows Standards of Evidence that are routinely employed by various interest groups in the EMF debate (Sage, 1997). It can be used to focus on various accepted standards for evidence that are legitimately used by scientific and professional groups to determine when an action is appropriate. The varying levels of certainty about an outcome will dictate different decision-making among different groups that may all be appropriate given their professional charge. Even though the evidence required to make a scientific determination about causality has a far higher standard than a legal determination on the 'weight of the evidence' or 'preponderance of evidence' (a legal standard), neither negates the correctness of the other in its proper jurisdiction. Scientists typically want all possible evidence (animal, cell and epidemiological studies, with replications) showing a high degree of consistency. This can generally be described as a 95% to

99% degree of certainty before drawing conclusions (it does not refer to the 95% confidence interval in epidemiology, except as a part of the overall proof).

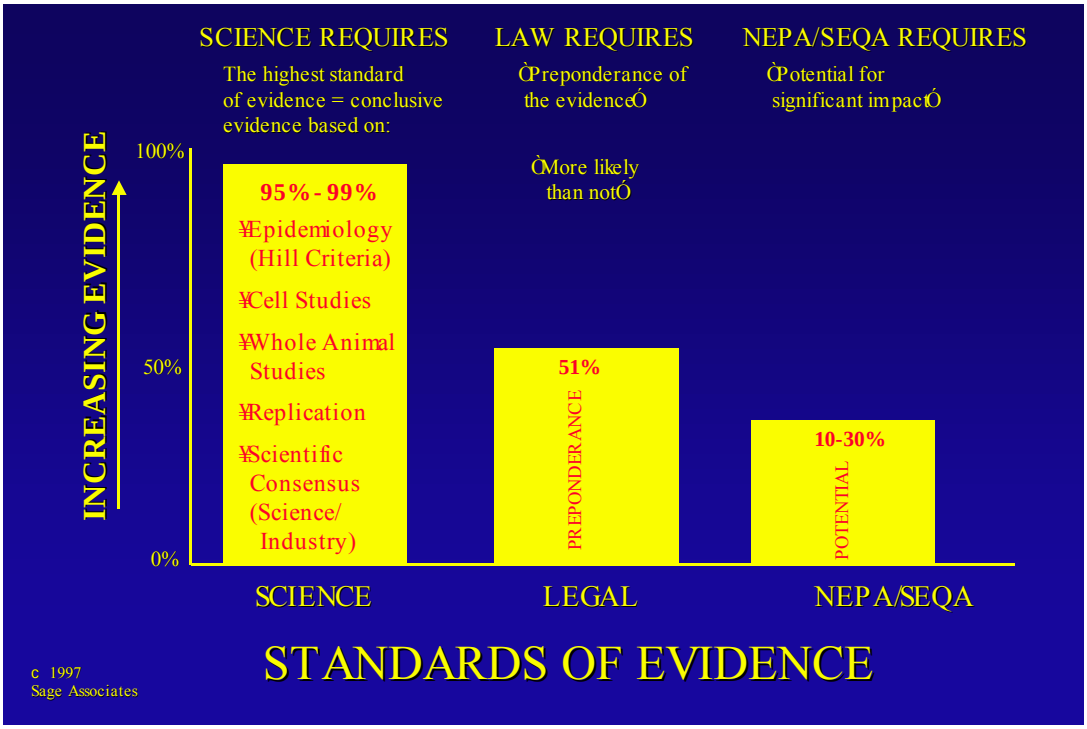

Figure 1 Variable Standards of Evidence (By Profession)

B. Legal Standard of Evidence

The second level of proof is the standard applied in legal proceedings, which is 'more likely than not' or 'preponderance of the evidence' (Figure 1). This is to say if there is a 50%+ likelihood of harm, this is taken as evidence for a relationship (Sage, 1997). At least this level of evidence is reached for the studies of adult cancer and neurodegenerative diseases and 50/60 Hz magnetic field exposures. As with childhood leukemia, while we have documented associations, this does not necessarily indicate causation. Failure to meet either the scientific or the legal standard of proof does not mean that there is no relationship between exposure and disease. In the case of EMF exposure, where everyone is exposed, the societal implications may be huge if there is a real risk whose magnitude has simply just not yet been clarified. Public policies are needed to address this issue of decision-making in the face of this scientific uncertainty.

C. Environmental Protection Standard of Evidence

National and state environmental quality acts (The National Environmental Policy Act) and various state environmental quality acts (SEQA) require that assessments use a standard of "potential for a significant impact on the environment which is a relatively low level of certainty (10% to 30%). The potential for a significant impact requires that mitigation strategies be developed, i.e, require precautionary or preventative actions when only the potential for risk is present (Figure 1).

For example, the potential for risk to humans from building on an active earthquake fault will require a finding of potentially significant impact, and will require mitigative action; even when there is no certainty (no causal evidence) that the fault will rupture and cause damage within the design lifetime of the building. Proof of harm is not a pre-condition for taking action, and the level of certainty is low in comparison to a scientific or legal standard of certainty. Nonetheless, each standard has validity, and will have a different level of evidence required to take action. What decision-makers need to address is what standard of evidence is appropriate now to guide them with respect to EMF exposures that are clearly of environmental and public health concern.

D. Public Health Standard of Evidence

The prudent approach from a public health point of view is to take preventive actions as if causation had been proven, while at the same time to continue to search for mechanisms of action. In the case of childhood leukemia and ELF exposure there is a consistent and statistically significant association in most studies, while for many of the other diseases the results are less consistent although strong associations are found in some studies (Figure 2). This bar graph should be considered illustrative only, since the level of certainty may be higher or lower (above or below 50%) depending on the circumstances of the potential risk, and costs of those risks to society.

Whether magnetic fields actually cause childhood leukemia and the other cancers and neurological diseases documented in this Report; or whether it is some other component in the electromagnetic environment that is responsible for the association is a subject of debate within the scientific community, but from a public health point of view it doesn't matter. The fact that there are unknowns does not negate or override the ultimate public health responsibility, which is to protect the population from exposures which cause disease. Those who make public health decisions, as well as policymakers who rely on them and who approve construction of new schools and homes near power lines, those who provide insurance or financing of new construction, those who must choose siting routes for new electrical facilities all face making decisions with some uncertainty about the potential health risks from EMF exposure. Important social issues must often be decided on the basis of incomplete or uncertain scientific information.

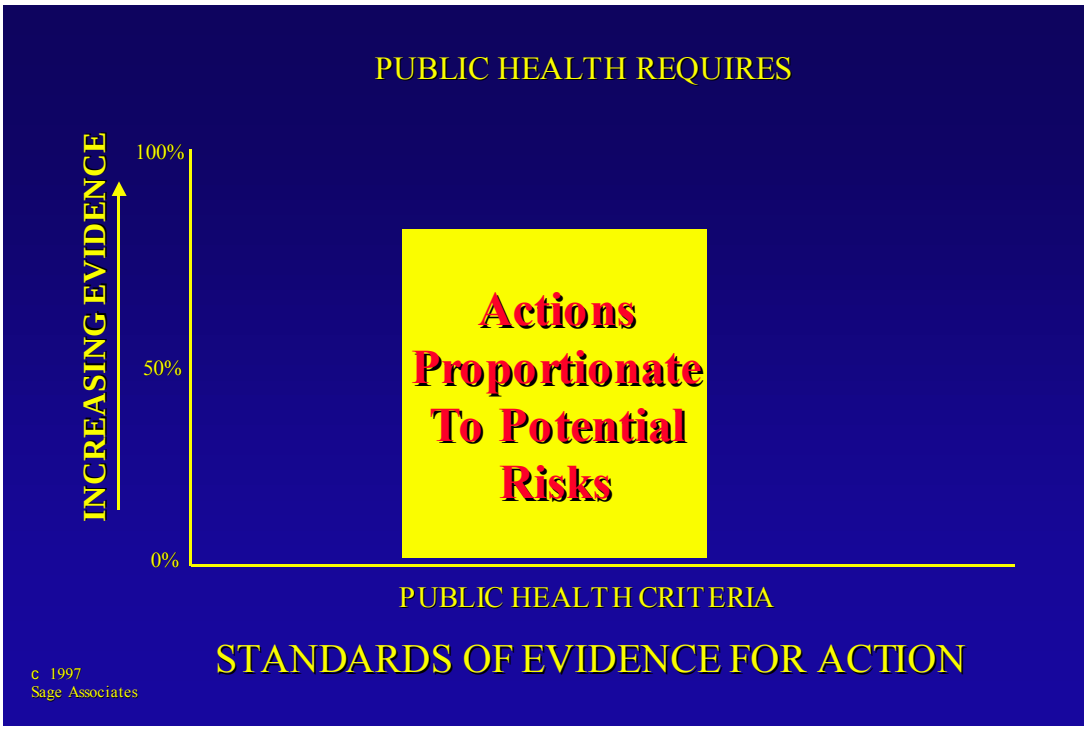

Figure 2 **Public Health Standard of Evidence for Decisions**

Acknowledgements

The BioInitiative Working Group gratefully acknowledges the many independent scientists, researchers and experts who have labored, some for decades - many of whom are no longer with us - to bring this body of science into the public arena. There would be no BioInitiative without their perseverance and generous contributions of intellect and resources.

We deeply appreciate the Santa Barbara Foundation for serving as our fiscal agent. Thanks go to Jan Campbell, Senior Vice President of Philanthropic Services, Communications and Marketing, and to Cheri Savage. Assistant Treasurer of the Santa Barbara Foundation for making this relationship possible. In addition, Mr. Nick Munday gave us brilliant technical help in refining our graphic products.

Web designer Julie Faber of Mountain Studio has our gratitude for her artful guidance in the redesign and layout of the BioInitiative 2012 website. She is both professional and intuitive, helping us communicate complex ideas with precision and flair.

Personally, I am indebted to my husband Dr. Orrin Sage and our family for their encouragement and understanding during the long months of immersion and irregular hours this project demanded. Working with colleagues in time zones spanning Russia, Sweden, Canada, Austria, the Slovak Republic, Italy, Greece, and India makes a 24-hr workday seem normal. Finally, gratitude to Avery, Drake, Ford, Jenner, Luke, Solei, and all the children whose trusting faces remind us that we hold their future in our hands. (Cindy Sage).

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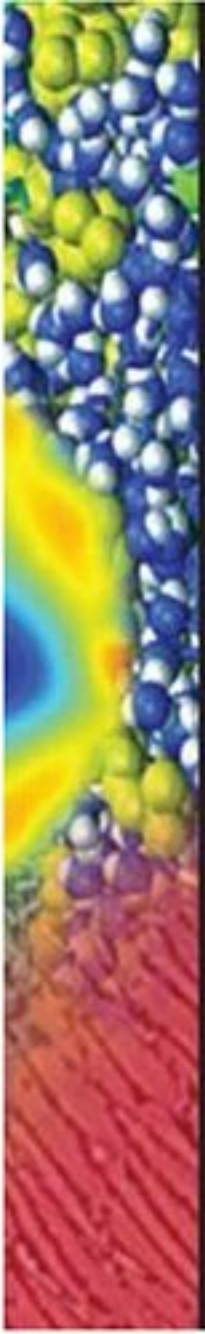

HANDBOOK OF BIOLOGICAL EFFECTS OF ELECTROMAGNETIC FIELDS

THIRD EDITION

Bioengineering and Biophysical Aspects of Electromagnetic Fields

EDITED BY

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Preface

We are honored to have been asked to carry on the tradition established by Dr. Postow and the late Dr. Polk in the first two editions of the *Handbook of Biological Effects of Electromagnetic Fields*. Their editions of this handbook were each recognized as the authoritative standards of their time for scientists working in bioelectromagnetics, the science of electromagnetic field effects on biological systems, and for others seeking information about this field of research.

In revising and updating this edition of the *Handbook of Biological Effects of Electromagnetic Fields*, we have expanded the coverage to include more material on diagnostic and therapeutic applications. At the same time, in updating and expanding the previous editions' coverage of the basic science and studies related to the possible biological effects of the electromagnetic fields, we have added new material on the related physics and chemistry as well as reviews of the recent developments in the setting standards for exposure limits. Following the previous edition's lead, we have charged the authors of the individual chapters with providing the reader, whom we imagine is fairly well founded in one or more of the sciences underlying bioelectromagnetics but perhaps not in the others or in the interdisciplinary subject of bioelectromagnetics itself, with both an introduction to their topic and a basis for further reading. We asked the chapter authors to write what they would like to be the first thing they would ask a new graduate student in their laboratory to read. We hope that this edition, like its two predecessors, will be useful to many as a reference book and to others as a text for a graduate course that introduces bioelectromagnetics or some of its aspects.

As a ''handbook'' and not an encyclopedia, this work does not intend to cover all aspects of bioelectromagnetics. Nevertheless, taking into account the breadth of topics and growth of research in this field since the last edition, we have expanded the number of topics and the number of chapters. Unavoidably, some ideas are duplicated in chapters, sometimes from different viewpoints that could be instructive to the reader; and different aspects of others are presented in different chapters. The increased amount of material has led to the publication of the handbook as two separate, but inter-related volumes: *Biological and Medical Aspects of Electromagnetic Fields (BMA)* and *Bioengineering and Biophysical Aspects of Electromagnetic Fields (BBA)*. Because there is no sharp dividing line, some topics are dealt with in parts of both volumes. The reader should be particularly aware that various theoretical models, which are proposed for explaining how fields interact with biological systems at a biophysical level, are distributed among a number of chapters. No one model has become widely accepted, and it is quite possible that more than one will in fact be needed to explain all observed phenomena. Most of these discussions are in the *Biological and Medical* volume, but the *Bioengineering and Biophysics* volume's chapters on electroporation and on mechanisms and therapeutic applications, for example, also have relevant material. Similarly, the chapters on biological effects of static magnetic fields and on endogenous electric fields in animals could equally well have been in the *Biological and Medical* volume. We have tried to use the index and cross-references in the chapters to direct the reader to the most relevant linkages, and we apologize for those we have missed.

Research in bioelectromagnetics stems from three sources, all of which are important; and various chapters treat both basic physical science and engineering aspects and the biological and medical aspects of these three. Bioelectromagnetics first emerged as a

separate scientific subject because of interest in studying possible hazards from exposure to electromagnetic fields and setting exposure limits. A second interest is in the beneficial use of fields to advance health, both in diagnostics and in treatment, an interest that is as old as the discovery of electricity itself. Finally, the interactions between electromagnetic fields and biological systems raise some fundamental, unanswered scientific questions and may also lead to fields being used as tools to probe basic biology and biophysics. Answering basic bioelectromagnetic questions will not only lead to answers about potential electromagnetic hazards and to better beneficial applications, but they should also contribute significantly to our basic understanding of biological processes. Both strong fields and those on the order of the fields generated within biological systems may become tools to perturb the systems, either for experiments seeking to understand how the systems operate or simply to change the systems, such as by injecting a plasmid containing genes whose effects are to be investigated. These three threads are intertwined throughout bioelectromagnetics. Although any specific chapter in this work will emphasize one or another of these threads, the reader should be aware that each aspect of the research is relevant to a greater or lesser extent to all three.

The reader should note that the chapter authors have a wide variety of interests and backgrounds and have concentrated their work in areas ranging from safety standards and possible health effects of low-level fields to therapy through biology and medicine to the fundamental physics and chemistry underlying the biology. It is therefore not surprising that they have different and sometimes conflicting points of view on the significance of various results and their potential applications. Thus authors should only be held responsible for the viewpoints expressed in their chapters and not in others. We have tried to select the authors and topics so as to cover the scientific results to date that are likely to serve as a starting point for future work that will lead to the further development of the field. Each chapter's extensive reference section should be helpful for those needing to obtain a more extensive background than is possible from a book of this type.

Some of the material, as well as various authors' viewpoints, are controversial, and their importance is likely to change as the field develops and our understanding of the underlying science improves. We hope that this volume will serve as a starting point for both students and practitioners to come up-to-date with the state of understanding of the various parts of the field as of late 2004 or mid-2005, when authors contributing to this volume finished their literature reviews.

The editors would like to express their appreciation to all the authors for the extensive time and effort they have put into preparing this edition, and it is our wish that it will prove to be of value to the readers and lead to advancing our understanding of this challenging field.

Frank S. Barnes
Ben Greenebaum

Editors

Frank Barnes received his B.S. in electrical engineering in 1954 from Princeton University and his M.S., engineering, and Ph.D. degrees from Stanford University in 1955, 1956, and 1958, respectively. He was a Fulbright scholar in Baghdad, Iraq, in 1958 and joined the University of Colorado in 1959, where he is currently a distinguished professor. He has served as chairman of the Department of Electrical Engineering, acting dean of the College of Engineering, and in 1971 as cofounder/director with Professor George Codding of the Political Science Department of the Interdisciplinary Telecommunications Program (ITP).

He has served as chair of the IEEE Electron Device Society, president of the Electrical Engineering Department Heads Association, vice president of IEEE for Publications, editor of the *IEEE Student Journal* and the *IEEE Transactions on Education*, as well as president of the Bioelectromagnetics Society and U.S. Chair of Commission K—International Union of Radio Science (URSI). He is a fellow of the AAAS, IEEE, International Engineering Consortium, and a member of the National Academy of Engineering.

Dr. Barnes has been awarded the Curtis McGraw Research Award from ASEE, the Leon Montgomery Award from the International Communications Association, the 2003 IEEE Education Society Achievement Award, Distinguished Lecturer for IEEE Electron Device Society, the 2002 ECE Distinguished Educator Award from ASEE, The Colorado Institute of Technology Catalyst Award 2004, and the Bernard M. Gordon Prize from National Academy of Engineering for Innovations in Engineering Education 2004. He was born in Pasadena, CA, in 1932 and attended numerous elementary schools throughout the country. He and his wife, Gay, have two children and two grandchildren.

Ben Greenebaum retired as professor of physics at the University of Wisconsin–Parkside, Kenosha, WI, in May 2001, but was appointed as emeritus professor and adjunct professor to continue research, journal editing, and university outreach projects. He received his Ph.D. in physics from Harvard University in 1965. He joined the faculty of UW–Parkside as assistant professor in 1970 following postdoctoral positions at Harvard and Princeton Universities. He was promoted to associate professor in 1972 and to professor in 1980. Greenebaum is author or coauthor of more than 50 scientific papers. Since 1992, he has been editor in chief of *Bioelectromagnetics*, an international peer-reviewed scientific journal and the most cited specialized journal in this field. He spent 1997–1998 as consultant in the World Health Organization's International EMF Project in Geneva, Switzerland. Between 1971 and 2000, he was part of an interdisciplinary research team investigating the biological effects of electromagnetic fields on biological cell cultures. From his graduate student days through 1975, his research studied the spins and moments of radioactive nuclei. In 1977 he became a special assistant to the chancellor and in 1978, associate dean of faculty (equivalent to the present associate vice chancellor position). He served 2 years as acting vice chancellor (1984–1985 and 1986–1987). In 1989, he was appointed as dean of the School of Science and Technology, serving until the school was abolished in 1996.

On the personal side, he was born in Chicago and has lived in Racine, WI, since 1970. Married since 1965, he and his wife have three adult sons.

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Table of Contents

Introduction

Charles Polk*

Revised for the 3rd Edition by Ben Greenebaum

Much has been learned since this handbook's first edition, but a full understanding of biological effects of electromagnetic fields has is to be achieved. The broad range of what must be studied has to be a factor in the apparent slow progress toward this ultimate end. The broad range of disciplines involved includes basic biology, medical science and clinical practice, biological and electrical engineering, basic chemistry and biochemistry, and fundamental physics and biophysics. The subject matter ranges over characteristic lengths and timescales from, at one extreme, direct current (dc) or $\sim 10^4$ km-wavelengths, multimillisecond ac fields and large, long-lived organisms to, at the other extreme, submillimeter wavelength fields with periods below 10^{-12} s and subcellular structures and molecules with subnanometer dimensions and characteristic times as short as the 10^{-15} s or less of biochemical reactions.

This chapter provides an introduction and overview of the research and the contents of this handbook.

0.1 Near Fields and Radiation Fields

In recent years it has become, unfortunately, a fairly common practice—particularly in nontechnical literature—to refer to the entire subject of interaction of electric (E) and magnetic (H) fields with organic matter as biological effects of nonionizing radiation, although fields that do not vary with time and, for most practical purposes, slowly time-varying fields do not involve radiation at all. The terminology had its origin in an effort to differentiate between relatively low-energy microwave radiation and high-energy radiation, such as UV and x-rays, capable of imparting enough energy to a molecule or an atom to disrupt its structure by removing one or more electron\s with a single photon. However, when applied to dc or extremely low-frequency (ELF), the term ''nonionizing radiation'' is inappropriate and misleading.

A structure is capable of efficiently radiating electromagnetic waves only when its dimensions are significant in comparison with the wavelength λ. But in free space $\lambda = c/f$, where c is the velocity of light in vacuum (3×10^8 m/s) and f is the frequency in hertz (cycles/s); therefore the wavelength at the power distribution frequency of 60 Hz, e.g., is 5000 km, guaranteeing that most available human-made structures are much smaller than one wavelength.

The poor radiation efficiency of electrically small structures (i.e., structures whose largest linear dimension $L \ll \lambda$ can be illustrated easily for linear antennas. In free space the radiation resistance, R_r of a current element, i.e., an electrically short wire of length ℓ carrying uniform current along its length [1], is

$$R_r = 80\pi^2 \left(\frac{\ell}{\lambda}\right)^2 \tag{0.1}$$

*Deceased.

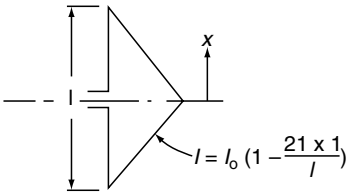

FIGURE 0.1
Current distribution on short, thin, center-fed antenna.

whereas the R_r of an actual center-fed radiator of total length ℓ with current going to zero at its ends, as illustrated in Figure 0.1, is

$$R_r = 20\pi^2 \left(\frac{\ell}{\lambda}\right)^2 \tag{0.2}$$

Thus, the R_r of a 0.01 λ antenna, 50 km long at 60 Hz, would be 0.0197 Ω. As the radiated power $P_r = I^2 R_r$ where I is the antenna terminal current, whereas the power dissipated as heat in the antenna wire is $I^2 R_d$; when I is uniform, the P_r will be very much less than the power used to heat the antenna, given that the ohmic resistance R_d of any practical wire at room temperature will be very much larger and R_r. For example, the resistance of a 50-km long, 1/2-in. diameter solid copper wire could be 6.65 Ω. At dc, of course, no radiation of any sort takes place, as acceleration of charges is a condition for radiation of electromagnetic waves.

The second set of circumstances, which guarantees that any object subjected to low-frequency E and H fields usually does not experience effects of radiation, is that any configuration that carries electric currents sets up E and H field components which store energy without contributing to radiation. A short, linear antenna in free space (short electric dipole) generates, in addition to the radiation field E_r, an electrostatic field E_s and an induction field E_i. Neither E_s nor E_i contribute to the P_r [2,3]. Whereas E_r varies as $1/r$, where r is the distance from the antenna, E_i varies as $1/r^2$, and E_s as $1/r^3$. At a distance from the antenna of approximately one sixth of the wavelength ($r = \lambda/2\pi$), the E_i equals the E_r, and when $r \ll \lambda/6$ the E_r quickly becomes negligible in comparison with E_i and E_s. Similar results are obtained for other antenna configurations [4]. At 60 Hz the distance $\lambda/2\pi$ corresponds to about 800 km and objects at distances of a few kilometers or less from a 60-Hz system are exposed to nonradiating field components, which are orders of magnitude larger than the part of the field that contributes to radiation.

A living organism exposed to a static (dc) field or to a nonradiating near field may extract energy from it, but the quantitative description of the mechanism by which this extraction takes place is very different than at higher frequencies, where energy is transferred by radiation:

1. In the near field the relative magnitudes of E and H are a function of the current or charge configuration and the distance from the electric system. The E field may be much larger than the H field or vice versa (see Figure 0.2).
2. In the radiation field the ratio the E to H is fixed and equal to 377 in free space, if E is given in volt per meter and H in ampere per meter.
3. In the vicinity of most presently available human-made devices or systems carrying static electric charges, dc, or low-frequency (<1000 Hz) currents, the E and H fields will only under very exceptional circumstances be large enough to produce heating effects inside a living object, as illustrated by Figure 0.3. (This statement assumes that the living object does not form part of a conducting path

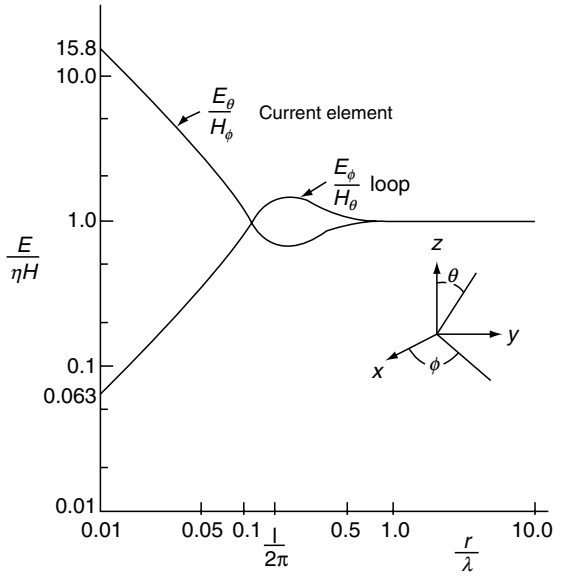

FIGURE 0.2
Ratio of E to H field (divided by wave impedance of free space $\eta = 377\ \Omega$) at $\theta = 90°$; for electric current element at origin along z-axis and for electrically small loop centered at the origin in x–y plane.

that permits direct entrance of current from a wire or conducting ground.) However, nonthermal effects are possible; thus an E field of sufficient magnitude may orient dipoles, or translate ions or polarizable neutral particles (see Chapter 3 and Chapter 4 in *BBA**).

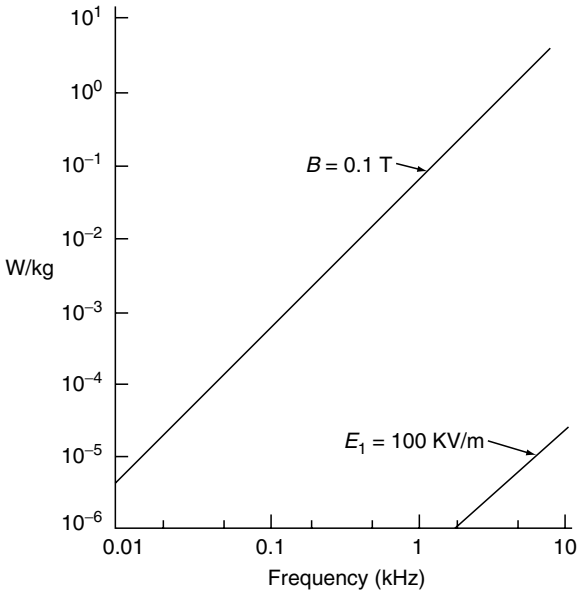

FIGURE 0.3
Top line: Eddy current loss produced in cylinder by sinusoidally time-varying axial H field. Cylinder parameters are conductivity $\sigma = 0.1\,\mathrm{S/m}$, radius 0.1 m, density $D = 1100\,\mathrm{kg/m^3}$, RMS magnetic flux density $0.1\,\mathrm{T} = 1000\,\mathrm{G}$. Watt per kilogram $= \sigma B^2 r^2 w^2 / 8D$; see Equation 0.15 and use power per volume $= J^2/\sigma$, *Lower line:* Loss produced by 60-Hz E field in Watt per kilogram $= \sigma\, E_{\mathrm{int}}{}^2/D$, where external field E_1 is related to E_{int} by Equation 0.9 with $\varepsilon_2 = \varepsilon_0 \times 10^5$ at 1 kHz and $\varepsilon_0 = 8 \times 10^4$ at 10 kHz.

**BBA*: *Bioengineering and Biophysical Aspects of Electromagnetic Fields* (ISBN 0-8493-9539-9); *BMA*: *Biological and Medical Aspects of Electromagnetic Fields* (ISBN 0-8493-9538-0).

4. With radiated power it is relatively easy to produce heating effects in living objects with presently available human-made devices (see Chapter 10 in *BBA* and Chapter 5 in *BMA*). This does not imply, of course, that all biological effects of radiated radio frequency (RF) power necessarily arise from temperature changes.

The results of experiments involving exposure of organic materials and entire living organisms to static E and ELF E fields are described in *BBA*, Chapter 3. Various mechanisms for the interaction of such fields with living tissue are also discussed there and in *BBA*, Chapter 5. In the present introduction, we shall only point out that one salient feature of static (dc) and ELF E field interaction with living organisms is that the external or applied E field is always larger by several orders of magnitude than the resultant average internal E field [5,6]. This is a direct consequence of boundary conditions derived from Maxwell's equations [1–3].

0.2 Penetration of Direct Current and Low-Frequency Electric Fields into Tissue

Assuming that the two materials illustrated schematically in Figure 0.4 are characterized, respectively, by conductivities σ_1 and σ_2 and dielectric permittivities ε_1 and ε_2, we write E-field components parallel to the boundary as E_{P} and components perpendicular to the boundary as $E_{\perp}$. For both static and time-varying fields

$$E_{\mathrm{P1}} = E_{\mathrm{P2}} \tag{0.3}$$

and for static (dc) fields

$$\sigma_1 E_{\perp 1} = \sigma_2 E_{\perp 2} \tag{0.4}$$

as a consequence of the continuity of current (or conservation of charge). The orientations of the total E fields in media 1 and 2 can be represented by the tangents of the angles between the total fields and the boundary line

$$\tan\theta_1 = \frac{E_{\perp 1}}{E_{\mathrm{P1}}}, \quad \tan\theta_2 = \frac{E_{\perp 2}}{E_{\mathrm{P2}}} \tag{0.5}$$

From these equations it follows that

$$\tan\theta_1 = \frac{\sigma_2}{\sigma_1}\frac{E_{\perp 1}}{E_{\mathrm{P1}}} = \frac{\sigma_2}{\sigma_1}\frac{E_{\perp 2}}{E_{\mathrm{P2}}} = \frac{\sigma_2}{\sigma_1}\tan\theta_2 \tag{0.6}$$

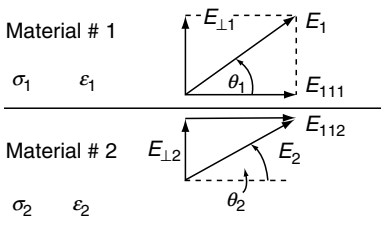

FIGURE 0.4
Symbols used in description of boundary conditions for E-field components.

If material 1 is air with conductivity [7] $\sigma_1 = 10^{-13}$ S/m and material 2 a typical living tissue with $\sigma_2 \approx 10^{-1}$ S/m (compare Chapter 3 in *BBA*), $\tan\theta_1 = 10^{12}\tan\theta_2$, and therefore even if the field in material 2 (the inside field) is almost parallel to the boundary so that $\theta_2 \cong 0.5^\circ$ or $\tan\theta_2 \approx (1/100)$, $\tan\theta_1 = 10^{10}$ or $\theta_1 = (\pi/2 - 10)^{-10}$ radians. Thus an electrostatic field in air, at the boundary between air and living tissue, must be practically perpendicular to the boundary. The situation is virtually the same at ELF although Equation 0.4 must be replaced by

$$\sigma_1 E_{\perp 1} - \sigma_2 E_{\perp 2} = -\mathrm{j}\omega\rho_s \tag{0.7}$$

and

$$\varepsilon_1 E_{\perp 1} - \varepsilon_2 E_{\perp 2} = \rho_s \tag{0.8}$$

where $\mathrm{j} = \sqrt{-1}$, ω is the radian frequency ($= 2\pi \times$ frequency), and ρ_s is the surface charge density. In Chapter 3 in *BBA* it is shown that at ELF the relative dielectric permittivity of living tissue may be as high as 10^6 so that $\varepsilon_2 = 10^6\ \varepsilon_0$, where ε_0 is the dielectric permittivity of free space $(1/36\ \pi)\ 10^{-9}$ F/m; however, it is still valid to assume that $\varepsilon_2 \leq 0^{-5}$. Then from Equation 0.7 and Equation 0.8

$$E_{\perp 1} = \frac{\sigma_2 + \mathrm{j}\omega\varepsilon_2}{\sigma_1 + \mathrm{j}\omega\varepsilon_1} E_{\perp 2} \tag{0.9}$$

which gives at 60 Hz with $\sigma_2 = 10^1$ S/m, $\sigma_1 = 10^{-13}$ S/m, $\varepsilon_2 \approx 10^{-5}$ F/m, and $\varepsilon_1 \approx 10^{-11}$ F/m

$$E_{\perp 1} = \frac{10^{-1} + \mathrm{j}_4 10^{-3}}{10^{-13} + \mathrm{j}_4 10^{-9}} E_{\perp 2} \approx \frac{\sigma_2}{\mathrm{j}\omega\varepsilon_1} = -\mathrm{j}\,(2.5 \times 10^7) E_{\perp 2} \tag{0.10}$$

This result, together with Equation 0.3 and Equation 0.5, shows that for the given material properties, the field in air must still be practically perpendicular to the boundary of a living organism: $\tan\theta_1$: $2.5(10^7)\tan\theta_2$.

Knowing now that the living organism will distort the E field in its vicinity in such a way that the external field will be nearly perpendicular to the boundary surface, we can calculate the internal field by substituting the total field for the perpendicular field in Equation 0.4 (dc) and Equation 0.9 (ELF). For the assumed typical material parameters we find that in the static (dc) case

$$\frac{E_{\text{internal}}}{E_{\text{external}}} \approx 10^{-12} \tag{0.11}$$

$$\rho_f = \frac{3(\sigma_2\varepsilon_1 - \sigma_1\varepsilon_2)E_0}{2\sigma_1 + \sigma_2} \cos\vartheta\ \text{C/m}^2$$

and for 60 Hz

$$\frac{E_{\text{internal}}}{E_{\text{external}}} \approx 4(10^{-8}) \tag{0.12}$$

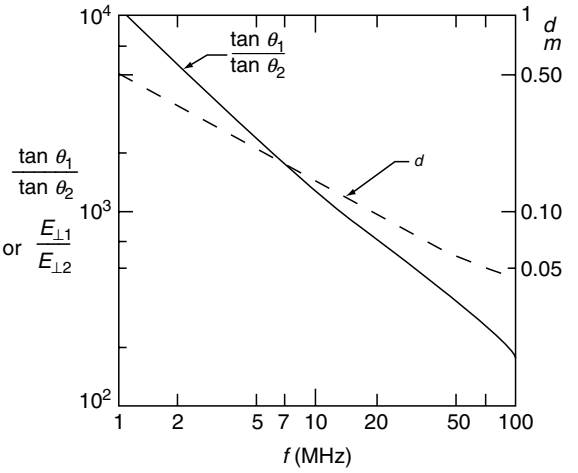

FIGURE 0.5
Orientation of *E*-field components at air–muscle boundary (or ratio of fields perpendicular to boundary); depth (d) at which field component parallel to boundary surface decreases by approximately 50% ($d = 0.6938$).

Thus, a 60-Hz external field of 100 kV/m will produce an average E_{internal} field of the order of 4 mV/m.

If the boundary between air and the organic material consists of curved surfaces instead of infinite planes, the results will be modified only slightly. Thus, for a finite sphere (with ε and σ as assumed here) embedded in air, the ratios of the internal field to the undisturbed external field will vary with the angle θ and distance r as indicated in Figure 0.5, but will not deviate from the results indicated by Equation 0.7 and Equation 0.8 by more than a factor of 3 [3,8]. Long cylinders ($L \ll r$) aligned parallel to the external field will have interior fields essentially equal to the unperturbed external field, except near the ends where the field component perpendicular to the membrane surface will be intensified approximately as above (see Chapter 9 and Chapter 10 in this volume).

0.3 Direct Current and Low-Frequency Magnetic Fields

Direct current H fields are considered in more detail in the Chapter 3, Chapter 5, and Chapter 8 in *BBA*. ELF H fields are considered in various places, including Chapter 5 and Chapter 7 in *BBA* and Chapter 2 and Chapter 11 in *BMA*. As the magnetic permeability μ of most biological materials is practically equal to the magnetic permeability μ_0 of free space, $4\pi(10^{-7})$ H/m, the dc or ELF H field ''inside'' will be practically equal to the H field ''outside.'' The only exceptions are organisms such as the magnetotactic bacteria, which synthesize ferromagnetic material, discussed in Chapter 8 of *BBA*. The known and suggested mechanisms of interaction of dc H fields with living matter are:

1. Orientation of ferromagnetic particles, including biologically synthesized particles of magnetite.
2. Orientation of diamagnetically or paramagnetically anisotropic molecules and cellular elements [9].
3. Generation of potential differences at right angles to a stream of moving ions (Hall effect, also sometimes called a magnetohydrodynamic effect) as a result of the magnetic force $F_{\text{m}} = qvB \sin \theta$, where q is the the electric charge, v is the

velocity of the charge, B is the magnetic flux density, and sin θ is the sine of the angle θ between the directions v and B. One well-documented result of this mechanism is a ''spike'' in the electrocardiograms of vertebrates subjected to large dc H fields.

4. Changes in intermediate products or structural arrangements in the course of light-induced chemical (electron transfer) reactions, brought about by Zeeman splitting of molecular energy levels or effects upon hyperfine structure. (The Zeeman effect is the splitting of spectral lines, characteristic of electronic transitions, under the influence of an external H field; hyperfine splitting of electronic transition lines in the absence of an external H field is due to the magnetic moment of the nucleus; such hyperfine splitting can be modified by an externally applied H field.) The magnetic flux densities involved not only depend upon the particular system and can be as high as 0.2 T (2000 G) but also $<$0.01 mT (100 G). Bacterial photosynthesis and effects upon the visual system are prime candidates for this mechanism [10,11].
5. Induction of E fields with resulting electrical potential differences and currents within an organism by rapid motion through a large static H field. Some magnetic phosphenes are due to such motion [12].

Relatively slow time-varying H fields, which are discussed in the basic mechanisms and therapeutic uses chapters (Chapter 5 of *BBA* and Chapter 11 in *BMA*), among others, may interact with living organisms through the same mechanisms that can be triggered by static H fields, provided the variation with time is slow enough to allow particles of finite size and mass, located in a viscous medium, to change orientation or position where required (mechanism 1 and 2) and provided the field intensity is sufficient to produce the particular effect. However, time-varying H fields, including ELF H fields, can also induce electric currents into stationary conducting objects. Thus, all modes of interaction of time-varying E fields with living matter may be triggered by time-varying, but not by static, H fields.

In view of Faraday's law, a time-varying magnetic flux will induce E fields with resulting electrical potential differences and ''eddy'' currents through available conducting paths. As very large external ELF E fields are required (as indicated by Equation 0.9 through Equation 0.12) to generate even small internal E fields, many human-made devices and systems generating both ELF E and H fields are more likely to produce physiologically significant internal E fields through the mechanism of *magnetic* induction.

The induced voltage V around some closed path is given by

$$V = \oint E \cdot \mathrm{d}\ell = -\int\int \frac{\partial B}{\partial t}\mathrm{d}s \tag{0.13}$$

where E is the induced E field. The integration $\oint E\ \mathrm{d}\ell$ is over the appropriate conducting path, $\partial B/\partial t$ is the time derivative of the magnetic flux density, and the ''dot'' product with the surface element, ds, indicates that only the component of $\partial B/\partial t$ perpendicular to the surface, i.e., parallel to the direction of the vector ds, enclosed by the conducting path, induces an E field. To obtain an order-of-magnitude indication of the induced current that can be expected as a result of an ELF H field, we consider the circular path of radius r, illustrated by Figure 0.6. Equation 0.13 then gives the magnitude of the E field as

$$E = \frac{\omega B r}{2} \tag{0.14}$$

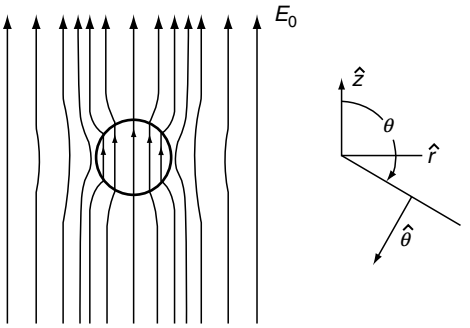

FIGURE 0.6
E field when sphere of radius R, conductivity σ_2, and dielectric permittivity ε_2 is placed into an initially uniform static field ($E = 2E_0$) within a medium with conductivity σ_1 and permittivity ε_1. The surface charge density is $\rho_r = \dfrac{3(\sigma_2\varepsilon_1 - \sigma_1\varepsilon_2)E_0}{2\sigma_1 + \sigma_2}\cos\theta$ C/m^2.

$$r < R \quad \bar{E} = \frac{3\sigma_1 E_0}{2\sigma_1 + \sigma_2}\hat{z} \qquad \varepsilon_2, \sigma_2$$

$$r < R \quad \bar{E} = E_0\cos\theta\left[1 + \frac{2R^3(\sigma_2 \propto \sigma_1)}{r^3(2\sigma_1 + \sigma_2)}\right]\hat{r} \qquad \varepsilon_1, \sigma_1$$

$$- E\sin\theta\left[1 - \frac{R^3(\sigma_2 \propto \sigma_1)}{r^3(2\sigma_1 + \sigma_2)}\right]\hat{\theta}$$

where ω is the $2\pi f$ and f is the frequency. The magnitude of the resulting electric current density J in ampere per square meter is*

$$J = \sigma E = \frac{\sigma\omega B r}{2} \tag{0.15}$$

where σ is the conductivity along the path in Siemens per meter. In the SI (Systeme Internationale) units used throughout this book, B is measured in tesla ($T = 10^4$ G) and r in meters. Choosing for illustration a circular path of 0.1 m radius, a frequency of 60 Hz, and a conductivity of 0.1 S/m, Equation 0.14 and Equation 0.15 give $E = 18.85$ B and $J = 1.885$ B. The magnetic flux density required to obtain a current density of 1 mA/m^2 is 0.53 mT or about 5 G. The E field induced by that flux density along the circular path is 10 mV/m. To produce this same 10 mV/m E_{internal} field by an external 60 Hz E_{external} field would require, by Equation 0.12, a field intensity of 250 kV/m.

As the induced voltage is proportional to the time rate of change of the H field (Equation 0.13), implying a linear increase with frequency (Equation 0.14), one would expect that the ability of a time-varying H field to induce currents deep inside a conductive object would increase indefinitely as the frequency increases; or conversely, that the magnetic flux density required to induce a specified E field would decrease linearly with frequency, as indicated in Figure 0.7. This is not true however, because the displacement current density $\partial D/\partial t$, where $D = \varepsilon E$, must also be considered as the frequency increases. This leads to the wave behavior discussed in Part III, implying that at sufficiently high frequencies the effects of both external E and H fields are limited

*Equation 0.15 neglects the H field generated by the induced eddy currents. If this field is taken into account, it can be shown that the induced current density in a cylindrical shell of radius r and thickness Δ is given by $\Delta r < 0.01$ m$^2/[1 + j\Delta r/\delta^2]$, where $H_0 = B_0/\mu_0$ and δ is the skin depth defined by Equation 0.17 below. However, for conductivities of biological materials ($\sigma < 5$ s/m) one obtains at audio frequencies $\delta > 1$ m and as for most dimensions of interest $\Delta r < 0.01$ m^2 the term $j\Delta r/\delta^2$ becomes negligible. The result $-jrH_0/\delta^2$ is then identical with Equation 0.15.

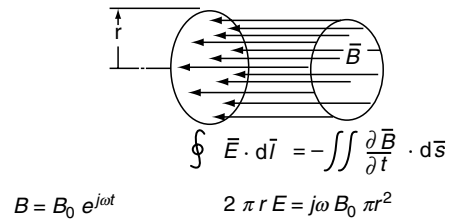

FIGURE 0.7
Circular path (loop) of radius r enclosing uniform magnetic flux density perpendicular to the plane of the loop. For sinusoidal time variation $B = B_0 e^{j\omega t}$.

by reflection losses (Figure 0.8 through Figure 0.10) as well as by skin effect [13], i.e., limited depth of penetration d in Figure 0.5.

0.4 RF Fields

At frequencies well below those where most animals and many field-generating systems have dimensions of the order of one free space wavelength, e.g., at 10 MHz where $\lambda = 30$ m, the skin effect limits penetration of the external field. This phenomenon is fundamentally different from the small ratio of internal to external E fields described in Equation 0.4 (applicable to dc) and Equation 0.9.

Equation 0.9 expresses a ''boundary condition'' applicable at all frequencies, but as the angular frequency ω increases (and in view of the rapid decrease with frequency of the dielectric permittivity ε_2 in biological materials—see Chapter 3 of *BBA*, the ratio of the normal component of the external to the internal E field at the boundary decreases

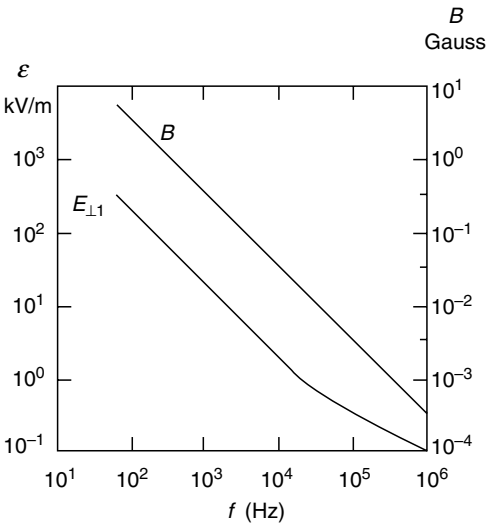

FIGURE 0.8
External E and H field required to obtain an internal E field of 10 mV/m (conductivity and dielectric permittivity for skeletal muscle from Foster, K.R., Schepps, J.L., and Schwan, H.P. 1980. *Biophys. J.*, 29:271–281. H-field calculation assumes a circular path of 0.1-m radius perpendicular to magnetic flux).

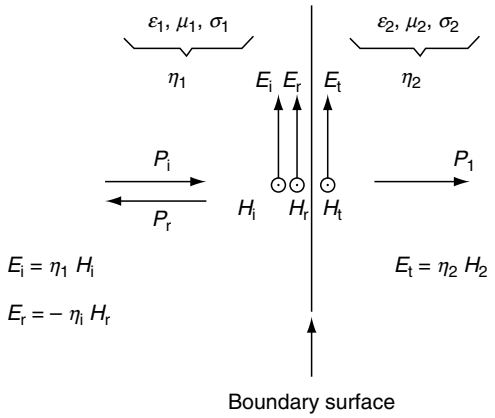

FIGURE 0.9
Reflection and transmission of an electromagnetic wave at the boundary between two different media, perpendicular incidence; P_i = incident power, P_r = reflected power, P_t = transmitted power.

with increasing frequency. This is illustrated by Figure 0.10 where $\tan\theta_1/\tan\theta_2$ is also equal to $E_{\perp 1}/E_{\perp 2}$ in view of Equation 0.3, Equation 0.5, and Equation 0.9. However, at low frequencies the total field inside the boundary can be somewhat larger than the perpendicular field at the boundary; and any field variation with distance from the boundary is not primarily due to energy dissipation, but in a homogeneous body is a consequence of shape. At RF, on the other hand, the E and H fields of the incoming

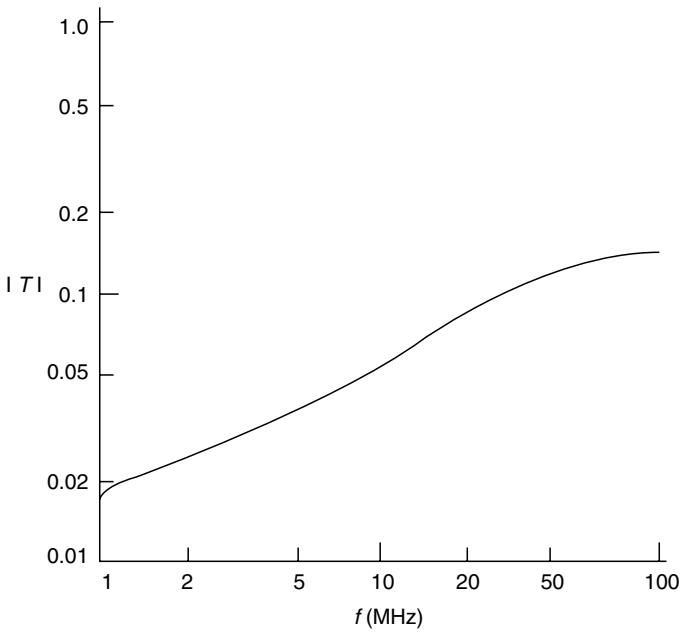

FIGURE 0.10
Magnitude of transmission coefficient T for incident E field parallel to boundary surface. $T = E_t/E_i$: reflection coefficient $r = E_r/E_i = T\text{-}1$. Γ and T are complex numbers; ε_r and σ for skeletal muscle from Chapter 3 in *BBA*.

electromagnetic wave, after reflection at the boundary, are further decreased due to energy dissipation. Both E and H fields decrease exponentially with distance from the boundary

$$g(z) = Ae^{-\frac{z}{\delta}} \tag{0.16}$$

where $g(z)$ is the field at the distance z and A is the magnitude of the field just *inside* the boundary.

As defined by Equation 0.16 the skin depth δ is the distance over which the field decreases to $1/e$ ($= 0.368$) of its value just *inside* the boundary. (Due to reflection, the field A just inside the boundary can already be very much smaller than the incident external field; see Figure 0.8 and Figure 0.9.)

Expressions for δ given below were derived [2,3,13,14] for plane boundaries between infinite media. They are reasonable accurate for cylindrical structures if the ratio of radius of curvature to skin depth (r_0/δ) is larger than about five [13]. For a good conductor

$$\delta = \frac{1}{\sqrt{\pi f \mu \sigma}} \tag{0.17}$$

where a good conductor is one for which the ratio p of conduction current, $J = \sigma E$, to displacement current, $\partial D/\partial t = \varepsilon\,(\partial E/\partial t) = j\omega\varepsilon E$ is large:

$$p = \frac{\sigma}{\omega\varepsilon} \gg 1 \tag{0.18}$$

Since for most biological materials p is of the order of one ($0.1 < p < 10$) over a very wide frequency range (see Chapter 3 of *BBA*), it is frequently necessary to use the more general expression [13]

$$\delta = \frac{1}{\omega\left[\frac{\mu\varepsilon}{2}(\sqrt{1+p^2}-1\right]^{1/2}} \tag{0.19}$$

The decrease of field intensity with distance from the boundary surface indicated by Equation 0.16 becomes significant for many biological objects at frequencies where $r_0/\delta \geq 5$ is not satisfied. However, the error resulting from the use of Equation 0.16 and Equation 0.17 or Equation 0.19 with curved objects is less when $z < \delta$. Thus at $z = 0.693\,\delta$, where $g(z) = 0.5$ A from Equation 0.16 and Equation 0.17, the correct values of $g(z)$, obtained by solving the wave equation in cylindrical coordinates, differs only by 20% (it is 0.6 A) even when r_0/δ is as small as 2.39 [14]. Therefore, Figure 0.10 shows the distance $d = 0.693\,\delta$, at which the field decreases to half of its value just inside the boundary surface, using Equation 0.19 with typical values for σ and ε for muscle from Figure 0.11. It is apparent that the skin effect becomes significant for humans and larger vertebrates at frequencies >10 MHz.

Directly related to skin depth, which is defined for fields varying sinusoidally with time, is the fact that a rapid transient variation of an applied magnetic flux density constitutes an exception to the statement that the dc H field inside the boundary is equal to the H field outside. Thus, from one viewpoint one may consider the rapid application or removal of a dc H field as equivalent to applying a high-frequency field during the switching period, with the highest frequencies present of the order of $1/\tau$, where τ is the rise time of the applied step function. Thus, if $\tau < 10^{-8}$ s, the skin effect will be important during the transient period, as d in Figure 0.5 is <5 cm above 100 MHz. It is also possible to calculate directly the magnetic flux density inside a conducting cylinder as a function of radial position r and time t when a magnetic pulse is applied in the axial

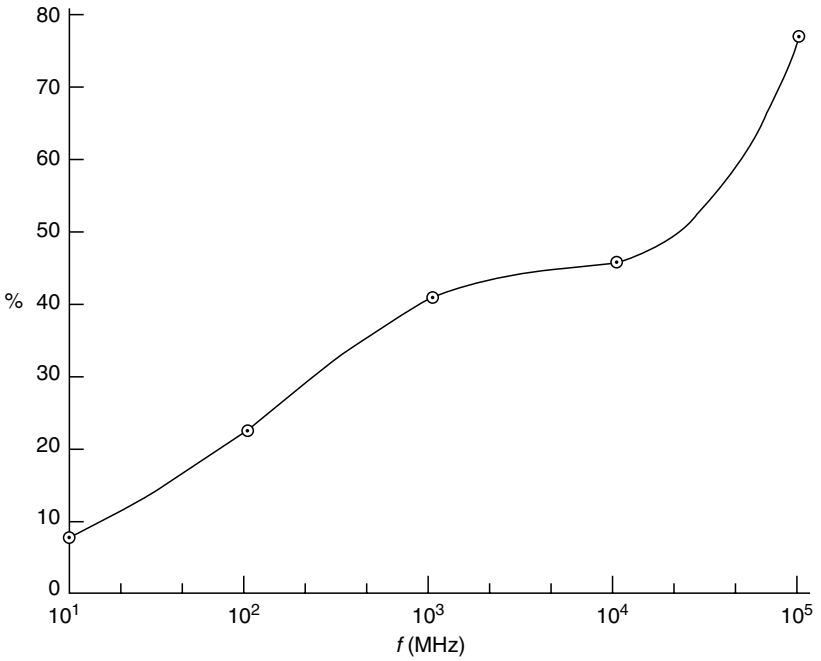

FIGURE 0.11
Ratio of transmitted to incident power expressed as percent of incident power. Air–muscle interface, perpendicular incidence (Equation 0.31, Table 0.1).

direction [15,16]. Assuming zero rise time of the applied field B_0, i.e., a true step function, one finds that the field inside a cylinder of radius a is

$$B = B_0\left[1 - \sum_{k=1}^{\infty} J_0\left(r\frac{v_k}{a}\right)\mathrm{e}^{-t/T_k}\right] \tag{0.20}$$

where $J_0\,(r\,v_k/a)$ is the zero-order Bessel function of argument $r\,v_k/a$ and the summation is over the nulls of J_0 designated v_k (the first four values of v_k are 2.405, 5.520, 8.654, and 11.792).* T_k is the rise time of the kth term in the series and is given by

$$T_k = \frac{\mu_0 \sigma a^2}{v_k} \tag{0.21}$$

As v_k increases, the rise time decreases and therefore the longest delay is due to the first term in the summation with $k = 1$

$$T_1 = \frac{\mu_0 \sigma a^2}{2.405} \tag{0.22}$$

For a cylinder with 0.1 m radius and a conductivity $\sigma \approx 1$ S/m, which is a typical value for muscle between 100 and 1000 MHz, Equation 0.22 gives $T_1 = 2.6 \times 10^{-8}$ s. This finite rise time (or decay time in case of field removal) of the internal H field may be of some importance when pulsed H fields are used therapeutically [17]. It might also be used

*This result is based on solution of $\partial B/\partial t = (1/\mu_0)\nabla^2 B$, which is a consequence of Ampere's and Farraday's laws when displacement is disregarded. Equations 0.20 to 0.22 are therefore only correct when $\mathrm{p} \gg 1$.

to measure noninvasively the conductivity of biological substances *in vivo* through determination of the final decay rate of the voltage induced into a probe coil by the slowly decaying internal field after the applied field is removed [16].

The properties of biological substances in the intermediate frequency range, above ELF (>300 Hz), and below the higher RFs, where wave behavior and skin effect begin to be important (~20 MHz), are discussed in Chapter 3 of *BBA*. However, many subsequent chapters are concerned with biological effects at dc and ELF frequencies below a few kilohertz, while others deal primarily with the higher RFs, >50 MHz. One reason for this limited treatment of the intermediate frequency range is that very little animal data are available for this spectral region in comparison with the large number of experiments performed at ELF and microwave frequencies in recent years.* Another reason is that most electrical processes known to occur naturally in biological systems—action potentials, EKG, EEG, ERG, etc.—occur at dc and ELF frequencies. Therefore, one might expect some physiological effects from external fields of appropriate intensity in the same frequency range, even if the magnitude of such fields is not large enough to produce thermal effects. As illustrated by Figure 0.3 and Figure 0.7, most *E* fields below 100 kHz set up by currently used human-made devices, and most *H* fields below 10 kHz except the very strongest, are incapable of producing thermal effects in living organisms, excluding, of course, fields accompanying currents directly introduced into the organism via electrodes. Thus, the frequencies between about 10 and 100 kHz have been of relatively little interest because they are not very likely to produce thermal or other biological effects. On the other hand, the higher RFs are frequently generated at power levels where enough energy may be introduced into living organisms to produce local or general heating. In addition, despite skin effect and the reflection loss to be discussed in more detail below, microwaves modulated at an ELF rate may serve as a vehicle for introducing ELF fields into a living organism of at least the same order of magnitude as would be introduced by direct exposure to ELF. Any effect of such ELF-modulated microwaves would, of course, require the existence of some amplitude-dependent demodulation mechanism to extract the ELF from the microwave carrier.

Among the chapters dealing with RF, Chapter 10 and Chapter 11 of *BBA* give the necessary information for establishing the magnitude of the fields present in biological objects: (1) experimental techniques and (2) analytical methods for predicting field intensities without construction of physical models made with ''phantom'' materials, i.e., dielectric materials with properties similar to those of living objects which are to be exposed. As thermal effects at microwave frequencies are certainly important, although one cannot assume *a priori* that they are the only biological effects of this part of the spectrum, and as some (but not all) thermal effects occur at levels where the thermoregulatory system of animals is activated, thermoregulation in the presence of microwave fields is discussed in Chapter 5 of *BMA*, as well as in Chapter 10 of *BBA*. Not only are the therapeutic applications of microwaves based upon their thermal effects, but also the experimental establishment of possible nonthermal effects at the threshold of large scale tissue heating in particular living systems and also requires thorough understanding of thermoregulatory mechanisms. The vast amount of experimental data obtained on animal systems exposed to microwave is discussed in Chapter 3 and Chapter 4 in *BMA*. Both nonmodulated fields and modulated fields, where the type of modulation had no apparent effect other than modification of the average power level, are considered. These chapters and the Chapter 9 in *BMA* are considered to be very new extension of experiments into exposures to ultra-short and to ultra-high power pulses.

*Though this statement was written in for the second edition in 1995, it continues to be true in 2005—Ben Greenebaum.

At the higher RFs, the external E field is not necessarily perpendicular to the boundary of biological materials (see Figure 0.4 and Figure 0.10), and the ratio of the total external E field to the total internal field is not given by Equation 0.9. However, the skin effect (Equation 0.16 through Equation 0.19) and reflection losses still reduce the E field within any biological object below the value of the external field. As pointed out in Chapter 3, dielectric permittivity and electrical conductivity of organic substances both vary with frequency. At RF, most biological substances are neither very good electrical conductors nor very good insulators, with the exception of cell membranes, which are good dielectrics at RF but at ELF can act as intermittent conductors or as dielectrics and are ion-selective [18–20]). The ratio p (Equation 0.18) is neither much smaller nor very much larger than values shown for typical muscle tissue [21,22] in Table 0.1.

Reflection loss at the surface of an organism is a consequence of the difference between its electrical properties and those of air. Whenever an electromagnetic wave travels, from one material to another with different electrical properties, the boundary conditions (Equation 0.3 and Equation 0.8) and similar relations for the H field require the existence of a reflected wave. The expressions for the reflection coefficient

$$\Gamma = \frac{E_r}{E_i} \tag{0.23}$$

and the transmission coefficient

$$T = \frac{E_t}{E_i} \tag{0.24}$$

become rather simple for loss-free dielectrics ($p \ll 1$) and for good conductors ($p \gg 1$). As biological substances are neither the most general expressions for Γ and T, applicable at plane boundaries, are needed [3,13]. For perpendicular incidence, illustrated by Figure 0.8,

$$\Gamma = \frac{\eta_2 - \eta_1}{\eta_2 + \eta_1} \tag{0.25}$$

$$T = \frac{2\eta_2}{\eta_2 + \eta_1} = 1 + \Gamma \tag{0.26}$$

TABLE 0.1

Ratio p of Conduction Current to Displacement as a Function of Frequency

f (MHz)	σ	ε_r	$p = \frac{\sigma}{\omega\varepsilon_0\varepsilon_r}$
1	0.40	2000	3.6
10	0.63	160	7.1
100	0.89	72	2.2
10^3	1.65	50	0.59
10^4	10.3	40	0.46
10^5	80	6	2.4

where η_1 and η_2 are the wave impedances, respectively, of mediums 1 and 2. The wave impedance of a medium is the ration of the E to the H field in a plane wave traveling through that medium; it is given by [13]

$$\eta = \left(\frac{j\omega\mu}{\sigma + j\omega\varepsilon}\right)^{1/2} \tag{0.27}$$

Clearly Γ and T are in general complex numbers, even when medium 1 is air for which Equation 0.27 reduces to the real quantity $\eta_0 = \sqrt{\mu_0/\varepsilon_0}$, because medium 2, which here is living matter, usually has a complex wave impedance at RFs.

The incident, reflected, and transmitted powers are given by [13]

$$P_i = R_1|E_i|^2\frac{1}{\eta_1^*} = \frac{|E_i|^2}{|\eta_1|^2}R_1 \tag{0.28}$$

$$P_r = R_1|E_r|^2\frac{1}{\eta_1^*} = \frac{|E_r|^2}{|\eta_1|^2}R_1 \tag{0.29}$$

$$P_t = R_1|E_t|^2\frac{1}{\eta_2^*} = \frac{|E_t|^2}{|\eta_2|^2}R_2 \tag{0.30}$$

where the E fields are effective values ($E_{\text{eff}} = E_{\text{peak}}/\sqrt{2}$) of sinusoidal quantities, R_1 signifies ''real part of,'' η^* is the complex conjugate of η, and R_1 and R_2 are the real parts of η_1 and η_2. If medium 1 is air, $\eta_1 = R_1 = 377\ \Omega$, it follows from Equation 0.23, Equation 0.24, and Equation 0.28 through Equation 0.30 and conservation of energy that the ratio of the transmitted to the incident real power is given by

$$\frac{P}{P_1} = |T|^2\frac{\eta_1\eta_2^* + \eta_1^*\eta_2}{2|\eta_2|^2} = 1 - \frac{P_r}{P_i} = 1 - |\Gamma|^2 \tag{0.31}$$

The magnitude of the transmission coefficient T for the air–muscle interface over the 1- to 100-MHz frequency range is plotted in Figure 0.9, which shows that the magnitude of the transmitted E field in muscle tissue is considerably smaller than the E field in air. The fraction of the total incident power that is transmitted (Equation 0.31) is shown in Figure 0.11, indicating clearly that reflection loss at the interface decreases with frequency. However, for deeper lying tissue this effect is offset by the fact that the skin depth δ (Equation 0.19) also decreases with frequency (Figure 0.12) so that the total power penetrating beyond the surface decreases rapidly.

In addition to reflection at the air–tissue boundary, further reflections take place at each boundary between dissimilar materials. For example, the magnitude of the reflection coefficient at the boundary surface between muscle and organic materials with low-water content, such as fat or bone, is shown in Table 0.2.

The situation is actually more complicated than indicated by Figure 0.9 and Figure 0.11, because the wave front of the incident electromagnetic wave may not be parallel to the air–tissue boundary. Two situations are possible: the incident E field may be polarized perpendicular to the plane of incidence defined in Figure 0.13 (perpendicular polarization, Figure 0.13a) or parallel to the plane of incidence (parallel polarization, Figure 0.13b). The transmission and reflection coefficients [8] are different for the two types of polarization and also become functions of the angle of incidence α_1:

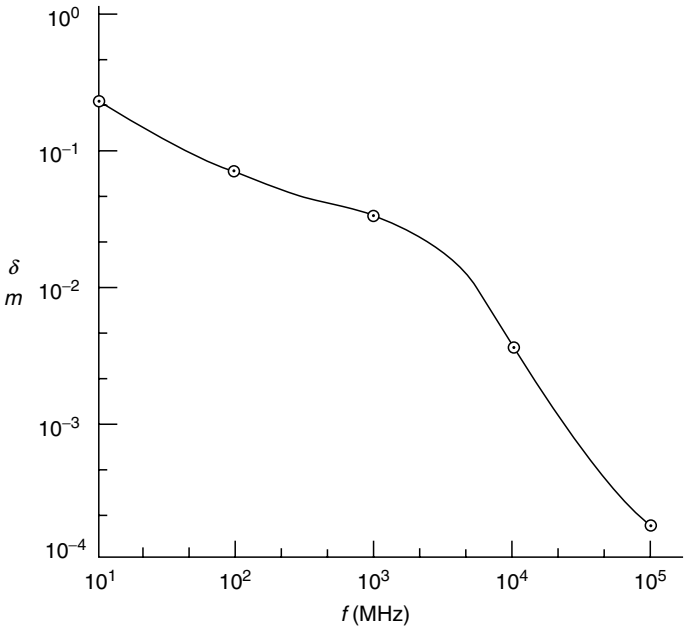

FIGURE 0.12
Electromagnetic skin depth in muscle tissue from plane wave expression (Equation 0.19, Table 0.1).

$$\text{Perpendicular polarization}\begin{cases} T_{\perp} = \dfrac{2\eta_2 \cos\alpha_1}{\eta_2 \cos\alpha_1 + \eta_1 \cos\alpha_2} \\ \Gamma_{\perp} = \dfrac{\eta_2 \cos\alpha_1 - \eta_1 \cos\alpha_2}{\eta_2 \cos\alpha_1 + \eta_1 \cos\alpha_2} \end{cases} \quad (0.32),(0.33)$$

$$\text{Parallel polarization}\begin{cases} T_{\mathrm{p}} = \dfrac{2\eta_2 \cos\alpha_1}{\eta_2 \cos\alpha_2 + \eta_1 \cos\alpha_1} \\ \Gamma_{\mathrm{p}} = \dfrac{\eta_1 \cos\alpha_1 - \eta_2 \cos\alpha_2}{\eta_2 \cos\alpha_2 + \eta_1 \cos\alpha_1} \end{cases} \quad (0.34),(0.35)$$

where α_2 is given by the generalized Snell's law (when both the media have the magnetic permeability of free space) by

TABLE 0.2
Reflection Coefficient ''Capital Gamma'' for Low–Water-Content Materials

	Fat or Bone		
f (MHz)	σ (S/m)	ε_r	Muscle[a]–Fat (Γ)
10^2	0.048	7.5	0.65
10^3	0.101	5.6	0.52
10^4	0.437	4.5	0.52

[a] σ and ε_r for muscle from Table 0.1.

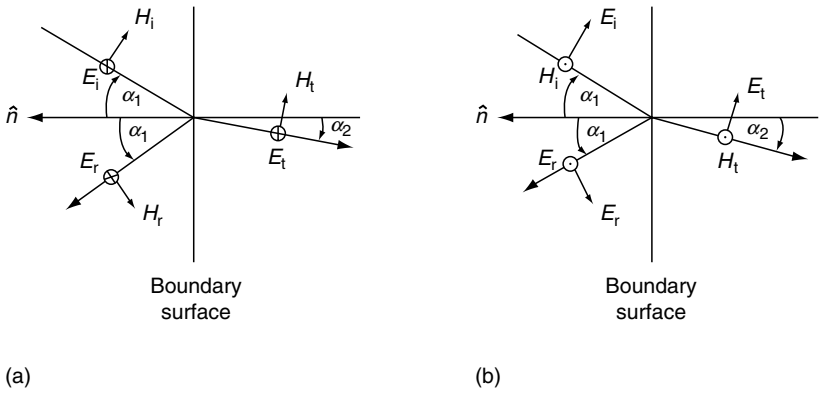

FIGURE 0.13
Oblique incidence of an electromagnetic wave at the boundary between two different media. (a) Perpendicular polarization (E vector perpendicular to plane of incidence); (b) parallel polarization (E vector parallel to plane of incidence). The plane of incidence is the plane formed by the surface normal (unit vector **n** and the direction of the incident wave); $\otimes$ indicates a vector into the plane of the paper; $\odot$ indicates a vector out of the plane of the paper. The orientation of the field vectors in the transmitted field is shown for loss-free dielectrics. For illustration of the transmitted wave into a medium with finite conductivity, where the wave impedance η_2 becomes a complex number, see Stratton, J.A., *Electromagnetic Theory*, McGraw-Hill, New York, 1941, p. 435.

$$\sin\alpha_2 = \frac{\sqrt{\varepsilon}_1}{\sqrt{\varepsilon_2 - \mathrm{j}\frac{\sigma_2}{\omega}}} \tag{0.36}$$

so that $\cos\alpha_2 = \sqrt{1-\sin^2\alpha_2}$ is a complex number unless $\rho_2 = (\sigma_2/\omega\varepsilon_2) = 1$.

As illustration, the variation with angle of incidence of the transmission coefficient for parallel polarization at the air–muscle interface at 10 MHz, is shown in Figure 0.14. It is apparent that the transmitted field is not necessarily maximized by perpendicular incidence in the case of parallel polarization. Furthermore, whenever $p \approx 1$ or $p > 1$ (see Table 0.1, above), α_2 is complex, which causes the waves entering the tissue to be inhomogeneous—they are not simple plane waves, but waves where surfaces of constant phase and constant amplitude do not coincide [3,23]; only the planes of constant amplitude are parallel to the boundary surface.

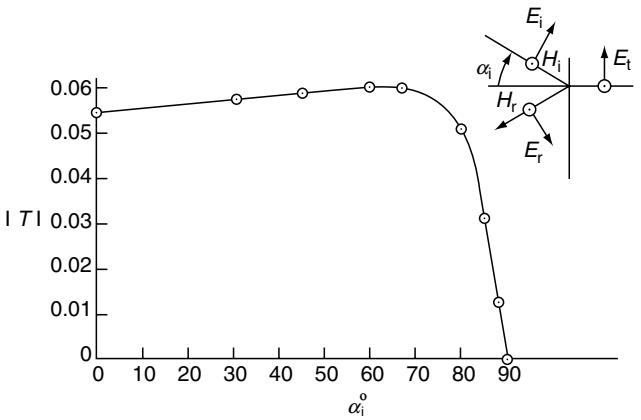

FIGURE 0.14
Magnitude of complex transmission coefficient for parallel polarization versus angle of incidence α_1 at 10 MHz (E field in plane of incidence, H field parallel to boundary plane; $\sigma_2 = 0.7\,\mathrm{S/m}$, $\varepsilon_{r2} = 150$, $T = E_t/E_r$).

Analytical solutions for nonplanar structures taking into account size and shape of entire animals have been given [24] and are also described in the RF modeling Chapter 10 of *BBA*.

0.5 Biophysical Interactions of Fields: Ionization, Ionizing Radiation, Chemical Bonds, and Excitation

RF fields can be characterized as nonionizing radiation. By this we mean that there is not enough energy in a single quantum of energy, hf, to ionize an atom or a molecule at RFs, where h is Planck's constant and f is the frequency. By comparison radiation in the UV or x-rays often lead to ionization. It is desirable to begin by reviewing the differences between ionizing and nonionizing radiations, to explain ionization phenomena and also to discuss related excitation phenomena, which require less energy than ionization. Then a number of the proposed models concerning atomic or molecular-level interactions of fields will be introduced. A number of these theories will be discussed and their predictions compared with experimental results in later chapters, including Chapter 5 through Chapter 7 and Chapter 9 in *BBA*; Chapter 9 and Chapter 11 in *BMA*. Heating, cell excitation, electroporation, and other results of high-intensity fields have been accepted as explanations for many bioelectromagnetic phenomena. For low-intensity exposure, however, no theory is widely accepted as a general explanation for bioelectromagnetic phenomena, and few specific phenomena have accepted explanations. It is quite possible that no general explanation exists and that more than one mechanism of interaction between fields will be found to be operating, depending on the situation. Binhi's book [25] contains a good summary of most recent theoretical proposals, including comparisons with data and critiques of their strong and weak points, as well as his own theory.

We note first that the energy of electromagnetic waves is quantized with the quantum of energy (in joules) being equal to Planck's constant ($h = 6.63 \times 10^{-34}$ J s) times the frequency. This energy can also be expressed in electron volts, i.e., in multiples of the kinetic energy acquired by an electron accelerated through a potential difference of 1 eV (1 eV $\approx 1.6 \times 10^{-19}$ J). Energy quanta for a few frequencies are listed in Table 0.3.

Quantized energy can ''excite'' molecules; appropriate frequencies can couple to vibrational and rotational oscillation; and if the incident energy quantum has sufficient magnitude it can excite other changes in the electron configuration, such as changing an electron to another (unoccupied) energy level or tearing an electron away from one of the constituent atoms, the latter process called as ionization. The energy required to remove one electron from the highest energy orbit of a particular chemical element is called its ''ionization potential.'' Typical ionization potentials are of the order 10 eV; for example, for the hydrogen atom it is 13.6 eV and for gaseous sodium it is 5.1 eV. As chemical binding forces are essentially electrostatic, ionization implies profound chemical changes. Therefore ionization by any outside agent of the complex compounds that make up a living system leads to profound and often irreversible changes in the operation of that system.

Table 0.3 shows that even the highest RF (millimeter waves) has quantum energies well below the ionization potential of any known substance; thus one speaks of nonionizing radiation when referring to electromagnetic waves below UV light frequencies. Ionizing radiation includes UV and higher frequency electromagnetic waves (x-rays, γ-rays).

TABLE 0.3

Wave and Quantum Characteristics of Various Types of Radiation

Name of Radiation or Application	Frequency (Hz)	Wavelength (m)	Energy of 1 Quantum of Radiation (eV)
UHF TV	7×10^8	0.43	2.88×10^{-6}
Microwave radar	10^{10}	3×10^{-2}	4.12×10^{-5}
Millimeter wave	3×10^{11}	1×10^{-3}	1.24×10^{-3}
Visible light	6×10^{14}	5×10^{-7}	2.47
Ionizing UV	10^{16}	3×10^{-4}	41.2
Soft x-ray	10^{18}	3×10^{-10}	4120
Penetrating x-ray	10^{20}	3×10^{-12}	4.12×10^5

This explanation of the difference between ionizing and nonionizing radiation should not imply that nonionizing electromagnetic radiation cannot have profound effects upon inorganic and organic substances. As excitation of coherent vibrational and rotational modes requires considerably less energy than ionization, it could occur at RF; this will be discussed in later chapters. In addition, many other possible biological effects require energies well below the level of ionizing potentials. Examples are tissue heating, dielectrophoresis, depolarization of cell membranes, mechanical stress due to piezoelectric transduction, or dielectric saturation, resulting in the orientation of the polar side chains of macromolecules and leading to the breaking of hydrogen bonds. These and other mechanisms will be discussed by the authors of several chapters (see especially Chapter 5 through Chapter 7 of *BBA* and Chapter 9 of *BMA*), who will also give estimates of rates at which energy must be delivered to produce particular effects.

Returning to the discussion of ionization, it is important to note that ionization of a chemical element can be brought about not only by absorption of electromagnetic energy, but also by collision either with foreign (injected) atoms, molecules, or subatomic particles of the requisite energy, or by sufficiently violent collision among its own atoms. The latter process constitutes ionization by heating, or thermal breakdown of a substance, which will occur when the kinetic energy of the colliding particles exceeds the ionization potential. As the average thermal kinetic energy of particles is related to temperature [26] by $W = kT$ where k is Boltzmann's constant ($= 1.38 \times 10^{-23}$ J/K), we find that the required temperature is

$$1.38(10^{-23})T \approx 5 \text{ eV} \approx (5)1.6(10^{-19}) \text{ J}$$

$$T \approx 5(10^4) \text{ K}$$

which is about twice the temperature inside a lightning stroke [27] and orders of magnitude higher than any temperature obtainable from electromagnetic waves traveling through air.

Actually, initiation of lightning strokes is an example of ionization by collision with injected energetic particles. The few free electrons and ions always present in the air due to ionization by cosmic rays are accelerated by the E fields generated within clouds to velocities corresponding to the required ionization energy. Only when the field is large enough to impart this energy over distances shorter than the mean free path of the free electrons or ions at atmospheric pressure can an avalanche process take place: an accelerated electron separates a low-energy electron from the molecule with which it collides and in the process loses most of its own energy; thus, one high-energy free electron is exchanged for two free low-energy electrons and one positive ion. Both the

electrons are in turn accelerated again by the field, giving them high kinetic energy before they collide with neutral molecules; their collision produces four free electrons and the multiplication process continues. The breakdown field strength for air at atmospheric pressure is approximately 3×10^6 V/m, implying a mean free path of electrons

$$\Delta\ell \approx [5\,\text{eV}/3 \times 10^6\,\text{V/m}] \approx 10^{-6}\,\text{m}$$

However, this model is not entirely accurate because the actual mean free path corresponds to energies of the order of 0.1 eV, which is only sufficient to excite vibrational modes in the target molecule. Apparently such excitation is sufficient to cause ionization if the collision process lasts long enough [28].

Except for some laboratory conditions where a sufficiently high potential difference can be applied directly across a biological membrane to bring about its destruction, collisional ionization is generally not a factor in the interaction of electromagnetic waves with tissue: The potential difference required for membrane destruction [29] is between 100 nV and 300 mV, corresponding to a field strength of the order of 2×10^7 V/m, assuming a membrane thickness ($d = 100$ Å; $E = V/d$). However, there is a third mechanism of ionization that is particularly important in biological systems. When a chemical compound of the type wherein positive and negative ions are held together by their electrostatic attraction, such as the ionic crystal NaCl, is placed in a suitable solvent, such as H_2O, it is separated into its ionic components. The resulting solution becomes an electrolyte, i.e., an electrically conducting medium in which the only charge carriers are ions.

In this process of chemical ionization, the Na^+ cations and Cl^- anions are separated from the original NaCl crystal lattice and individually surrounded by a sheet of solvent molecules, the ''hydration sheath.'' If the solvent is H_2O, this process is called ''hydration,'' or more generally, for any solvent, ''solvation.''

A dilute solution of NaCl crystals in H_2O is slightly cooler than the original constituents before the solvation process, indicating that some internal energy of the system was consumed. Actually energy is consumed in breaking up the original NaCl bonds and some, but less, is liberated in the interaction between the dipole moment of the solvent molecule (H_2O in our example) and the electric charges on the ions. Thus, solvents with higher relative dielectric constant ε_r, indicating higher inherent electric dipole moment per unit volume (P), solvate ions more strongly ($\varepsilon_r = 1 + P/[\varepsilon_o E]$, where E is the electric field applied during the measurement of ε_r). For example, H_2O with $\varepsilon_r \approx 80$ solvates more strongly than methanol with $\varepsilon_r \approx 33$. For biological applications it is worth noting that solvation may affect not only ionic substances, but also polar groups, i.e., molecular components which have an inherent dipole moment, such as—C=O, —NH, or —NO_2. Details of the process are discussed in texts on electrochemistry [30,31].

In biological processes not only chemical ionization and solvation of ionic compounds, but also all kinds of chemical reaction take place. One of the central questions in the study of biological effects of E and H fields is therefore not only whether they can cause or influence ionization, but also whether they can affect—speed up, slow down, or modify—any naturally occurring biologically important chemical reaction.

In Table 0.4 typical energies for various types of chemical bonds are listed. For comparison the thermal energy per elementary particle at 310 K is also shown. Complementing the numbers in Table 0.4 one should also point out that:

1. The large spread in the statistical distribution of energies of thermal motion guarantees that at physiological temperatures some molecules always have sufficient energy to break the strongest weak bonds [32].

TABLE 0.4

Bond and Thermal Energies

Type of Bond	Change in Free Energy (Binding Energy) kcal/mol	eV/Molecule
Covalent	50–100	2.2–4.8
Van der Waals	1–2	0.04–0.08
Hydrogen	3–7	0.13–0.30
Ionic[a]	5	0.2
Avg. thermal energy at 310 K	0.62	0.027

[a]For ionic groups of organic molecules such as COO^-, $NH3_3^-$ in aqueous solution.

2. The average lifetime of a weak bond is only a fraction of a second.
3. The weak binding forces are effective only between the surfaces in close proximity and usually require complementary structures such as a (microscopic) plug and hole, such as are thought to exist, for instance, between antigen and antibody [33].
4. Most molecules in aqueous solution form secondary bonds.
5. The metabolism of biological systems continuously transforms molecules and therefore also changes the secondary bonds that are formed.

Comparison of the last columns in Table 0.3 and Table 0.4 shows that millimeter waves have quantum energies, which are only about one order of magnitude below typical Van der Waals energies (waves at a frequency of 10^{12} Hz with a quantum energy of 0.004 eV have a wavelength of 0.3 mm and can still be classified as millimeter waves). One might expect therefore that such waves could initiate chemically important events, such as configurational changes, by e.g., multiple transitions between closely spaced vibrational states at successively high-energy levels [46].

Energies associated with transition from one to another mode of rotation of a diatomic molecule are given by $W = \ell\,(\ell + 1)\,A$ [26,33], where $\ell = 0, 1, 2, 3 \ldots$ and $A = 6 \times 10^{-5}$ eV; thus an electromagnetic wave with a frequency as low as 29 GHz—still in the microwave region—can excite a rotational mode. Vibrational modes of diatomic molecules [26,33] correspond to energies of the order of 0.04 eV, requiring excitation in the IR region. Vibrational frequencies in a typical H-bonded system [34] are of the order of 3000 GHz; however, attenuation at this frequency by omnipresent free H_2O may prevent any substantial effect [34].

Kohli et al. [34] predict that longitudinal and torsional modes of double helical DNA should not be critically damped at frequencies >1 GHz, although relaxation times are of the order of picoseconds, and Kondepudi [36] suggests the possibility of an influence of millimeter waves at approximately 5×10^{11} Hz upon oxygen affinity of hemoglobin due to resonant excitation of heme plane oscillations. Although Furia et al. [37] did not find resonance absorption at millimeter waves in yeast, such was reported by Grundler et al. [38,47]. The latter experiment has been interpreted [39,40] as supporting Fröhlich's theory of cooperative phenomena in biological systems. That theory postulates ''electric polarization waves'' in biological membranes which are polarized by strong biologically generated [18] fields (10^7 V/m). Fröhlich [41,42] suggests that metabolically supplied energy initiates mechanical vibrations of cell membranes. The frequency of such vibrations is determined by the dimensions and the elastic constants of the membranes;

based on an estimate of the sound velocity in the membrane of 10^3 m/s and a membrane thickness of 100 Å (equal to one half wavelength) one obtains a frequency of $5(10^{10})$ Hz. Individual molecules within and outside the membrane may also oscillate, and frequency estimates vary between 10^9 Hz for helical RNA [43] and 5×10^{13} Hz for hydrogen-bonded amide structures [44]. As the membranes and molecules involved are strongly polarized, the mechanically oscillating dipole electromagnetic fields that are able to transmit energy, at least in some situations, over distances much larger than the distance to the next adjacent molecule.

Electromagnetic coupling of this type may produce long-range cooperative phenomena. In particular, Fröhlich [45] has shown that two molecular systems may exert strong forces upon each other when their respective oscillation frequencies are nearly equal, provided the dielectric permittivity of the medium between them is strongly dispersive or excitation is supplied by pumping, i.e., by excitation at the correct frequency from an external source. The mechanism is nonlinear in the sense that it displays a steplike dependence on excitation intensity. Possible long-range effects may be, for example, attraction between enzyme and substrate [42]. These and related topics have been discussed in detail by Illinger [34] and are reviewed in the present volume in Chapter 11 and Chapter 5 of *BBA*.

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1

Environmental and Occupationally Encountered Electromagnetic Fields

Kjell Hansson Mild and Ben Greenebaum

CONTENTS

1.1 Introduction

We encounter electromagnetic (EM) fields every day, both naturally occurring and man-made fields. This leads to exposure both in our homes as well as in our various

workplaces, and the intensity of the fields varies substantially with the situation. Quite high exposure can occur in some of our occupations as well as our personal activities, for instance, in trains, where the extremely low-frequency (ELF) magnetic field can reach rather high levels. The frequency of the fields we are exposed to covers a wide range, from slowly changing static fields to the gigahertz range.

In this chapter, we give an overview of the fields we encounter in various situations.

1.2 Direct Current and ELF (0–3000 Hz) EM Fields

1.2.1 Naturally Occurring Fields

The most obvious naturally occurring field is the Earth's magnetic field, known since ancient times. The total field intensity diminishes from the poles, with a high of 67 μT at the south magnetic pole and a low of about 30 μT near the equator. In South Brazil, an area with flux densities as low as about 24 μT can be found. Indeed, the angle of the Earth's field to the horizontal (inclination) varies, primarily with latitude, ranging from very small near the equator to almost vertical at high latitudes. More information is available in textbooks (see, e.g., Dubrov [1]) and in databases available on the Web (see, e.g., the U.S. National Geophysical Data Center [2]).

However, the geomagnetic field is not constant, but is continuously subject to more or less strong fluctuations. There are diurnal variations, which may be more pronounced during the day and in summer than at night and in winter (see, e.g., König et al. [3]). There are also short-term variations associated with ionospheric processes. When the solar wind brings protons and electrons toward the Earth, phenomena like the Northern Lights and rapid fluctuations in the geomagnetic field intensity occur. The variation can be rather large; the magnitude of the changes can sometimes be up to 1 μT on a timescale of several minutes. The variation can also be very different in two fairly widely separated places because of the atmospheric conditions. There is also a naturally occurring direct current (DC) electric field at the surface of the Earth in the order of 100–300 V/m (Earth's surface negative) in calm weather and can be 100 kV/m in thunderstorms, caused by atmospheric ions [4].

EM processes associated with lightning discharges are termed as atmospherics or ''sferics'' in short. They consist mostly of waves in the ELF (strictly speaking 30–300 Hz but usually taken in the bioelectromagnetics literature to extend from 0 to 3000 Hz) and very low-frequency (VLF) ranges (3–30 kHz) (see König et al. [3]). Each second about 100 lightning discharges occur globally, and in the United States one cloud-to-ground flash occurs about every second, averaged over the year [3]. The ELF and VLF signals travel efficiently in the waveguide formed by the Earth and the ionosphere and can be detected many thousands of kilometers from the initiating stroke. Since 1994, several experiments studying the effects of short-term exposure to simulated 10-kHz sferics have been performed at the Department of Clinical and Physiological Psychology at the University of Giessen, Germany [5,6]. In the ELF range, very low-intensity signals, called Schumann resonances, also occur. These are caused by the ionosphere and the Earth's surface acting as a resonant cavity, excited by lightning [3,7] (see also http://www.oulu.fi/~spaceweb/textbook/schumann.html). These cover the low-frequency spectrum, with broad peaks of diminishing amplitude at 7.8, 14, 20, and 26 Hz and higher frequencies. Higher-frequency fields, extending into the microwave region, are also present in atmospheric or intergalactic sources. These fields are much weaker, usually by many

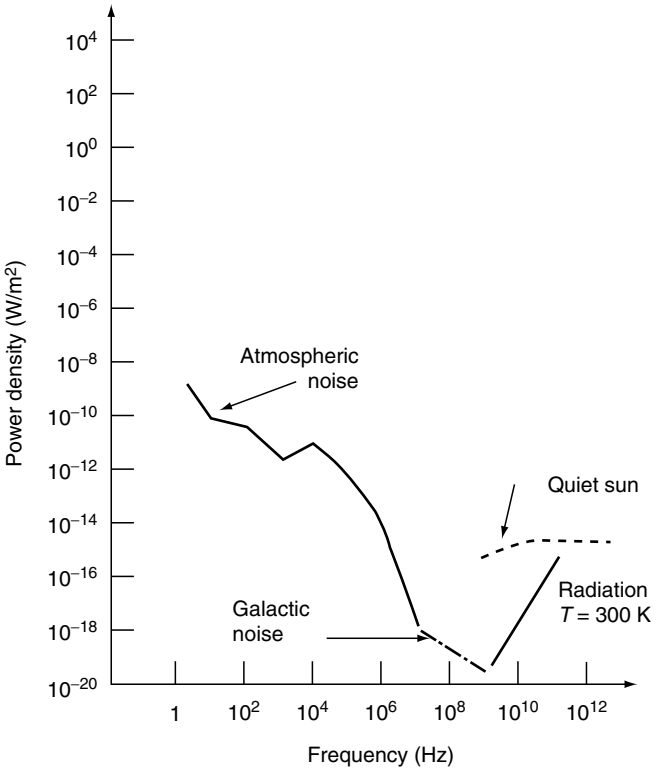

FIGURE 1.1
Power density from natural sources as a function of frequency. (Data from Smith, E. *Proceedings of the IEEE Symposium on Electromagnetic Compatibility*. Institute of Electrical and Electronic Engineering, Piscataway, NJ, 1982. Graph adapted from Barnes, F.S. *Health Phys*. 56, 759–766, 1989. With permission.)

orders of magnitude, than those caused by human activity (compare Figure 1.1 and subsequent tables and figures in this chapter).

1.2.2 Artificial DC and Power Frequency EM Fields in the Environment

1.2.2.1 DC Fields

Although alternate current (AC) power transmission is facilitated by the availability of transformers to change voltages, DC is also useful, especially since high-power, high-efficiency solid-state electronic devices have become available. Overland high-voltage DC lines running at up to ± 1100 kV are found in Europe, North America, and Asia [8] (see also, e.g., http://www.answers.com/topic/high-voltage-direct-current, accessed on August 17, 2005). Electric and magnetic fields near these lines are essentially the same as those for AC lines running at the same voltages and currents, which are discussed below. Because potentials on the cables do not vary in time and there are only two DC conductors ($+$ and $-$) instead of the three AC phases, the DC electric fields and space charge clouds of air ions that partially screen them are somewhat different from those near AC transmission lines, though the general features are the same, especially for positions away from the lines. Electric fields, corona, and air ions are discussed further in the AC transmission line section below; see also Refs. [9,10].

For transfer of electric power between countries separated by sea, undersea power cables are especially useful, since their higher capacity causes increased losses in AC.

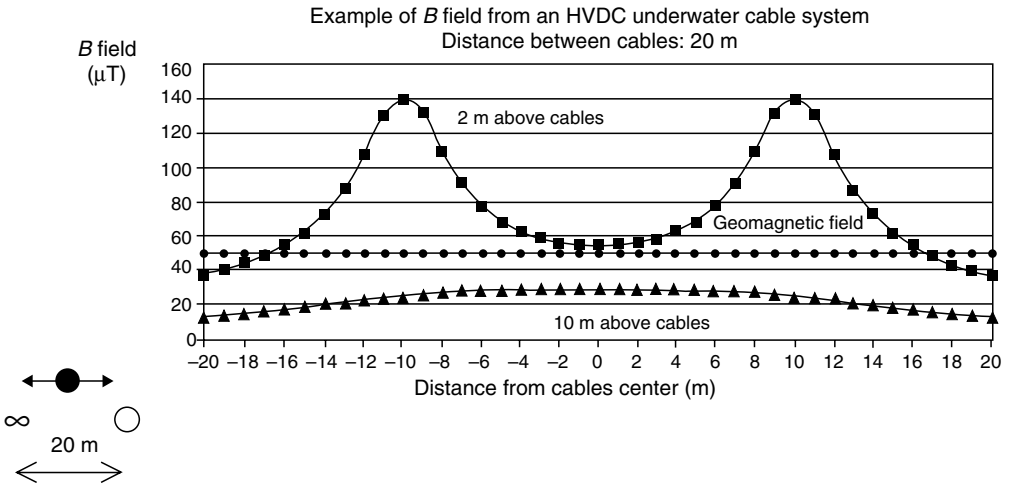

FIGURE 1.2
Predicted DC magnetic field from a high-voltage DC cable with the return cable placed at a distance of 20 m. The current in the cable was assumed to be 1333 A, which is the maximum design current. (From Hansson Mild, K. In Matthes, R., Bernhardt, J.H., and Repacholi, M.H., Eds. Proceedings from a joint seminar, *International Seminar on Effects of Electromagnetic Fields on the Living Environment*, of ICNIRP, WHO, and BfS, Ismaning, Germany, October 4–5, 1999, pp. 21–37. With permission.)

Examples are cables between Sweden and Finland, Denmark, Germany, and Gotland, a Swedish island in the Baltic Sea. Under construction at present is a cable from Sweden to Poland (SwePol). In these cables DC is used, and the ELF component of the current is less than a few tenths of a percent. The maximum current in these cables is slightly above 1000 A, and the estimated normal load is about 30% or 400 A. Depending on the location of the return path, the DC magnetic field will range from a maximum disturbance of the geomagnetic field (with a return through water) to a minimal disturbance (with a return through a second cable as close as possible to the feed cable). With a closest distance of 20 m between the cables, the predicted field distribution can be seen in Figure 1.2, immediately above the cables (2 m), practically the same value as that obtained for a single wire. When the distance between cables is increased beyond 20 m, the distortion at a given distance rises above that of Figure 1.2. Since the cables are shielded, no electric field will be generated outside the cable. For a more detailed discussion of the fields associated with this technique, the reader is referred to the paper by Koops [11].

Few other DC fields from human activity are broadly present in the environment, though very short-range DC fields are found near permanent magnets, usually ranging from a few tenths of a millitesla to a few millitesla at the surface of the magnet and decreasing very rapidly as one moves away. Occupationally encountered DC fields are discussed below.

1.2.2.2 High-Voltage AC Power Lines

The electric and magnetic fields from high-voltage power lines have been figuring for a long time in the debate on the biological effects of EM fields. Although the AC power systems in the Americas, Japan, the island of Taiwan, Korea, and a few other places are 60 Hz, while most of the rest of the world is 50 Hz, the frequency difference has no effect on high-voltage transmission line fields. In the early days of bioelectromagnetics research, the electric field was considered the most important part, and measurements of field strengths were performed in many places. Figure 1.3 shows an example of such

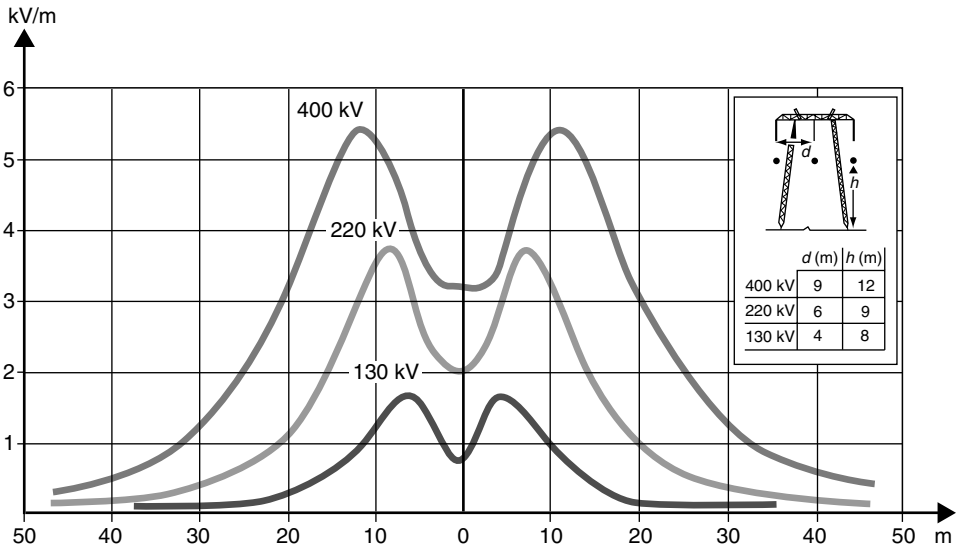

FIGURE 1.3
Electric field from three different high-voltage power lines as a function of the distance from the center of the line. In the inset the distance between the phases as well as the height above ground of the lines are given. (From Hansson Mild, K. In Matthes, R., Bernhardt, J.H., and Repacholi, M.H., Eds. Proceedings from a joint seminar, *International Seminar on Effects of Electromagnetic Fields on the Living Environment*, of ICNIRP, WHO, and BfS, Ismaning, Germany, October 4–5, 1999, pp. 21–37. With permission.)

measurements from three different types of lines: 400, 220, and 130 kV lines, respectively. The field strength depends not only on the voltage of the line but also on the distance between the phases and the height of the tower. The strongest field can be found where the lines are closest to the ground, and this usually occurs midway between two towers. Here, field strengths up to a few kilovolts per meter can be found. Since the guidelines of the International Commission on Non-Ionizing Radiation Protection (ICNIRP) [12] limit public exposure to 5 kV/m and there is no time averaging for low-frequency fields, people walking under high-voltage power lines may on some occasions be exposed in excess of existing international guidelines.

Because electric fields are well shielded by trees, buildings, or other objects, research in the 1970s and 1980s did not turn up any major health effects (see, e.g., Portier and Wolf [13]), and because of the epidemiological study by Wertheimer and Leeper [14] (see also Chapter 6 on ELF epidemiology in this volume), attention turned from electric to magnetic fields in the environment. The magnetic field from a transmission line or any other wire depends on the current load carried by the line, as well as the distance from the conductors; in Figure 1.4 calculations of the magnetic flux density from several different types of transmission lines are shown. There is a very good agreement between the theoretical calculation and the measured flux density in most situations. The flux density from two-wire power lines is directly proportional to the electric current, generally inversely proportional to the square of the distance to the power line for distances greater than several times the distance between the phase lines, and directly proportional to the distance between the phase wires. For three and six-wire systems the fields decrease more rapidly with distance at a rate that is dependent on the phase sequences and the spacing between the wires. For most lower-voltage lines, around 10–20 kv, the distance at which the B field falls below 0.2 μT is generally less than 10 m; this distance still depends on current and the spacing of the wires.

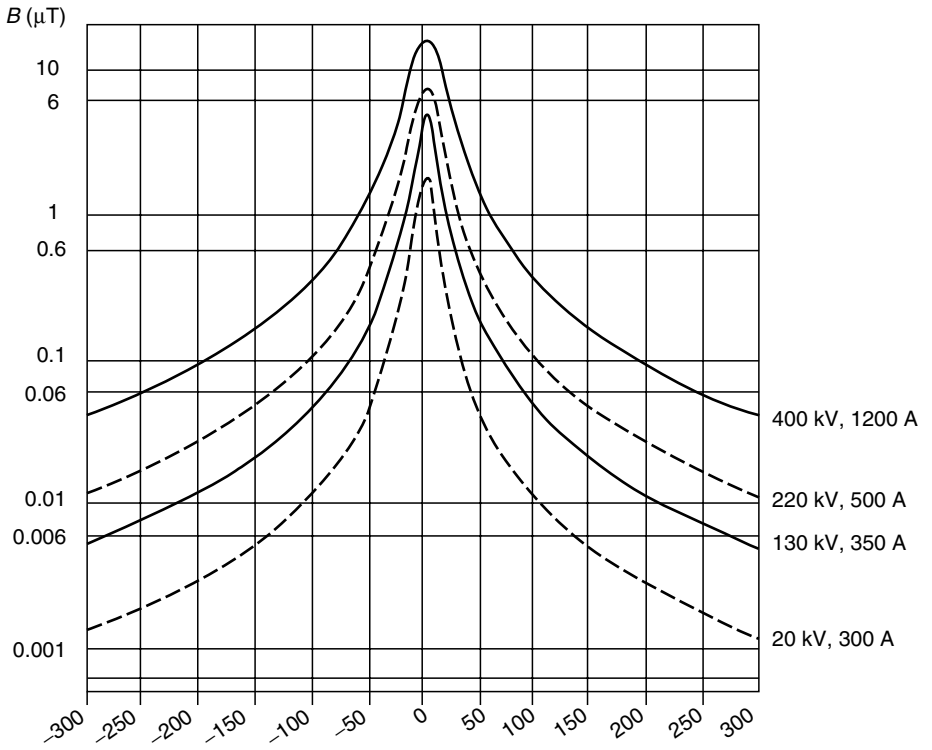

FIGURE 1.4
Magnetic flux density from different high-voltage power lines at a distance (in meters) from the center of the line. The currents in the lines are the maximum values allowed and are given to the right in the figure. (Figure courtesy of Swedish National Institute for Working Life.)

The electric or magnetic field vector from a single AC conductor displays a sinusoidal waveform, oscillating back and forth through zero intensity in a single direction determined by the observation position with respect to the wire, ignoring any small distortions due to harmonics, etc. However, near a three-phase high-voltage transmission line, the electric and magnetic field vectors from the group of conductors, which are at some distance from each other and whose individual sinusoidal variations are out of phase, rotate in space as well as change in magnitude, but their magnitude never decreases exactly to zero [15]. This so-called elliptical polarization may or may not have a different biological significance than the single conductor's ''plane polarization.''

Several approaches have been used for reducing the magnetic field from a line, and in Figure 1.5 some examples are given. Instead of hanging the three phases at the same height and in parallel, the lines can be arranged in a triangular form, thereby reducing the distance between the phases and thus also the flux density. The reduction is of the order of about 1.6. An even greater reduction is obtained if the so-called split phase arrangement is used. Here, five lines are used. One phase is placed in the center, and the other two phases are split into two lines each, which are placed diagonally (see Figure 1.4). The reduction is almost tenfold.

When high voltage is present, there is a possibility of the insulation breaking down, causing a catastrophic discharge—a spark; lightning is an obvious example. There is also the more common possibility of very minor discharges occurring, in which one or a relatively small number of molecules near the high-voltage element become

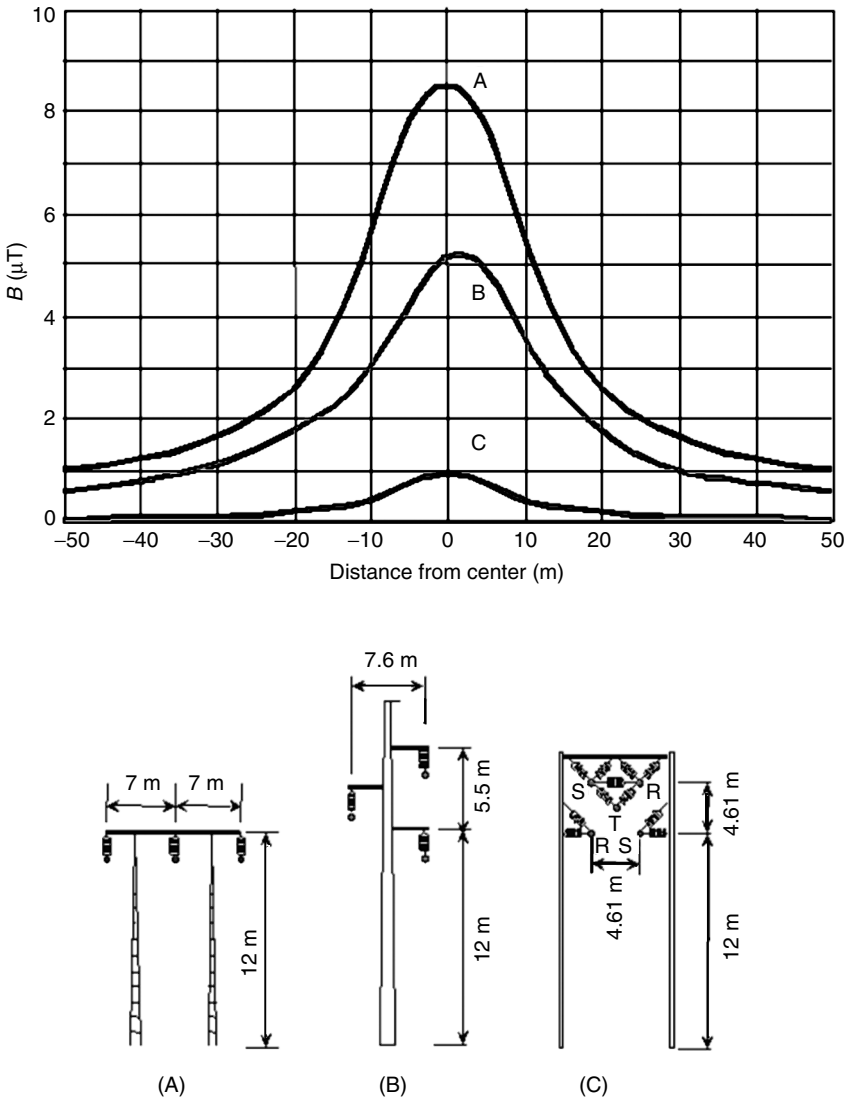

FIGURE 1.5
Examples of reduction of the magnetic flux density from a 220-kV line with a maximum phase current of 500 A. In (A) the normal configuration is used and the maximum flux density is about 8 μT, and in (B) a delta arrangement is used which gives a reduction to about 5 μT maximum under the line. In (C) the split-phase arrangement is used leading to a maximum value of only 1 μT. (Figure courtesy of Swedish National Institute for Working Life.)

ionized; this is often called a *corona*, since in extreme cases a small glow can be seen near parts of the high-voltage system. Corona discharge can also occur at grounded objects near a high voltage and is more likely to occur at more pointed objects; this is the principle of the lightning rod. Minor corona damage has been observed on pine tree needles very close to a 1200 V transmission line [16]. (No other environmental damage to plants or animals from either fields or corona has been found [17].) The resulting ions screen the electric field of the transmission line cables to varying extents, because their number depends on a variety of factors, including humidity, dust, rain, and wind [9,10]. While a hypothesis has been put forward that ions from power lines make small airborne

particles, particularly those carrying naturally occurring radioactive atoms, more likely to enter and remain in the lungs and cause cancer or various other diseases [18], it has not found much acceptance.

1.2.2.3 Exposure in Homes

Although Wertheimer and Leeper [14] initially used transmission and distribution line sizes and configurations as surrogates for estimating magnetic field exposure from transmission lines, it quickly became apparent that the correlation was not very good and that sources of exposure inside the home were at least as important, unless the home was very close to a transmission line [13]. Several studies have explored the exposure to ELF electric and magnetic fields in homes in different countries. Deadman et al. [19] investigated the exposure of children in Canada. A logging device was used, which recorded the fields during two consecutive 24-h periods. For 382 children up to the age of 15 they found an arithmetic mean (AM) of the magnetic field of 0.121 μT with a range of 0.01–0.8 μT. The corresponding values for the electric field were AM 14.4 V/m, range 0.82–64.7 V/m. Hansson Mild et al. [20] compared the ELF fields in Swedish and Norwegian residential buildings. The overall mean values were as follows: E fields 54 V/m (SD = 37) and 77 V/m (SD = 58) in Sweden and Norway, respectively; the corresponding values for B fields were 40 nT (SD = 37) and 15 nT (SD = 17). Table 1.1 shows additional comparisons.

Mccurdy et al. [21] measured women's exposure in the United States by using personal magnetic field exposure meters that were worn during a working day or a day at home. The geometric mean of the time-weighted average for the working day was 0.138 μT with a range of 0.022–3.6 μT, and for the homemakers the corresponding values were 0.113 μT, range 0.022–0.403 μT.

In the meta-analysis by Ahlbom et al. [22] on childhood cancer and residential magnetic fields, it was stated that 99.2% of the population resided in homes with $B \leq 0.4$ μT.

Exposure varies widely in time, according to the time of day and the season. One may be outdoors, far from any field sources at one time, indoors near an operating appliance at another, riding in an electric transit vehicle at some other time, and so forth. Sample exposure values for an individual, recorded as a function of time over a 24-h period in spring and summer, are shown in Figure 1.6.

TABLE 1.1

Comparison of Personal Exposure and Background Fields

Country		Geometric Mean of Personal Exposure (nT)	Geometric Mean of Long-Term Background Field (nT)	Ratio, Personal Mean to Background Mean
United States	Adults at home	134	58	2:3
	Adults at home, not in bed	111	74	1:5
	Children, residential	96	99	1:0
	Children, at home	96	67	1:4
Canada	Children at home	117	107	1:1
	Adults at home	133		1:2
U.K.	Adults at home	54	37	1:5
	Adults	42	29	1:5

Source: From Swanson, J. and Kaune, W.T. *Bioelectromagnetics* 20, 244–254, 1999.

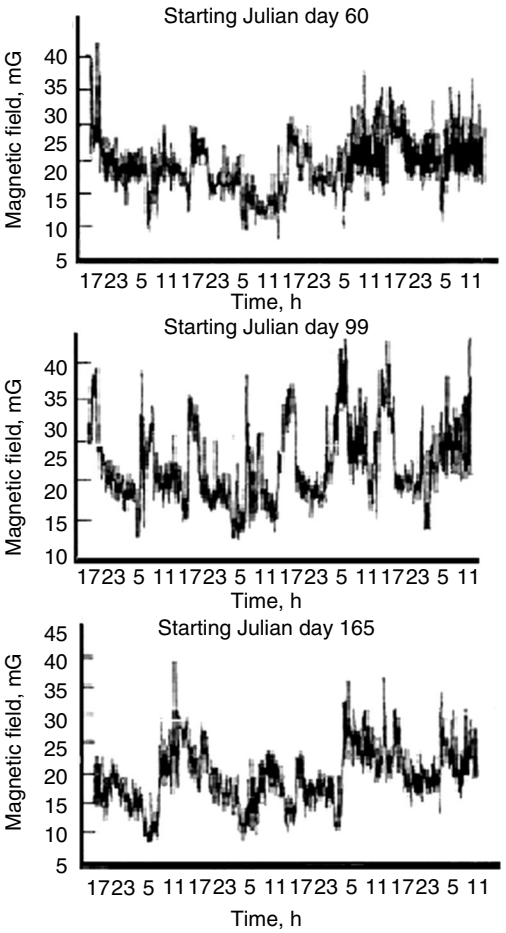

FIGURE 1.6
An individual's measured magnetic field exposure over the course of a day. Note that 1 mG = 0.1 μT. (From Koontz, M.D., Mehegan, L.L., Dietrich, F.M., and Nagda, N.L. Assessment of Children's Long Term Exposure to Magnetic Fields [The Geomet Study]. Final Report TR-101406, Research Project 2966-04, Electric Power Research Institute, Palo Alto, CA, 1992. With permission.)

Since the three-phase systems used for electrical distribution are dimensioned for sinusoidal fields, the harmonic content can create problems. Today we may find large stray currents, usually resulting from unbalanced currents between phases, in water pipes, ventilation systems, concrete reinforcement mesh, etc., and the current flowing also contains these harmonics. Figure 1.7 gives an example of a measurement of a current flowing in a cable in a large apartment building, and Figure 1.8 shows the corresponding Fourier frequency analysis. The magnetic field in the building thus also has these harmonic components. Often, the largest stray currents, which generate large domestic fields, are due to errors in wiring that violate the building code [23] or to a poorly planned wiring layout that has currents flowing in open loops instead of both wires of a circuit being laid next to each other in the same conduit [24].

From Figure 1.6 through Figure 1.8, as well as the data in the rest of this chapter, it is easy to see that average field strength is far from being the only parameter that is needed to characterize electric or magnetic field exposure. Other parameters include frequency or frequencies present (or the related parameters, the rise and fall times of up-and-down excursions or ''transients''), numbers and height of transients, number of

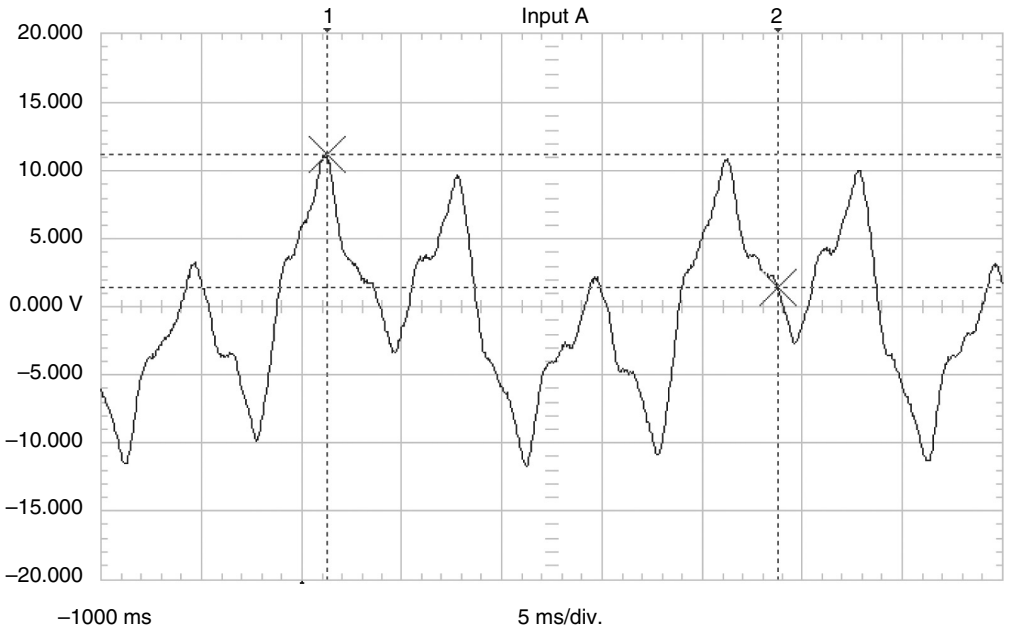

FIGURE 1.7
Stray current wave shape in the 50 Hz power delivery cable in an office building. The peak to peak current is of the order 20 A. (Figure courtesy of Swedish National Institute for Working Life.)

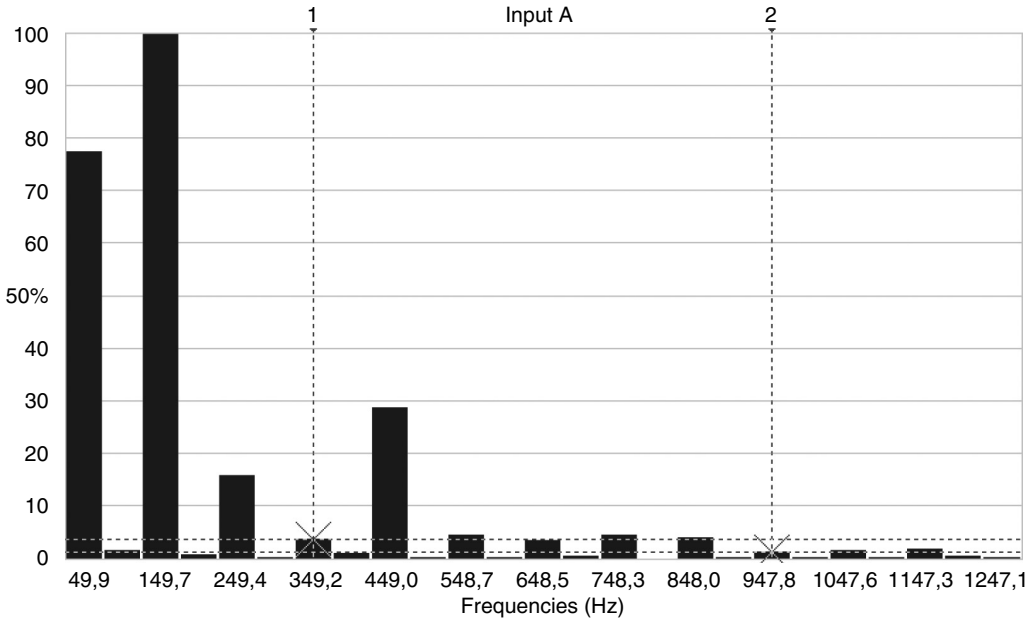

FIGURE 1.8
The Fourier spectrum of the wave shape in Figure 1.5. Note the high 150 Hz (third harmonic) component. (Figure courtesy of Swedish National Institute for Working Life.)

times the field exceeds or falls below a certain fraction of its average value, whether both DC and time-varying fields are present, relative direction of multiple fields, etc. As discussed elsewhere (e.g., the Introduction and chapters such as Chapter 5, Chapter 6, and Chapter 9 in this volume and Chapter 5 through Chapter 8 and Chapter 11 in *BMA*), it is not clear, in most cases, which one or group of these parameters is related to a particular biological effect. To date, average field strength is the most commonly used parameter, partly because it is the most easily obtainable summary of exposure over an extended period. For a given frequency range, average field strength is related to some other parameters, such as fraction of time over a certain threshold, but not to others, such as number of transients per hour. For further discussion of various parameters and their interrelationships, see, for example, Refs. [25,26].

Most measurements have been done in detached houses, even though many city dwellers live in apartment buildings. In apartment buildings, the current in the wiring in the ceiling of one unit, for instance, for ceiling lamps, may most strongly affect the magnetic field level of the unit above. Also, some apartment buildings have an electric substation in the basement, where a transformer reduces the medium-voltage distribution line power to 110 or 220 V for domestic use. The low-voltage conductors of the substation may carry substantial currents and create magnetic fields up to several tens of microtesla directly above the substation; reduction through placing conductors away from the substation ceiling and shielding with aluminum plates is possible [27].

In the United States and Canada, though not in other countries, the neutral wire of the AC power distribution system is required to be physically connected to the earth (grounded) at regular intervals to avoid injury from electric shocks; building wiring systems' neutral wires must also be grounded, often by connection to the buried water pipe as it enters the building. Unbalanced loading of the system can produce currents in the ground system, sometimes including currents that leave one residence through the grounding system and return to the power grid through another, which further contributes to the residential magnetic fields [28,29].

Kavet and colleagues [30–32] have proposed that effects observed in children, which epidemiology has associated with domestic magnetic fields, are in fact due to small shocks that arise due to potential differences that build up between the water tap and the grounded drain of a tub. Shocks received in the bath can still induce in a small child's body current densities of a magnitude known to induce a biological effect. This alternative hypothesis is still under investigation.

1.2.2.4 Electrical Appliances

The United States, Japan, Canada, and some other countries use 110 V_{rms} AC for basic electrical power, while most of the rest of the world uses 230 V. Since transmission and distribution voltages in the two types of system are about the same, only differences due to appliances or building wiring would be expected. For a given power consumption and similar design, 110 V appliances draw twice as much current and create twice as strong a local magnetic field, although their local electric fields are half as strong. However, because both types of field fall off rapidly with increasing distance from the appliance and metal appliance cabinets shield electric fields, measurements of exposure to magnetic fields have not yielded great differences between the two systems (see Table 1.1). Measurements of magnetic fields from a sample of various appliances show that the fields have a rapid falloff with distance from the device [33]. Very close, the values may exceed international guidelines, but at a distance of 0.5–1 m the fields are seldom higher than few tenths of a microtesla. In general, it can be said that the more power the equipment uses, the higher the magnetic field. Table 1.2 presents some representative values from 110 V appliances.

TABLE 1.2

Ratios (B_{on}/B_{off}) of Magnetic Fields Measured with Appliances Turned On and Off

Appliance	Measurement Location	B_{on}/B_{off} 6–54 Hz	54–606	606–3066 Hz	8–200 kHz
Hair dryer	5 cm from nozzle	8.3	57	76	11
	10 cm from nozzle	3.2	17	31	—
	15 cm from nozzle	2.1	7.9	16	—
	25 cm from nozzle	1.4	3.1	6.1	—
Headset playing music	Forehead	1.5	1.0	1.2	—
	Center of head	<1.0	1.0	1.2	1.1
	Above ear	2.0	1.0	2.5	—
	Sternum	1.4	1.0	1.1	—
	Hip	2.7	1.0	2.6	—
Home sewing machines	Front of abdomen	2.7	2.8	2.4	1.5
	Left side of abdomen	1.7	2.0	1.8	—
	Right side of abdomen	1.7	1.6	1.5	—
Motorized clock	10 cm from clock	<1.0	13	4.3	1.1
	25 cm from clock	<1.0	4.0	<1.0	—
	50 cm from clock	<1.0	1.7	<1.0	—
	100 cm from clock	<1.0	1.0	1.0	—
	At subject's head	<1.0	1.4	1.0	—
Electronic clock	10 cm from clock	<1.0	4.7	1.5	1.5
	25 cm from clock	<1.0	1.8	1.0	—
	50 cm from clock	<1.0	1.1	<1.0	—
	100 cm from clock	1.1	1.0	1.0	—
	At subject's head	1.1	1.1	1.0	—

Note: B_{off} was estimated using linear interpolation at those measurement locations where it was not directly measured.

Source: From Kaune, W.T., Miller, M.C., Linet, M.S., Hatch, E.E., Kleinerman, R.A., Wacholder, S., Mohr, A.H., Tarone, R.E., and Haines, C. *Bioelectromagnetics* 23, 14–25, 2002.

Vistnes [34] recently gave some examples of flux densities near 220 V appliances. Of special interest may be a clock radio, which because of bad electrical design may give rise to exposure of the order of 100 μT close to the equipment. Since people are likely to place a clock radio very close to the pillow, the head may be exposed to quite a large magnetic field, exceeding the normal levels in the house.

The general range of magnetic and electric field magnitudes at various distances from transmission lines, local distribution lines, and appliances is shown in Figure 1.9.

Most modern electrical appliances are equipped with an electronically switched power supply in which an electronic circuit replaces the old-style transformer. This means that the current is no longer a pure sinusoidal 50- or 60-Hz signal but contains harmonics. The current used by a low-energy 50-Hz fluorescent lamp is illustrated in Figure 1.10, and the Fourier analysis is shown in Figure 1.11 indicating all the harmonics. Higher harmonics and transients (fast spikelike excursions) are also generated by motor-driven appliances and those run by vibrating mechanisms using make-and-break switching contacts, such as older electric shavers or doorbells (Table 1.2).

The magnetic field in different infant incubators used in hospital nurseries varied between 0.23 and 4.4 μT, with an arithmetic average of 1.0 μT [35]. Most of these values are considerably higher than the exposure that can be measured in residential areas close to transmission lines. The technology to reduce the exposure is at hand and can be easily applied.

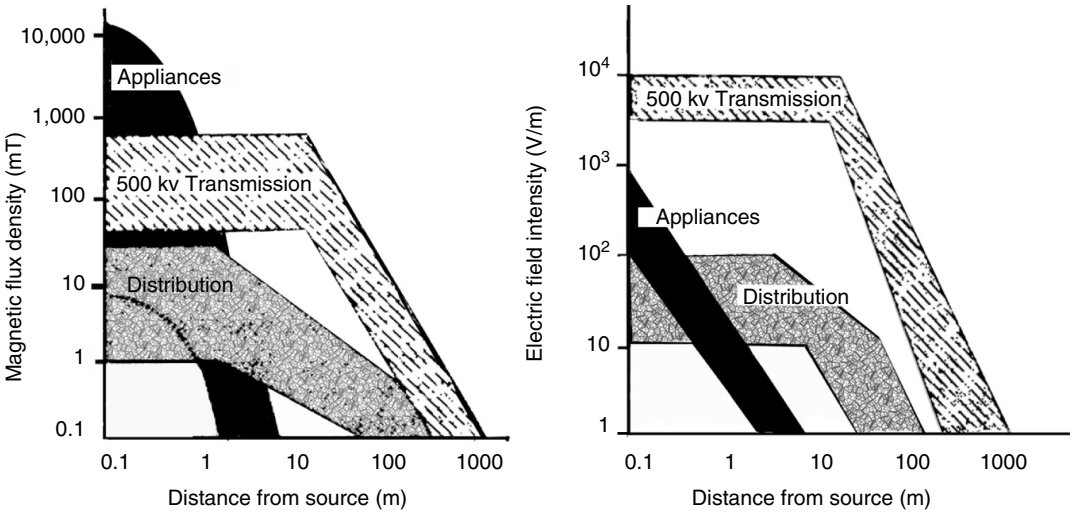

FIGURE 1.9
Magnetic flux density (left) and electric field strength (right) as a function of distance from transmission lines, local distribution lines, and appliances. (From U.S. Office of Technology Assessment. Biological Effects of Power Frequency Electric and Magnetic Fields. U.S. Government Printing Office, Washington, DC, Background Paper OTA-BP-E-53, 1989.)

Occupational exposure from handheld electrical appliances can be quite high. This is mainly equipment that is held close to the body and that uses high power, such as drills and circle saws. These devices usually have adjustable speed, which is done through the switched power supply. Values for the magnetic field of the order 100–200 μT are not uncommon, and in order to show compliance with standards the measurements have to take into account the harmonic contents of the waveform.

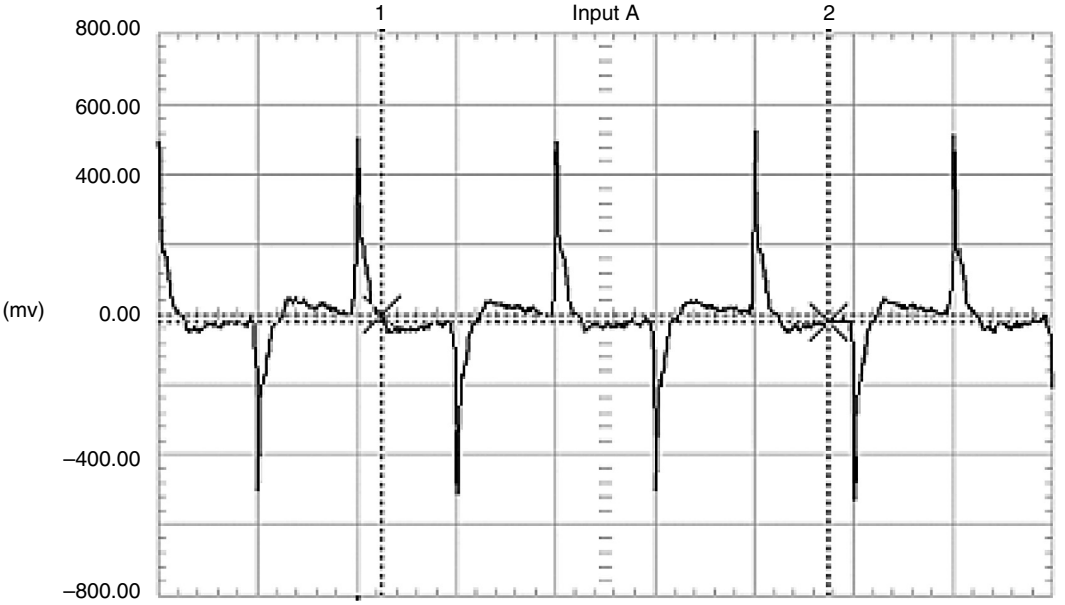

FIGURE 1.10
Wave shape of the current to a low-energy fluorescent lamp. The timescale is 10 ms/div. (Figure courtesy of Swedish National Institute for Working Life.)

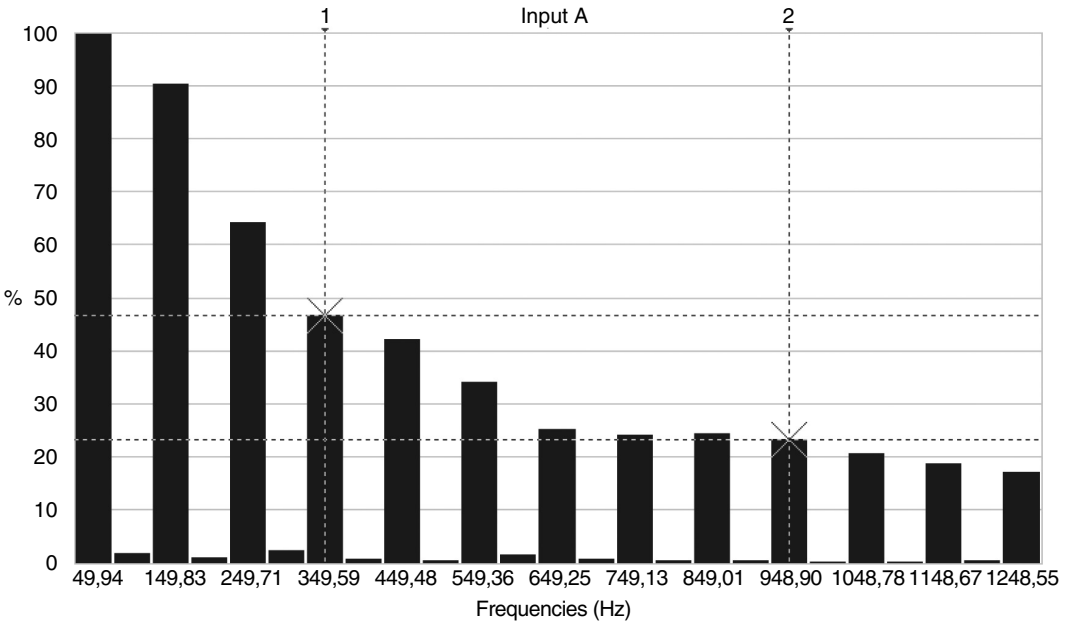

FIGURE 1.11
The Fourier spectrum of the wave shape in Figure 1.7. Note the high 150-Hz component. (Figure courtesy of Swedish National Institute for Working Life.)

1.2.2.5 ELF Fields in Occupational Settings

Wertheimer and Leeper [14] were not only the first to publish evidence in support of increased childhood cancer risk with magnetic field exposure, but they also pointed to increased cancer risk in occupations with high magnetic field exposure. Since then, hundreds of studies have looked into this problem, and the assessment of workers' exposure has been debated. There are studies where individual estimates of the exposure have been made for male [36] and females [37]. For workday means, the 25th, 50th, and 75th percentiles were 0.13, 0.17, and 0.27 μT, respectively, for males, and the corresponding values for females were almost similar: 0.14, 0.17, and 0.23 μT. The study on exposure of males investigated the 1000 most common occupations in Sweden, and the study on female exposure included 61 job categories. Table 1.3 shows additional estimates for various professions.

Sewing machines—Near sewing machines increased magnetic fields can be found, and depending on the type of machines used the values differ. The mean average value logged during some working hours is of the order of several tenths of a microtesla [38].

Welders—Among the occupations where quite high exposure exists, electric arc welders are a prominent example. They handle cables carrying hundreds of amperes very close to their bodies. The welder normally grasps the cable, and it sometimes also is in contact with other parts of the body, for instance, it might be draped over the shoulder. Depending of the technique used—DC or AC, type of rectification, etc.—the ELF magnetic field varies, but several studies report values in the range of tens to hundreds of microtesla [39]. Skotte and Hjøllund [40] found a mean of 21 μT for a full-shift average workday of manual metal arc welders. During the actual welding, the *B* field can be up to several millitesla.

The frequency content of the signal can be rather complex. In one of the most common situations the welding equipment is connected to a three-phase outlet, and the current for the weld is thus three-phase full-wave rectified. This means that we have first a DC

TABLE 1.3

EMF Exposures in Common Environments

Environment	Median[a] Exposure	Top 5th Percentile	Environment	Median[a] Exposure	Top 5th Percentile
Office Building			*Machine Shop*		
Support staff	0.6	3.7	Machinist	0.4	6.0
Professional	0.5	2.6	Welder	1.1	24.6
Maintenance	0.6	3.8	Engineer	1.0	5.1
Visitor	0.6	2.1	Assembler	0.5	6.4000
School			Office staff	0.7	4.7
Teacher	0.6	3.3	*Grocery Store*		
Student	0.5	2.9	Cashier	2.7	11.9
Custodian	1.0	4.9	Butcher	2.4	12.8
Administrative staff	1.3	6.9	Office staff	2.1	7.1
Hospital			Customer	1.1	7.7
Patient	0.6	3.6	—	—	—
Medical staff	0.8	5.6			
Visitor	0.6	2.4			
Maintenance	0.6	5.9			

Note: Magnetic fields are measured in milligauss (mG); 1 mG = 0.1 μT.

[a]The median of four measurements. For this table, the median is the average of the two middle measurements.

Source: National Institute for Occupational Safety and Health. From Portier, C.J. and Wolfe, M.S., Eds. Assessment of Health Effects from Exposure to Power-Line Frequency Electric and Magnetic Fields. NIH Publication 98-3981, National Institute of Health Sciences, Research Triangle Park, NC, 1998 (accessed April. 7, 2005, at http://www.niehs.nih.gov/emfrapid/html/WGReport/WorkingGroup.html).

component and on that a large AC ripple with main frequency 300 Hz (50 Hz power system), but it also has harmonics at 600, 900, 1200 Hz, etc. A newer type of equipment has a pulsed DC (50–200 Hz pulse frequency) as a base with a 53 kHz current applied between the pulses. This leads to frequencies in the current equal to the pulse frequency and its harmonics and also 53 kHz and harmonics. It is a very complex situation to evaluate with respect to compliance with guidelines, because of the complexity of the signal.

Since in many cases, high exposure results from the cables being very close to the body, much can be done to reduce the exposure of the welder by carefully arranging the workstation to keep the cables away from the body. By placing the welding machine on the right-hand side of the worker (if right-handed) and seeing that the return cable is as close as possible to the current cable, the exposure can be reduced by one order of magnitude.

Induction heaters—Induction heating is used for heating metals for purposes that include surface or deep hardening, welding, melting, soft soldering, brazing, annealing, tempering, and relieving stress. The frequency can be from 50 Hz to the low megahertz range, depending on the desired skin depth and purpose. Since high currents are used, the leakage magnetic field can be substantial. At the operator's position, values of the order of 0.5–8 μT are common, and the maximum field near the coil, where, for instance, the hands can be exposed, can reach several hundreds of microtesla. The field strength is in many cases high compared with recommended limits [12].

Railway workers—Engine drivers of AC electric engines experience rather high magnetic field exposure. The intensity depends of several factors, one of them being the age of the engine. Nordensson et al. [41] (see also Refs. [42,43]) found that drivers of Swedish model RC engines were exposed to flux densities of the order of 10–100 μT. The older

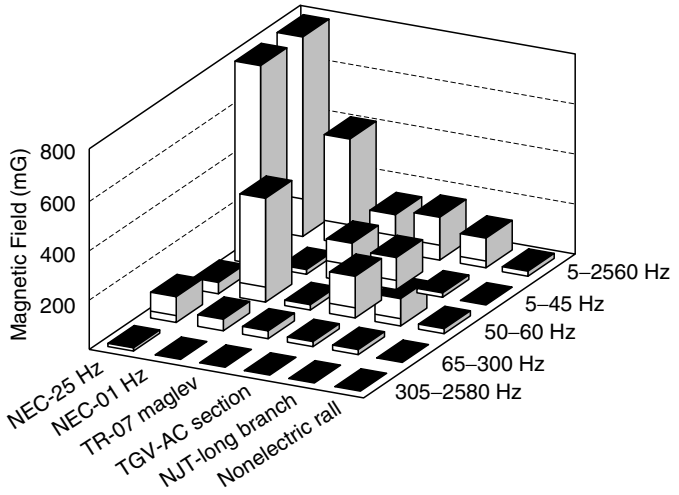

FIGURE 1.12
Maximum (top of bar) and average (horizontal bar) magnetic fields in various frequency bands in the passenger compartment of several intercity rail systems. NEC = U.S. Amtrak Northeast Corridor (Washington, DC, to Boston, MA), which has both 25- and 60-Hz segments; TR-07 = German Transrapid maglev system; TGV = French ''Train a Grande Vitesse,'' AC-powered segment of Paris-Tours line; NJT = New Jersey Transit, NJ Coast Line Long Branch section. (From Bernardi, A., Fraser-Smith, A.C., and Villard, O.G., Jr. *IEEE Trans. Electromagn. Compat*. 31, 413–417, 1989.)

models of engines had the higher values. The mean average values for a full workday ranged from 2 to 15 μT. The main input power frequency is $16\frac{2}{3}$ Hz, and this frequency was dominant at idle, but at full power, harmonics up to 150 Hz existed. Wenzl [44] measured the exposure of rail maintenance workers in the United States and found peak values ranging from 3.4 to 19 μT, and the time-weighted average was in the range 0.3–1.8 μT. Chadwick and Lowes [45] have examined the exposure of passengers on trains in the U.K., and they found static magnetic flux densities up to several microtesla. The alternating field was also substantial in some locations and reached up to 15 mT at floor level. However, none of the whole-body alternating magnetic flux densities approached the National Radiological Protection Board (NRPB) investigation levels.

Trains operating on DC, such as in the Washington, DC, and San Francisco, CA, transit systems, also produce time-varying fields in the passenger compartments, particularly below 5 Hz [46,47]. Figure 1.12 shows field intensity in various frequency bands in the passenger compartment of several representative electric rail systems and a nonelectric one. Interestingly, the figure shows that an experimental magnetic levitation (maglev) system does not exhibit substantially different field levels [48].

Electrochemical plants—In factories producing, for instance, aluminum, copper, or chloride through electrochemical processes, very high DC currents are used, often of the order of tens of kiloamperes. The DC current is obtained through rectification of the incoming three-phase AC power. Often there is still a substantial AC component of the current and hence an AC magnetic field. Measurements have shown broadband ELF measurements of the order of 10–50 μT, with many different frequencies present that need to be taken into account in the evaluation of the exposure situation. Typically, a 50 Hz component can be present, because of unbalance between the three phases, and the full-wave rectification gives 300, 600, and 900 Hz components. The exposure guidelines can often be exceeded in some locations in the plants, and special requirements may be needed to reduce the exposure. DC fields in these smelters are often on the order of several millitesla, with peaks of at least 20–30 mT; up to 70 mT has been reported [49,50].

1.2.2.6 *Internal ELF Fields Induced by External and Endogenous Fields*

Because the bodies of humans, other animals, and even plants contain ionic solutions and because cell cultures, as well as many one-celled and other organisms such as fish or the roots of plants, live in conductive media, external exposure to electric or time-varying magnetic fields can produce internal fields, which can be quite different than the unperturbed external fields.

In an electric field, as discussed in Chapter 3 and Chapter 4 in this volume on properties of materials, the conductivity and dielectric constants of tissue are quite different from those of air or vacuum, creating a layer of charge due to polarization at the surface of the body, which decreases the internal field, often by many orders of magnitude. For a human standing in the ELF electric field below a high-voltage transmission line, the field inside the body may be only 10^{-6} of the external field. The shape of the body also affects the amount of polarization. Since a standing humans body has more of a ''lightning rod'' shape than a crouching rat, a rat must be exposed to a much lower external field to achieve an equivalent internal electric field. A squatting human will experience lower and the rearing rat, higher fields. The body shape and foot area also affect the average current densities in various body locations because of the external electric field. Figure 1.13 illustrates these differences [51]. As shown in the figure, current densities increase in areas of smaller cross section, for example, the human neck or leg, and closer to the ground, for example, the upper and lower human torso. When calculated without averaging across a cross section, current densities are higher near a junction point; for instance, they are higher and more horizontal at the armpit than in the middle of the chest area [52].

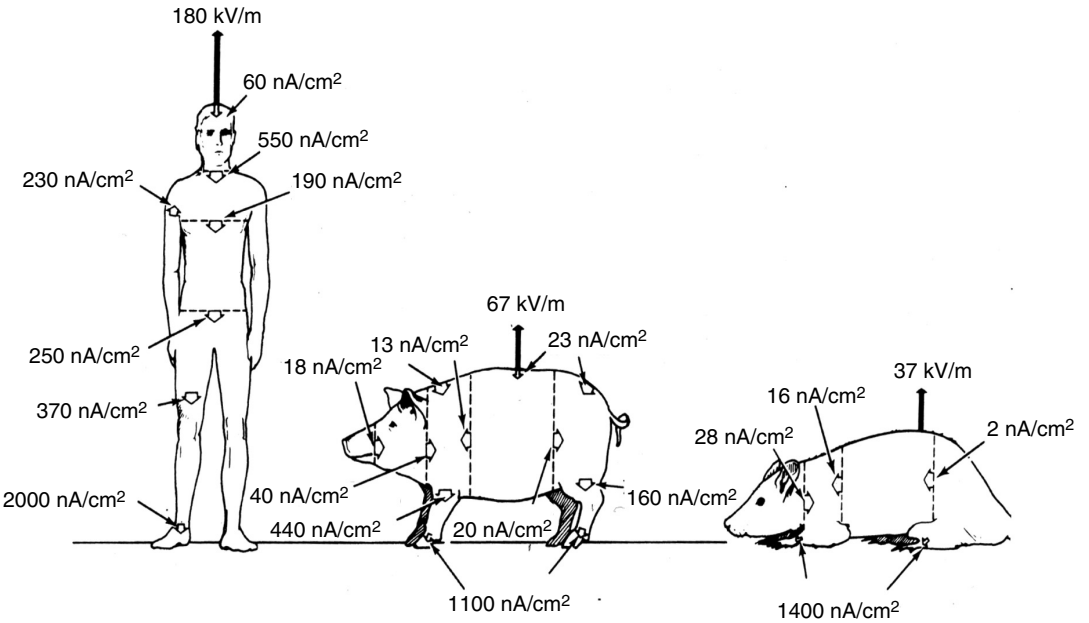

FIGURE 1.13
Estimated external electric field and current densities of a grounded man, pig, and rat exposed to a vertical 0-Hz, 6-kV/m electric field. Calculated internal current densities are averaged over sections through bodies as shown; calculated current densities perpendicular to the body surface are shown for man and pig. (From Figure 4 in Kaune, W.T. and Phillips, R.D. *Bioelectromagnetics* 1, 117–129, 1980; Copyright John Wiley & Sons, reproduced With permission.)

It is important to recognize that electric fields and current densities such as those in Figure 1.13 are averages, whether across the whole cross section of the body or a limb or across a localized region. Fields vary greatly across very small distances when one examines them at dimensions on the order of a cell or a molecule; this is called *micro-dosimetry*. Forming a good picture at this level of fields from either endogenous or external sources is an unsolved but very important problem. Chapter 5 in this volume on basic mechanisms discusses this issue further.

An external magnetic field's value is little changed as it enters a biological system, whether the human body or cells in culture, since the average biological magnetic susceptibilities are very close to those of air or vacuum (see Chapter 3 and Chapter 4 in this volume on magnetic properties of materials). However, the internal electric fields and currents induced in the body according to Faraday's Law are strongly determined by bodys (or specimen) shape, electric conductivity, and orientation with respect to the field. Table 1.4 gives some comparisons between the current induced in a human by the ELF magnetic fields generated in various situations and the external vertical 60 Hz electric field needed to produce the same current densities.

As discussed further in several chapters in this volume, especially Chapter 2 on endogenous fields, Chapter 5 on the basic interactions of fields and biological systems, and Chapter 7 on noise, as well as in the various discussions of models of field–biological system interaction, an externally applied field is unlikely to cause a biological effect unless the part of the biological system with which the field interacts is able to distinguish the external field from the internal electric fields and currents that are an integral part of the system. Exactly how to formulate the aspects of the endogenous field or current

TABLE 1.4

Magnetically Induced Total Body Current and Current Densities and Vertical 60-Hz Electric Field Inducing Equivalent Currents

Source	Current (μA)	Current Density (A/m^2)	Electric Field (kV/m)
Sinusoidal waveforms			
Cord-connected household appliance	20–500	0.5–12[a]	1.5–38
Man in 8-kV/m electric field	120	3[a]	8
Electric blanket (not low field)	7–25	2–40[b]	0.5–1.7
Man in 0.16-kV/m electric field	2.2	0.05[a]	0.16
Nonsinusoidal waveforms—medical devices			
Electric anesthesia device (100-Hz square wave)	10,000	71,000[c]	670
Pacemaker electrode in myocardium[d,e]	6,000	20,000	400
Pacemaker electrode implanted in abdomen[d,f]	6,000	300	400

[a]Through 40-cm^2 ankle.
[b]0.63 cm from electric wire in blanket.
[c]Next to electrode.
[d]Peak pulse current $\sim 10^{-3}$-s duration, repeated every 0.8 s.
[e]Electrode area, 0.3 cm^2.
[f]Electrode area, 20 cm^2.
Source: After Bridges, J.E. and Preache, M. *Proc. IEEE* 69, 1092–1120, 1981. (Slightly modified from Table 1.3, Chapter 2 of second edition.)

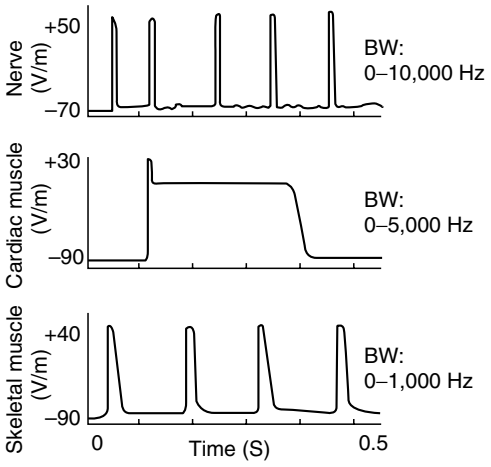

FIGURE 1.14
Typical time course and amplitudes of time-varying membrane potentials (V_m) of various cells. BW is the equivalent frequency bandwidth containing the main Fourier components of each voltage excursion. (From H. Wachtel, University of Colorado, private communication, copyright 1992; reprinted with permission.)

density that should be compared with the local field or currents in a particular situation is still an open research question; for example, over what region (how many molecules or cells) and over what range of frequencies (very narrow or broad) does the biological system average?

These endogenous fields range from the normal ~50–100 mV DC transmembrane potentials of most cells (negative in animals, sometimes positive in plants) to the relatively rapid pulses of nerve cell depolarization or repolarization spikes and the less rapid pulses of, for instance, muscle cells (see Figure 1.14 for examples). They also include the very large and often highly local and hence very nonuniform fields because of local charge densities on some macromolecules or changes in the double ion layer next to a membrane because of the inclusion of a protruding structure, such as a channel, at a particular location (see, e.g., diagrams in Chapter 5 in this volume on basic interactions of fields and biological systems).

1.3 EM Fields at Intermediate and Radio Frequencies (3 kHz to 300 MHz)

1.3.1 Electronic Article Surveillance

Many libraries and stores are currently equipped with electronic article surveillance systems, which generate EM fields ranging from ELF to radio frequencies (RFs). Sometimes, employees spend long periods of time close to parts of these systems, and they might therefore be exposed to strong EM fields, well in excess of the reference levels (RLs). RLs are the levels of easily measured fields in air that exposure-limiting regulations or guidelines state may, but do not necessarily, create health questions in those exposed to them. Above RLs, more precise measurements or calculations are needed for each specific situation to determine whether limits for the actual fields inside the body, the basic restrictions (BRs), are exceeded (for a discussion of RLs and BRs, see Chapter 8 in *BMA*) on standards in [82]).

Kjellsson et al. [53] made measurements on two different systems, one used in a shop and one in a library. The coils in the library at the exit were working at 920 Hz, and the

flux density at the center of the coils was of the order of 10 μT, compared with the RL for the general public of 6.25 μT. When the books are returned to the library, the electronic tag in the book has to be activated before the book is put back into the library. The system used for deactivating operates at 50 Hz, and at close range the flux densities were of the order of some millitesla, thus again above the RL for occupational exposure at 500 μT. In the store the signal was a mixture of 17 Hz and 6.25 kHz. The flux densities at the lower frequency were of the order of 200–300 μT, and at the higher frequency the values were well in excess of 100 μT. The RLs at 6.25 kHz for the general public is 6.25 μT, so the RLs are clearly exceeded, and more in-depth analysis is needed to see if the BRs are still not violated. See also Harris et al. [54] for a technical description of these devices.

Both at the shop and in the library there are situations and places where the general public as well as the employees are exposed to magnetic fields that exceed the RL. Logging the exposure during a work shift at the shop also showed that the cashiers are exposed to magnetic fields generated by the transmitter signal of the detection gates, which were often activated by customers during the work shift studied. The cashiers are therefore a highly exposed category of personnel and hence are of interest to include in epidemiological studies. Eskelinen et al. [55] have published similar results and conclusions in a previous study.

In the library not only the detection gates but also the activators and deactivators contribute to the high magnetic fields. One problem is the handheld activator used by the employees. Because of its small size, it is possible to hold the activator against almost every part of the body. If for example, a user is wearing a pacemaker and is not aware of the magnetic fields, the worst case could lead to disturbances in the pacemaker.

1.3.2 EM Fields from Video Display Terminals

A very commonly used appliance emitting EM fields is the computer video display terminal (VDT). Flat panel displays are increasingly replacing the cathode ray tube (CRT)-based VDTs at present, but a great many CRTs are still in use. There are five different types of fields present in the vicinity of the CRT: an electrostatic field, VLF electric and magnetic fields at the horizontal sweep frequencies, and various ELF electric and magnetic fields at the screen refreshing rate, related to the power frequency. These are considered separately in the next few sections. Measurements show that the equivalent electrostatic surface potential on the screen can reach up to 20 kV for some VDTs, and the ELF electric fields in front of the VDT at a distance of 0.5 m range from a few to tens of volts per meter, although most of the time it is not distinguishable from the office background 50 or 60 Hz electric field. The ELF magnetic field can reach a few tenths of a microtesla, and close to the tube the values are up to a few microtesla. The VLF electric fields range from a few to tens of volts per meter, and the corresponding magnetic field is of the order of a few tenths of a microtesla at 0.5 m in front of the VDT. The VLF B field time derivative ranges from a few to a few hundreds of millitesla per second (see Ref. [56]).

In Figure 1.15 a schematic drawing of a CRT-based VDT is shown with the deflection coils. Since these coils are to move the electron beam horizontally, from left to right, the magnetic field affecting the electrons has to be vertically directed; therefore, the coils are in horizontal planes above and below the neck of the tube as shown in Figure 1.15. The stray field from these coils at the operator's position is mainly vertical. The sawtooth wave shape of the magnetic field is also schematically shown in Figure 1.10. The times, 3 and 30 μs, given in the figure are typical examples of values found on some VDTs. Also shown in the figure is the time derivative of the signal. Since the vertical deflection requires a horizontal magnetic field, the coils for the vertical deflection (omitted in the drawing in

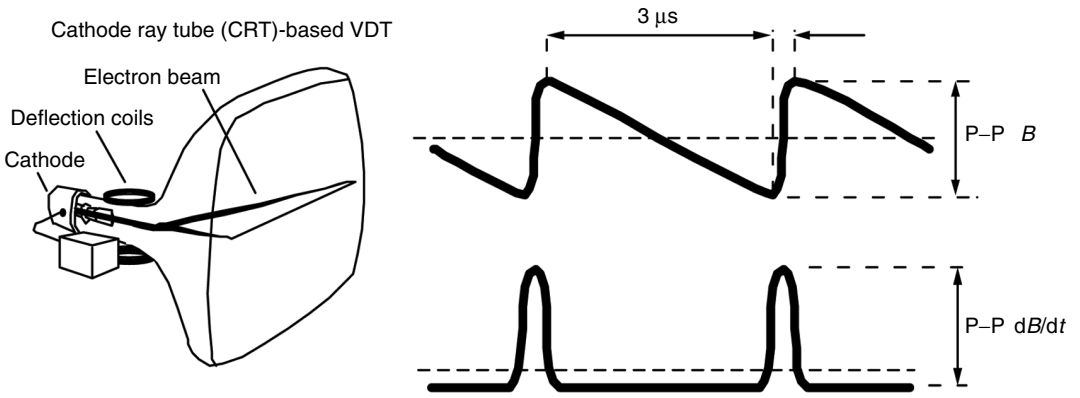

FIGURE 1.15
Schematic drawing of CRT-based VDT. To the right, examples of an idealized waveform of the VLF magnetic field and its time derivative are given. (Figure courtesy of Swedish National Institute for Working Life.)

Figure 1.15) lie in vertical planes on each side of the neck of the tube, giving a horizontal field and, thus, a corresponding stray field. The field from these coils has a frequency equal to the refresh rate, usually equal to or a small harmonic of the line frequency, and has a sawtooth wave shape. The electric field experienced by the operator is usually due to charge accumulating on the screen and is directed between the screen and the operator's body.

The time derivative, dB/dt, is usually measured only for the maximum field component in front of the VDTs. The median values found are 0.63 and 15 mT/s for the ELF and VLF frequency ranges, respectively. The corresponding maximum values are 1.9 and 101 mT/s for the ELF and VLF fields. For the ELF magnetic field in front of the VDT the median value was 0.21 μT. This is then a combination of the general magnetic field level in the office (median value 0.07 μT) and the emission from the VDT [56].

Flat panel displays for computers are presently based primarily on liquid crystal technology, particularly in portable computers. Compared with VDTs they use much lower internal voltages and currents and do not use magnetic field deflection, leading to the presumption that users' exposures are quite low. Even with a flat panel display, it or various sources inside the computer may expose portions of an operator's body to some fields that can approach few tenths of a microtesla in the ELF and VLF regions, especially for a portable computer that is held on the knees. At the time of writing, any values of the fields from laptop computers or other flat panel displays do not seem to have been published in the peer-reviewed literature. Swedish and Australian trade union tests on several laptop computers have shown magnetic field emissions below their internal certification limits for exposure (see Swedish levels in Table 1.5), initially established for VDTs. The Australians found two exceptions: a peak of up to 10 mG for up to 5 s during the program loading and a 0.01–0.16-μT fluctuating field at 30 cm, emanating from the computer transformer (frequencies not given) [57]. Computers with flat panel displays that have ungrounded power supplies, including laptops running either on batteries or on an ungrounded charger, can generate considerable static charges on their screens, producing DC potentials that exceed the Swedish unions' specifications. Older displays using cold-cathode backlighting sometimes also exceed the specifications for ELF or intermediate RF electric fields (Y. Hamnerius, Chalmers University, private communication, 2005).

Computers equipped for local area RF networking, such as ''Wi-Fi'' systems, and hubs for such networks emit and receive fields in the same general ranges of frequency and

TABLE 1.5

Swedish Tjänstemännens Central Organisation (TCO) Certification Limits for Computer Display Terminal Fields

Frequency Band	Quantity	Field Strength	Measurement Distance From Screen
DC	Electric potential	±0.5 kV	0
Band I	Electric field	≤10 V/m	30 and 50 cm
5 Hz–2 kHz	Magnetic field	≤200 nT	30 and 50 cm
Band II	Electric field	≤1 V/m	30 and 50 cm
20–400 kHz	Magnetic field	≤25 nT	30 and 50 cm

Source: TCO'03 Displays Flat Panel Displays, version 2.01 (translated by Y. Hamnerius), January. 2, 2004 (http://www.tcodevelopment.com).

intensity and are subject to the same sorts of limits as other portable RF devices, such as portable or cell phones. These are discussed later.

CRT-based VDTs use magnetic deflection of the electron beam, and therefore an external magnetic field can cause jitter and flicker on the screen. Sandström et al. [58] applied both 50 and 60 Hz magnetic fields to monitors with different refresh rates. The distortion was detectable from 0.6 up to 1.1 μT for seven monitors investigated. Background magnetic fields higher than 0.5 μT are not uncommon in offices; Sandström et al. [56] found that 5% of the workplaces measured exceeded this value. The ability to detect jitter depends, among other things, on the frequency of the disturbance. Since the frequency of the jitter oscillation is equal to the difference between the frequency of applied magnetic field and the refresh rate, the sensitivity to the external magnetic field will be different with different frequencies of the applied magnetic field.

1.3.3 RF Transmissions

1.3.3.1 Shortwave Transmission

High-power shortwave transmitters (approximately 2–25 MHz) are used for international broadcasts. Often the power supplied to the antenna system can be several hundreds of kilowatts. The antenna systems used are most often movable log-periodic or steerable curtain-type antennas.

Measurements of field strengths from such transmitters have been recently presented by Altpeter et al. [59] in connection with their study on health effects on people living near a station. The magnetic field values ranged from tens of milliamperes per meter for those at a distance of 500 m from the antenna to some tenths of a milliampere per meter for those at a distance of a few kilometers. In a study of leukemia and residence near a high-power shortwave transmitter in Italy, Michelozzi et al. [60] reported spot measurements of the electric field in some of the closest houses to be between 3 and 20 V/m. (Under far-field conditions 3 V/m corresponds to a magnetic field of 8 mA/m and 20 V/m to 53 mA/m.) For a review of measured field strengths see also Mantiply et al. [61].

1.3.3.2 FM Radio and TV Transmission

Exposures to RF fields have been occurring for as long as we have had radio broadcasting. Since the antenna towers are usually quite high and the emissions are directed for reaching a long distance, exposure levels near the towers are minimal. The Environmental Protection Agency has done field strength measurements in the United States, and an

TABLE 1.6

Electric Field Strengths

Source	Distance		
	1 km	**10 km**	**50 km**
(a) Combined electric field strengths from large radio and TV transmitters and one type of base station for mobile phones[a]			
Radio	1	0.1	0.02
UHF TV	5	0.5	0.1
(b) Electric field strengths from radio base stations for Mobile Communication			
	10 m	**100 m**	**1000 m**
Base station	7	0.7	0.07

Note: E field in V/m.

[a]Radio: 60 kW ERP; TV1: 60 kW ERP; TV2: 1000 kW ERP. $S = PG/(4\pi R^2) = E^2/120\pi$. (ERP is the effective radiated power, also expressed as PG, where P is the total power to the antenna and G is the gain; R is the distance to the antenna.)

overview is given by Mantiply et al. [61]. At a distance, the fields can be estimated from calculations using the far-field formula, and some examples are given in Table 1.6. The input power is often highest for UHF TV broadcasting. The TV signal consists of an amplitude-modulated video signal and a frequency-modulated audio signal. In Sweden, for instance, 30 kW of power is used for the video signal and about 5 kW for the audio. With the antenna gain this gives an effective radiated power (ERP) of 1000 kW.

There have not been many radio and TV towers built during the last 10 y or so, although a number have been moved or upgraded, e.g., moved to taller buildings for greater range, but we have seen an increase in the number of terrestrial channels available. New ways of transmitting information have also come into play with digital radio and TV. However, with these the output RF power may be lower; instead, this technique uses a much larger frequency bandwidth.

The total power density of RF exposure of the public has undeniably increased during the last 10 y. Tell and Mantiply [62] reported in 1980 that the average level in the United States from FM radio and TV transmitters was about 50 $\mu W/m^2$. Today, exposure due to such sources is about the same [50], but with mobile phone base stations added, the total power density is now often found to be on the order of 100 $\mu W/m^2$ or so (see Figure 1.16). Despite the proliferation of mobile telephone systems, most of the power is still due to broadcasting (Figure 1.11). Although the total level of RF exposure of the general public has increased during the last few years, it should be clearly stated that at all distances the RF field levels on the ground from base stations are well within the international guidelines for RF exposure of the general public.

1.3.3.3 Wireless Communication Systems (Base Stations, Personal Wireless Devices Such as Cellular Telephones and Pagers)

1.3.3.3.1 Mobile Phone Base Stations

Current mobile telephone systems operate at frequencies between 800 and 2100 MHz, but some older systems operating near 450 MHz are still in use (see Table 1.7). With the rapid increase in the use of mobile phones, the number of base stations has also increased. The phones operate by communicating with a nearby base station, which is a low-powered

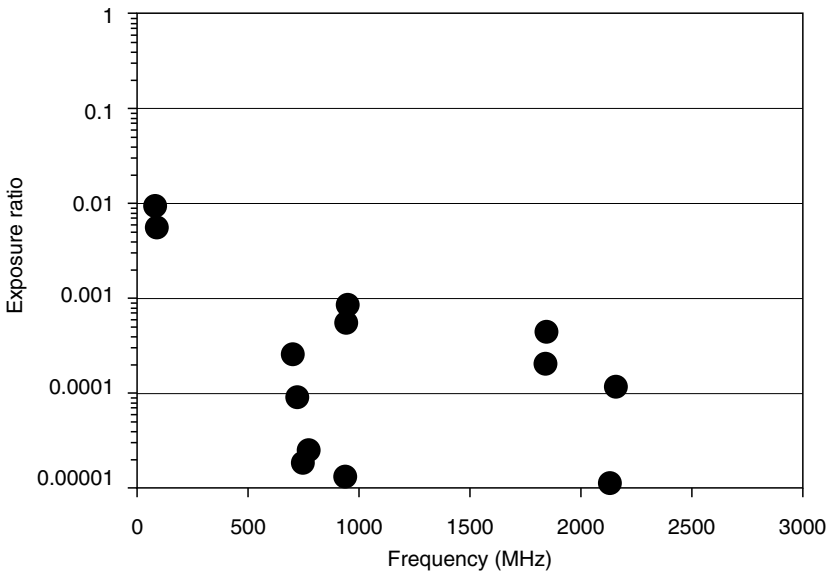

FIGURE 1.16
Power and frequency of environmental RF fields at a sample urban location in Sweden, plotted at each frequency as a comparison to the ICNIRP guideline power limit for personal exposure at the same frequencies, which is set equal to 1 (for plot of limits as a function of frequency, see Chapter 8 in *BMA* on standards in Ref. [82]). (From Hamnerius, Y. COST 281 Workshop 2004/09, Workshop on RF Exposure Assessment, Paris, September 20–21, 2004. With permission.)

radio transmitter, typically mounted on a tower or the roof of a building, that relays calls between the user and the telephone system. In Nordic countries the market penetration is over 100%; that is, there are more mobile phone subscribtions than people; many have more than one phone, and practically everone in the working population has access to a mobile phone. The number of base stations in Sweden is estimated at over 20,000. In 2000,

TABLE 1.7

Frequencies and Modulation Characteristics of Various Mobile Telephone Systems

System	Carrier Frequency	Modulation	Multiplexing Type
TETRA	380–470 MHz	17 Hz	TDMA
MIRS	806–821 MHz	11.1 Hz	TDMA
NADC	824–849 MHz	50 Hz	TDMA
CDMA	824–849 MHz	800 Hz	Multichannel
Analog	824–849 MHz	FM	None
GSM	890–915 MHz	217 Hz	TDMA
PDC	929.2 MHz/1.5 GHz	50 Hz	TDMA
Iridium	1616–1626 MHz	11 Hz	TDMA
CDMA	1765 MHz	800 Hz	Multichannel
PCS	1805–1880 MHz	217 Hz	TDMA
GSM	1800 MHz	217 Hz	TDMA
GSM	1900 MHz	217 Hz	TDMA
NMTS	1920–2170 MHz	100 Hz–1.5 kHz FDD	

Notes: TDMA = Time division multiple access; conversations use different time slices of shared channels. CDMA = code division multiple access; digital identifiers signal phone when the conversation is using one of many closely spaced channels.
Source: Data courtesy of M. Swicord, private communication, 2005.

the United States had more than 82,000 cellular base station sites, some with more than one base station in operation, while there were some 20,000 base stations sites in the U.K. [63].

The antenna system used for base stations comprises often either omnidirectional (whip) antennas, which radiate in all directions in the horizontal plane, or directional (panel) antennas, which radiate energy primarily from their front surfaces. Most commonly employed is a sectorized panel arrangement with three sets of directional transmitting and receiving antennas, oriented 120° apart.

The antennas have a high gain, giving a narrow beam in the vertical direction but a quite wide one in the horizontal direction. In the main beam of the antenna, that is, several meters or more directly in front of and at the same height as the antenna, the intensity of the beam (i.e., the power density) decreases as the inverse square of the distance from it. The RF exposure a person receives from a base station thus depends both on the distance from the antenna and on the angle with respect to the direction of the main beam. At ground level, the signal is relatively weak near the base of the antenna tower since the main beam is passing directly overhead. The ground level signal characteristically increases with distance from the tower to a maximum at between 10 and 100 m from the base of the tower and then decreases at still greater distances. Panel antennas only radiate significant amounts of energy in the forward direction. Thus, for panel antennas mounted facing outward on building parapets, the exposure is low for people on the rooftop or in rooms below the antenna. (See further the 1999 report on cellular telephones and health by the U.K. House of Commons Committee on Science and Technology [64].)

In rural areas, where there is a lower user density, base stations are typically a couple of kilometers apart. In towns and cities where there are more users the cells are smaller and transmitter base stations can be as little as a few hundred meters apart. The actual levels of transmitted power vary widely between urban and rural areas. Since a longer reaching distance is wanted in rural areas, the output power tends to be greater, whereas the large increase in the number and density of base stations within the cities will make the cells smaller and thereby also permit a reduction of output power from the surrounding base stations. Therefore, the levels of public exposure to RF energy from any system will not increase in proportion to the number of its base stations in an area.

In Table 1.6b an example is given of the calculation of electric field strength under far-field conditions. The values given are for the main beam, and since the beam would not be aimed at the ground in the near zone, the theoretical values are presumably overestimating the field strength for close distances. Measurements of field strength from base stations have recently been reported by Thuroczy et al. [65] and Hamnerius and Uddmar [66]. They found levels encountered within about 20 m from the antenna in the range of a few to some tens of volts per meter. However, at distances where most people would be exposed, the field strength is down to tens of millivolts per meter within cities, and in rural area values as low as a few millivolts per meter can be measured. For an estimation of maximum encountered levels, the formula used in Table 1.6b above may be used, and as can be seen from this table values in the range of tens of millivolts per meter are estimated for a distance of 1000 m from the station.

1.3.3.3.2 Handheld Mobile Phones

The technical details of analog and digital systems used for mobile phones have been described in detail [67,68], and only a short background is given here. The Nordic Mobile Telephone (NMT) system operates at 900 MHz with a continuous carrier wave. The maximum output from the handheld NMT900 phones is 1 W. The NMT phones have their output power regulated through the base station in two levels, 0.1 or 1 W; the closer to the station, the lower is the output power likely to be.

To make more efficient use of the available frequencies, various schemes that take advantage of the relatively slow way speech transmits information have allowed more than one conversation to occur in the same frequency channel. Some of these systems include pulsing the RF signal at various frequencies, often in the ELF frequency region, or otherwise modulating it. The result is a departure from a pure, continuous sinusoidal field. In the digital Global System for Mobile Communications (GSM), which is in very common use worldwide, the information is sent in pulses with a repetition rate of 217 Hz. The pulse length and repetition frequency give a duty cycle of 1/8. The maximum output power is 2 W, which gives a time-averaged value of 0.25 W maximum. The GSM system also provides a battery-saving function, which in practice reduces the output power to about half of the maximum. The output power is also regulated from the base station, from a maximum of 2 W down to a minimum of 20 mW, depending on the strength of the signal received at the phone; with the newest phones sold today an even lower value of 5 mW is used. The mean output power is thus normally well below 0.1 W. Frequencies and coding patterns of some other current or proposed mobile telephone signal systems are indicated in Table 1.7.

Different models of phones have different specifications for the antenna design position and physical dimensions, for instance, a dipole antenna or a helical antenna. Kuster [69] measured 16 different European digital phones and found a very wide variation in the SAR values. The phone giving the lowest value, when averaged over time and 10 g of tissue, had a specific absorption rate (SAR) of 0.28 W/kg in the user's head, and the one with the highest value had an SAR of 1.33 W/kg, all normalized to an antenna input power of 0.25 W, which is the maximal value for a GSM phone. If the averaging was done over 1 g of tissue, the span was from a low of 0.42 W/kg to a high of 2.0 W/kg. Anger [70] reported the measurement of SAR on 21 different phones, and his result is similar. The SAR ranged from 0.3 to 1.7 W/kg over 10-g tissues. He also reported the telephone communication power value, that is, how much of the output power can be used for communication, and he found values ranging from only about 5% in the lowest phone to just less than 50% in the ''best'' phone. Thus, more than half of the output power from the phone is lost because of mismatch between the phone and the antenna, and some is deposited as SAR in the user.

These SAR measurements were done under normal user conditions. However, when the phone is slightly tilted toward the head, Kuster [69] shows that the value can go up from 0.2 to 3.5 W/kg. Thus, for different phones under maximal output, we have a factor of about 5 between the extremes, and to this the personal handling of the phone gives a factor of tenfold or more. It should be noted that all given values are the maximum SAR values found, regardless of the anatomical location. An equal weight is given to the values, independent of whether they are obtained on the external ear, in the middle or inner ear, or behind the ear. In the future, it will be necessary to make the comparison at the same anatomical location. Presumably then, the values as given by Kuster [69] might differ even more.

Taken together there is a rather large uncertainty in estimating the actual SAR that depends on the specific situation, including a factor of 100 from the distance to the base station and at least a factor 10–50 depending on the make and model of the telephone and the personal style of use.

The currents from the battery also give rise to magnetic fields near the phone. For GSM phones magnetic flux densities of a few microtesla near the phone have been measured [66,71]. The fields are pulsed DC fields with a frequency of 217 Hz. For the NMT phones the magnetic field from the battery current can be regarded as pure DC. Jokela et al. [72] recently measured seven different GSM phones and examined the frequency content of the magnetic pulse, and he found that a considerable amount is found in the low kilohertz range. It was even found that some phones exceeded the ICNIRP guideline reference values when the multiple frequency formula was applied, but calculations show that the BRs were not exceeded.

1.3.4 RF EM Fields in Industrial Settings (RF Dielectric Heaters, Worker Exposure to Broadcast Systems)

1.3.4.1 RF Sealers

Operators of RF plastic sealers (RF operators) are an occupational category highly exposed to RF with frequencies around 27 MHz. RFs are used to produce heat to seal, for instance, plastics for tarpaulins, tents, rain clothes, and covers. Around an RF plastic sealer (RF sealer), both a magnetic and an electric field will be present, and close to the machine the coupling between the two is complex since far-field conditions are not at hand.

During RF exposure, a current is induced in the body, the magnitude of which is dependent on many factors such as the electric and magnetic field strength, the polarization of the field, and the grounding conditions. See further Wilén et al. [73], who tested different techniques to measure the induced current in grounded as well as ungrounded conditions.

Within the category of RF sealer operators, many different exposure situations exist, which can roughly be divided into two main types: tarpaulin workers and readymade clothing workers. Tarpaulin workers often stand in front of the RF sealer and will experience whole-body exposure, which often causes a high current to pass through the ankles. Readymade clothing workers often sit down in front of the RF sealer, often without perfect contact with the ground, but with their hands close to the electrode.

To get a good weld, both the welding time and the total power can be adjusted. The combination of the two will produce enough energy to seal the plastic. Typical welding times range from 1 to 10 s, depending on the material being sealed. The total exposure time will also vary between different RF-sealing processes; in the same amount of time, more welds are made in the readymade clothing industry than in the tarpaulin industry. For more information about the welding process see Refs. [74–76].

In a recent study, Wilén et al. [77] studied the exposure among RF sealer operators. The mean values of the calculated 6-min spatially averaged field strengths, in line with ICNIRP recommendations, are 107 V/m and 0.24 A/m, respectively. The maximum measured field strengths were 2 kV/m and 1.5 A/m, respectively. The induced current in ankles varied depending on the work situation, with a mean value of 101 mA and a maximum measured value of 1 A. In total, 16 out of the 46 RF plastic sealers measured exceeded the ICNIRP guidelines.

1.3.4.2 Occupational Exposure from Broadcasting and Radars

Workers in the fields of communication and radar are only exposed to low-level field strength in most situations. However, when climbing FM or TV towers, for instance, accidental exposure can be intense if proper safety precautions are not taken to keep exposure below the regulated limits. The same is true when someone is working near transmitter cabinets with the interlocks defeated and doors open. In these instances, the exposure, usually inadvertent, can be substantial.

Radar is used to detect the presence and directions of aircraft, ships, or other usually movable objects. The systems usually operate in the frequency range from 300 MHz to 15 GHz depending on the purpose of their use. The output power can range from a few milliwatts from police radar to several kilowatts for large air surveillance systems. A short description of various systems can be found, for example, on the WHO Fact Sheet No. 226 [78]. Here, as an example, a short description is given of one usual system where environmental exposure may occur. For civilian air traffic control, radars operating at 1305 MHz are used. The systems use a pulsed field with pulse duration of 2 μs and

repetition rate of 625 pps. The peak power is 1.8 MW, and with the antenna gain this gives 3590 MW peak ERP in the maximum direction. Calculations using the far-field formula then give a peak electric field at 5 km of 65 V/m (equivalent power density of 11 W/m^2). However, with the pulsing this comes down to a time-averaged power density of 1.4 μW/cm^2, and since the antenna is rotating at 9 rpm and the lobe width is 1.2° this is then further reduced to 3×10^{-5} μW/cm^2. For a review of measurements on different systems see Mantiply et al. [61]

In all known exposure situations of exposure of the general public to EMF from radar systems, the level is below the limiting values given in international guidelines. However, occupational exposure in the near field can occur, and strict adherence to safety instructions is needed, in form of both engineering controls, for example, interlocks, and administrative controls, for instance, strong training and enforcement of safety policies.

1.3.4.3 Exposure in Medical Applications

When medical uses of EM devices are considered, a distinction is made between exposure of patients and medical workers operating the equipment. The balance between any possible risks and the anticipated benefit of exposure of the patient has to be considered by consultation between the patient and the prescribing physician; as a result, exposures are often in excess of limits for workers or the general public. However, operator exposure is governed by the usual rules for occupational exposures; hence, only operator exposure is considered here.

One of the earliest applications of RF energy was shortwave diathermy, which usually operates at 27 MHz. Usually, unshielded electrodes are used, and this may lead to high stray fields. The person operating the equipment, therefore, may be exposed to high field strengths, and the time-averaged guideline for exposure may be exceeded for both RF electric (E) and magnetic (H) fields, depending on the working conditions at hand. Microwave diathermy at 2.45 GHz is also being used in therapy. In this case, the antenna is such that the beam can be directed toward the area to be treated, but the microwave beam may easily be directed toward the patients. Although the beam may not be exposed to the therapist, it may be exposed to the people in the immediate vicinity, including people waiting in the next room. It is therefore necessary to take this into account when planning the space where the microwave diathermy treatment is to be performed.

Electrosurgical units are commonly used in operating suites. They employ RF energy for cutting and coagulation and typically operate at frequencies from about 0.5 MHz to a few megahertz. The energy is supplied to the cutting tool via unshielded cable, which may pass close to the arm and hand of the surgeon, resulting in exposure of operating room personnel to RF energy. The electric and magnetic field near the active lead may be quite high, from a few hundred volts per meter to several kilovolts per meter [79,80]. The induced current in the tissue is of the same order of magnitude as the basic guideline limit for these frequencies, about 5 A/m^2. Since the exposure is rather high, precautionary action would be wise, and shielded wires should be used for the active lead.

Operator and general public exposure to static and RF fields may occur in connection with the use of magnetic resonance imaging (MRI) and nuclear magnetic resonance spectrometers. MRI systems use strong DC magnets, typically from 0.05 to about 3 T, as well as rapidly changing gradient magnetic fields with time derivatives (dB/dt) typically from 1 to 3 mT/ms (1–3 T/s). The RF fields (10–100 MHz) are low and almost fully contained within the patient enclosure, and the RF exposure of the operators is negligible. Inside treatment rooms, near MRI equipment, the maximum exposure level is about 1 T in front of the magnet, and nurses and technicians staying with patients can be exposed to magnetic flux densities up to 200 mT, approaching the protection guideline. When professional activities

take place very close to or inside the magnet's tube, workers can be exposed to higher fields (up to 1–2 T), for example, when assisting the patient, plugging in RF cables of treatment coils, or device cleaning. Reduction of the workers' exposure level is possible if MRI device design is required to include operation with workers no less than 0.5 m from the magnet. Workers' training should also include methods for exposure reduction.

Transcranial magnetic stimulation (TMS) has been introduced recently as a noninvasive and focal stimulation tool for the study of connectivity of brain regions, localization of functions, and pathophysiology of neuropsychiatric disorders and a therapeutic intervention method in the treatment of chronic depression. A high-intensity, fast magnetic field pulse produces a cortical stimulus through the induction of locally confined eddy currents; therefore, tailored coil arrangements can be used to achieve controlled local levels of stimulus. The TMS makes use of magnetic fields that can have intensities of up to 1 T with pulse durations in the range of ~0.05 to 0.2 ms. The resulting time derivative of the field can be several tens of kilotesla per second. This impulsive field transient is able to induce a rapid depolarization of the nerve cells within a volume of about 5 mm^3 at the cortical level.

In some instances, the operator holds the TMS transducer coil in place during exposure. Measurements of the leakage magnetic field at different distances from the coils of the transducer show that the intensity of the field decays proportionally to $1/r^3$ (r = distance). The regulations set limits aimed at avoiding excitation of the central nervous system, while TMS or repetitive TMS aims at just reaching the level of local exposure high enough to produce cortical excitations in patients. For the pulse trains in use, one group found a pulse spacing of ~0.3 ms and about 72-μs active pulse width, which gives an equivalent frequency of about 3.5 kHz. For this the limit value is about 1 T/s, and this is transgressed at distances of about 0.7 m from the surface of the transducer's coils under normal treatment conditions [81].

1.4 Conclusion

EM fields, both natural and of human origin, are ubiquitous. Fields of human origin are primarily a result of technological developments that did not begin until late in the 19th century. In general, the natural fields in the environment are much smaller than those inside organisms; natural environmental fields are also usually smaller than fields of human origin at the same frequency. Inside an organism, naturally occurring charges, currents, and fields in cells, tissues, and organs are very important physiologically, and electric charges and magnetic moments are crucial factors in determining molecular structure and chemical reaction rates. Since organisms, including humans, evolved in the natural fields alone, it is not clear how their adaptation to artificial ones might affect them. The other chapters of this handbook explore this question.

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2

Endogenous Electric Fields in Animals

Richard Nuccitelli

CONTENTS

2.1 Introduction

In a volume presenting the biological effects of electromagnetic fields it is appropriate to review the information we have regarding endogenous electric fields in the body. After all, imposed electromagnetic fields may augment the naturally occurring ones, so a complete understanding of the possible effects of imposed fields requires consideration of those electric fields already present. Here, I will provide a brief overview of the direct current (DC) endogenous fields that have been best characterized in animals and will touch on the evidence that these electric fields are required for the function of various cellular and organ systems. Other well-known variable fields that are generated by various electrically excitable organs such as the heart (electrocardiogram), brain (electroencephalogram), and

eye (electrooculogram) will not be covered here. Another very comprehensive review of endogenous fields that will be of interest has appeared quite recently in *Physiological Reviews* by McCaig et al. (2005), and another review of the roles of such fields in development was presented by Levin (2003).

In order to put these endogenous fields in perspective for the reader, I would like to summarize here their main characteristics. Unlike much of the material considered in this volume, these endogenous fields are small and very slowly changing. Endogenous fields typically fall into the 10- to 100-V/m range and are generally very steady, DC fields generated by the flow of ionic currents through cells and embryos. This can be compared with the much higher fields required to electroporate cells (3 V/cell diameter or 3×10^5 V/m for a 10-μm-diameter cell), which are usually only applied for a short time on the order of a millisecond.

2.1.1 Sources of Endogenous Electric Fields

In order to generate an electric field in the body, a voltage generator or power source is required. There are two main sources of such a power source in living systems: (1) the plasma membrane surrounding every cell in the body and (2) the epithelium that surrounds every organ in the body as well as the entire body itself in the form of the skin. The plasma membrane forms the defining boundary for every cell and is a lipid bilayer with many embedded transporter proteins whose main function is to control the movement of molecules inside or outside of the cell. One of these transporter proteins is the Na^+/K^+-ATPase, which is responsible for maintaining two ion concentration gradients across the plasma membrane (high internal [K^+] and low internal [Na^+]). The K^+ concentration gradient, in combination with a large number of K^+ channels in the plasma membrane, results in the outward diffusion of K^+. This outward movement of K^+ leaves behind the anion that was associated with maintaining electroneutrality and thereby separates charge across the membrane. This separation of charge generates a voltage difference or membrane potential (inside negative). This membrane potential is used for a wide variety of cellular functions, from capturing nutrients to signaling the occurrence of important events, such as sperm–egg fusion in many egg types or light absorption in retinal rods. Indeed, we expend more than half of our energy in maintaining this voltage across all of the cells in our brain and kidney, where excitatory events and Na^+-dependent transport constitute major functions (Clausen et al., 1991).

Voltage differences are also found across all epithelial layers, and this is called the transepithelial potential (TEP). Both organs and embryos are surrounded by one or more monolayers of cells called an epithelium. The outer epithelium belongs to the organ while the plasma membrane to the cell, and epithelia pump ions across themselves to generate the TEP. One clear difference between these two voltage sources (plasma membrane and epithelial layer) is their opposite polarity. Whereas the plasma membrane potential is usually negative on the inside with respect to the outside, the TEP is usually positive on the inside or basal side of the epithelial monolayer with respect to the outside or apical side of the monolayer.

This polarity difference results from the opposite flow of charge across these layers. The plasma membrane of most animal cells generates a potential difference across itself that is negative on the interior. This results from the outward diffusion of K^+ that separates charge across the membrane. In contrast, most animal epithelia are composed of highly polarized cells in which Na^+ channels are localized to the apical end of the cell and both the K^+ channels and the Na^+/K^+ ATPases are localized at the basal end. This polarized distribution of these transport proteins leads to Na^+ influx at the apical end and both Na^+ and K^+ efflux at the basal end to drive positive charge to the interior of the epithelial

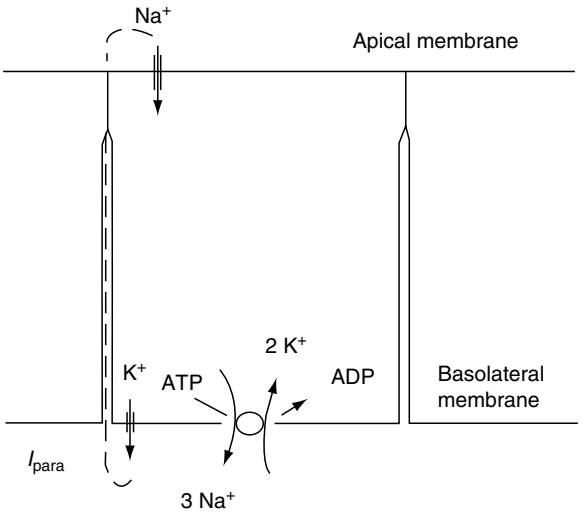

FIGURE 2.1
Diagram of a typical epithelial cell in a monolayer with Na^+ channels localized on the apical plasma membrane and K^+ channels localized on the basolateral membranes along with the Na^+/K^+-ATPase. This asymmetric distribution of ion channels generates a transcellular flow of positive current that must flow back between the cells through the paracellular pathway (I_{para}). This current flow generates a TEP that is positive on the basolateral side of the monolayer.

layer. However, this current cannot flow freely in the extracellular medium because these polarized epithelial cells are attached to each other with both tight and adherent junctions. As the apical–basal transcellular current flows back extracellularly, it must follow a pathway between the cells called the paracellular pathway (Figure 2.1). Current flow through this pathway encounters a high-resistance region at the tight junctions near the apical end, and the current flow through this resistance leads to a TEP that is positive on the basal side of the monolayer with respect to the apical side. The TEP will be proportional to the resistance of this paracellular pathway, and typical values for this TEP range from 15 to 60 mV, basal side positive.

It is this TEP that is the driving force for most endogenous ionic currents in embryos and adults. This voltage across epithelia will drive current out of regions of low resistance where there has been a break in the epithelium (wounds) or where tight junction resistance is low, such as along the primitive streak (Jaffe and Stern, 1979; Winkel and Nuccitelli, 1989), the posterior intestinal portal (Hotary and Robinson, 1990) in chick or mouse embryos, or at the forming limb bud in amphibian, chick, and mouse embryos (Borgens et al., 1983; Robinson, 1983; Altizer et al., 2001). This ''leakage current'' will in-turn generate a lateral electric field along its path that will be proportional to the resistivity in that region. This electric field results from Ohm's law in a conductive medium,

$$E = \rho J$$

where J is the current density and ρ is the local resistivity.

The earliest measurements of the leakage current associated with wounds were made more than a century ago. DuBois-Reymond (1843) used a unique galvanometer that he built himself with more than two miles of wire and measured about 1 μA flowing out of a cut in one of his fingers. This was confirmed in 1849 and 1910 by other investigators, and the history of these measurements is presented in a scholarly review by Vanable (1991). More modern techniques have also been used to study this wound current as discussed. Direct measurements of electric fields *in situ* have been made, and I will discuss them next.

2.1.2 Methods for Measuring Endogenous Electric Fields

2.1.2.1 Self-Referencing Probe

Lionel Jaffe and I developed a technique for exploring transcellular ionic currents, called the vibrating or self-referencing probe (Jaffe and Nuccitelli, 1974). This instrument vibrates a small platinum sphere between two points about 10 μm apart at about 300 Hz and measures the voltage between those points using signal averaging to improve the signal-to-noise ratio. In a conducting medium where most cells find themselves, a voltage difference can exist only where there is a current flowing through the medium. Ionic currents entering or leaving cells can be readily detected by measuring the voltage they generate as they flow through the extracellular medium, and the past 30 years of research on more than 30 cell types has revealed that most cells have an asymmetrical distribution of ion channels that naturally leads to a transcellular current density on the order of 1–10 $\mu A/cm^2$ (Nuccitelli, 1988, 1990). Most epithelia that have been studied exhibit extracellular current densities on the order of 10–100 $\mu A/cm^2$ flowing through the organ or embryo with which they are associated. This technique detects the current that is flowing outside the cell or tissue, and the exact electric field that is generated by this current when it flows inside the cell or tissue can only be estimated based on tissue resistivity. It is more accurate to directly measure the electric fields in the tissue or cells as described here.

2.1.2.2 Microelectrode Techniques for Measuring Endogenous Electric Fields

The classic approach to these measurements is to use KCl-filled glass microelectrodes to penetrate the outer epithelium and measure the voltage just beneath it in several positions. Such electrodes are typically connected via a Ag–AgCl junction to a very high-input impedance preamplifier, so that they do not drain current from the system under study, and their tips are small (on the order of 0.1–1 μm) to minimize tissue damage (Wallis, 1993). If ionic currents are flowing within a tissue, these currents will generate an electric field that can be detected as the difference in potential at various sites along the current path. We will see below that this is the most commonly used approach to measure intraembryonic electric fields.

2.1.2.3 Voltage-Sensitive Fluorescent Dyes for Measuring Endogenous Electric Fields

Another popular technique for measuring the voltage across lipid membranes uses lipophilic fluorescent dyes whose fluorescence is voltage sensitive (Loew, 1992; Loew et al., 2002). For some of these dyes, their fluorescence intensity is dependent on their position within the lipid bilayer, which is in turn influenced by the membrane potential drop across this region. Membrane potential changes can be monitored by measuring the fluorescence intensity of these dyes, and differences in the membrane potential of cells making up an organ or embryo can also be detected. One example of the use of this approach, which will be discussed below, is to provide information about electric fields within sheets of cells that are electrically coupled via gap junctions in the chick embryo.

2.2 Measurements of Endogenous Extracellular Electric Fields

2.2.1 Amputated Limbs

Among the earliest direct measurements of endogenous extracellular electric fields were those made in the regenerating amphibian limb (McGinnis and Vanable, 1986). Upon

amputation, the skin battery of the amphibian limb drives 10–100 $\mu A/cm^2$ out of the cut end of the limb stump. This current flow generates an electric field within the limb tissue that is 60 mV/mm near the lesion during the first hours after amputation, and this field drops to about 25 mV/mm within 6 h as the healing process leads to an increase in the resistance of the wound.

Electric fields of this magnitude have been found to stimulate the growth of neurons into the limb via galvanotropism, and the presence of enhanced nerve in limbs has been correlated with enhanced regeneration (Borgens et al., 1979). The study of nerve galvanotropism has a long and fascinating history that is thoroughly reviewed by McCaig et al. (2005). Briefly, most neurons exhibit sensitivity to imposed electric fields by either bending their outgrowth direction toward the negative pole of the field or in the case of a neural ganglion, exhibiting a higher density of outgrowths on the side of the ganglion facing the negative pole. This galvanotropism may play a role in the guidance of neurons to their targets during development and has also been found to play an important role in regeneration.

2.2.2 Embryonic Electric Fields Beneath the Skin

Direct measurements of electric fields have been made in both avian and amphibian embryos during normal development. Hotary and Robinson (1990) used both the self-referencing probe and microelectrodes to first detect the transembryonic current in the 2- to 4-day-old chick embryo and then measure the electric field that the transembryonic current generates beneath the epidermis. They measured current entering much of the epidermis during stage 14 of development with the outward current focused mainly at the posterior intestinal portal, where up to 105 $\mu A/cm^2$ was measured (Figure 2.2). One would expect that this large anterior–posterior current would generate an internal electric field, so they then used microelectrodes to measure the TEP along this axis. Here, they measured electric fields of 5–20 mV/mm.

They then proceeded to test the hypothesis that these fields are important for normal development by perturbing them (Figure 2.3). They implanted a glass capillary that was filled with either conductive saline agar or nonconducting glass, used as a control, through the ectoderm at the dorsal trunk of the embryo (Hotary and Robinson, 1992). The conductive capillary allowed large currents of about 5 $\mu A/cm^2$ to leak out of the embryo. While the control embryos developed quite normally, most embryos with the implanted conducting capillary exhibited abnormalities in posterior structures where the endogenous electric field is normally the largest but was reduced by the capillary shunt. Perturbing the normal voltage pattern within the embryo resulted in striking tail abnormalities; and an investigation of a genetic mutant, rumpless, that exhibits similar tail abnormalities led to a very interesting correlation. They found that most rumpless mutants exhibited a much lower transembryonic current density and lower electric field within the embryo and those mutants that exhibited a normal electric field pattern also exhibited normal development. Therefore, they found a good correlation between the internal electric field and the normal posterior development. These observations certainly support the hypothesis that the endogenous field is important for the development of posterior structures.

Studies of endogenous fields have also been carried out on the stage 14–21 developing axolotl embryo (Metcalf et al., 1994; Shi and Borgens, 1995). Current is driven out of the lateral walls of the neural folds and the blastopore and enters most of the rest of the embryo's body surface (Figure 2.4). Measurements of the TEP indicate an internal, caudally negative electrical field beneath the neural plate ectoderm. The magnitude of the endogenous field is on the order of 10–20 mV/mm (Figure 2.5). When these embryos

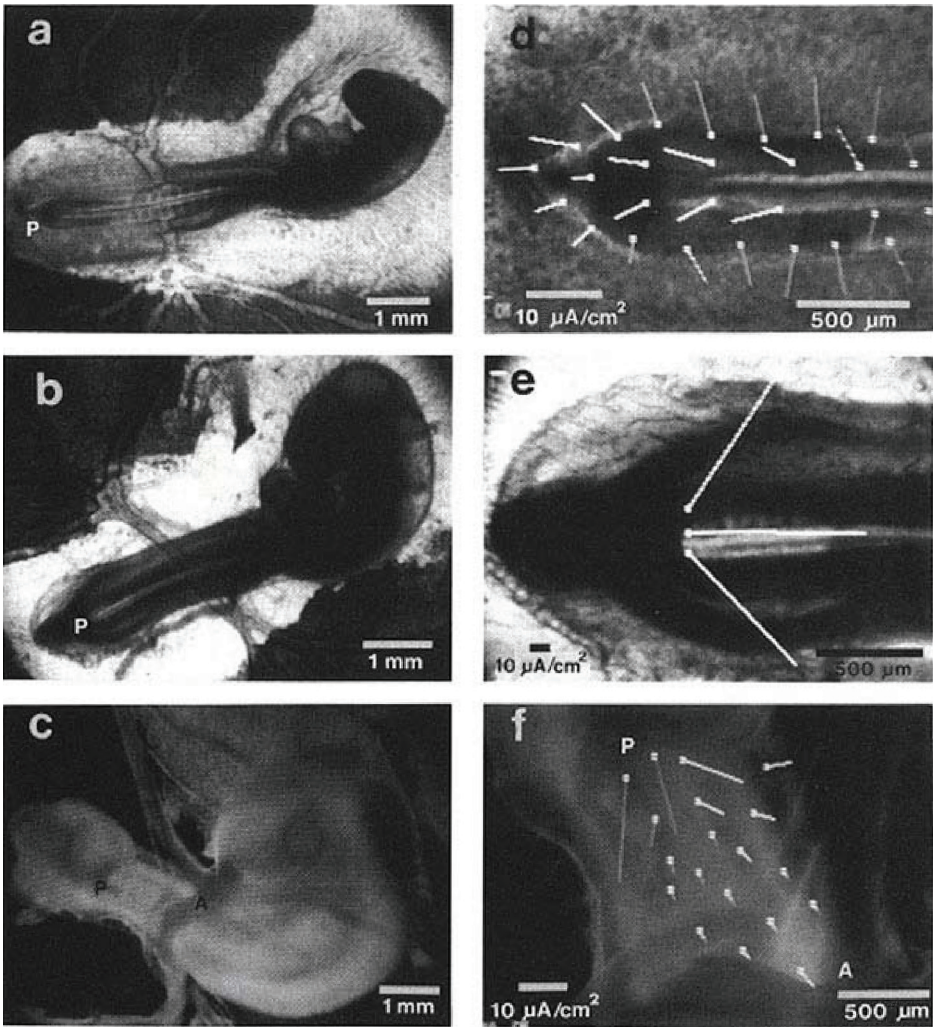

FIGURE 2.2
Ventral surface of three chick embryos at stages 14 (a and d), 17 (b and e), and 20 (c and f). Low-magnification views of the whole embryo are shown in (a)–(c), while (d)–(f) show the current pattern around the posterior intestinal portals of the embryos. Current vectors are represented by lines originating at a dot that indicates the position of the self-referencing probe when the measurement was made. The direction of the vector line away from the dot indicates the direction of current flow at that point, and the length of the line is proportional to the current density. At stage 14 (d), all vectors point toward the posterior intestinal portal or the lateral walls of the midgut. The three vectors shown at stage 17 (e) indicate large currents of about 100 $\mu A/cm^2$ leaving the posterior intestinal portal. At stage 20 (f), outward currents were also found at the posterior intestinal portal. Current densities were much lower by this stage. Note the inward current at the anterior intestinal portal (A). (From Hotary, K.B. and Robinson, K.R. (1990). *Dev. Biol. 140*, 149–160. With permission.)

were placed into an external electric field designed to modify the internal field, abnormalities were observed that depended on the developmental stage (Metcalf and Borgens, 1994). Gastrula-stage embryos exhibited normal development after exogenous field exposure, indicating that the imposed field does not harm the embryo in some nonspecific way. In contrast, neurula-stage embryos exhibited developmental abnormalities when exposed to similar electric fields of 25–75 mV/mm. These data support the hypothesis that the natural electric field within the embryo influences normal morphogenesis.

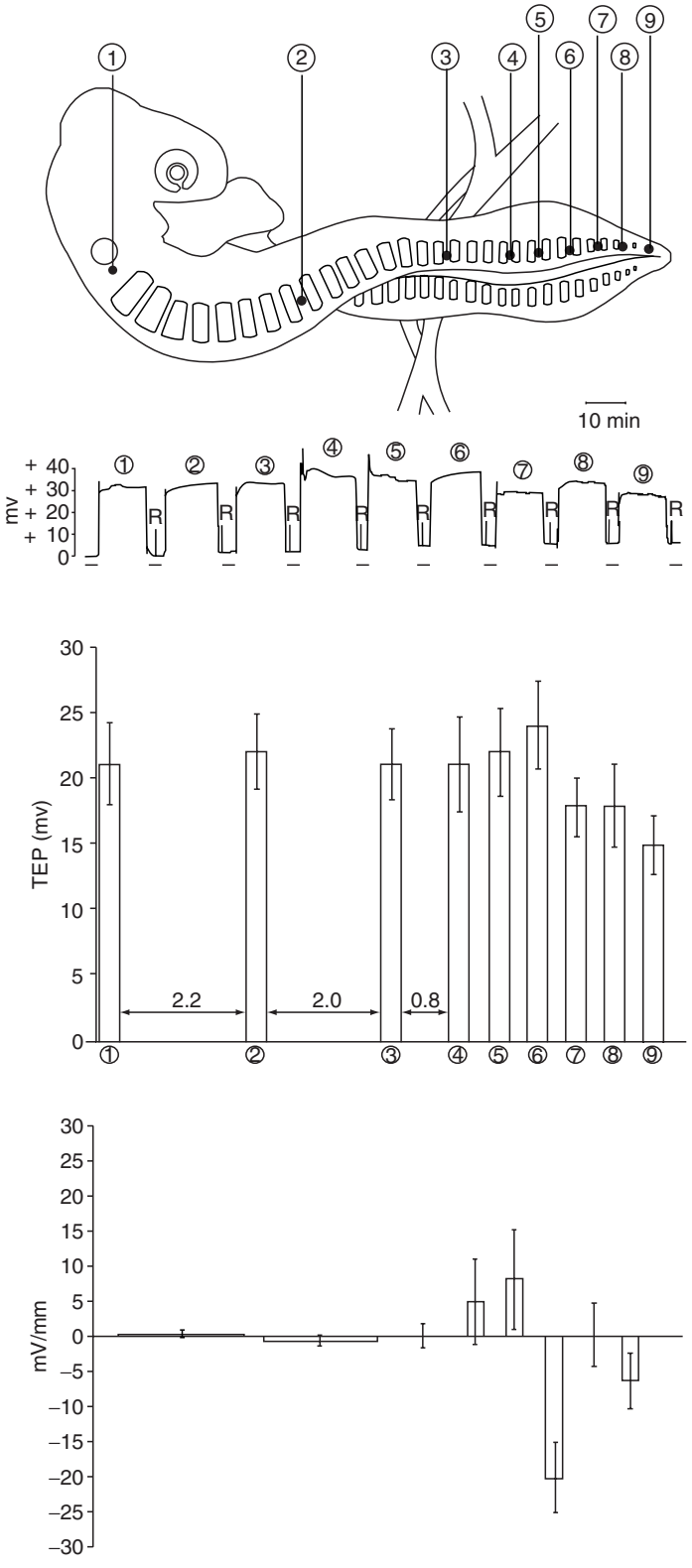

FIGURE 2.3
Stage 17 chick embryo TEP measured in nine rostral–caudal positions. Numbered measurement positions are shown in the drawing in the upper part of the figure. Below the drawing is a chart recording, tracing, and showing the TEP at the different measurement positions. At each numbered peak (corresponding to the positions shown in the drawing) the integument of the embryo was impaled and a stable positive potential was measured. Times at which the embryo was not impaled are indicated by a solid line below the recording. The upper bar chart shows the TEP at each position. The numbers below each bar correspond to the measurement positions indicated. The numbers between bars indicate the average distance (in mm) between each position. Where this is not indicated, the average distance is 0.3 mm. The lower chart shows the average voltage gradient between each consecutive position. Error bars indicate the standard error of the mean, $N = 6$. A steep voltage gradient was found between positions 6 and 7. (From Hotary, K.B. and Robinson, K.R. (1991). *Dev. Biol.* 140, 149. With permission.)

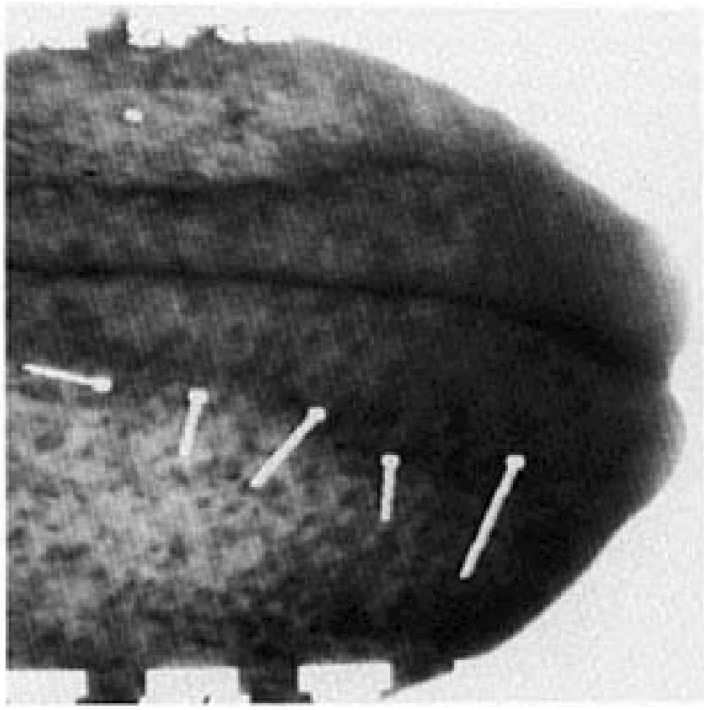

FIGURE 2.4
Neural fold currents in a stage 18 axolotl embryo measured with a two-dimensional self-referencing probe. Current vectors are displayed as a line originating at a dot that marks the measurement position. The direction of current flow from the dot is denoted by the line direction, and its length is proportional to the current density. Note the outwardly directed currents at the edge of the cranial neural folds. (From Metcalf, M.E.M., Shi, R.Y., and Borgens, R.B. (1994). *J. Exp. Zool. 268*, 307–322. With permission.)

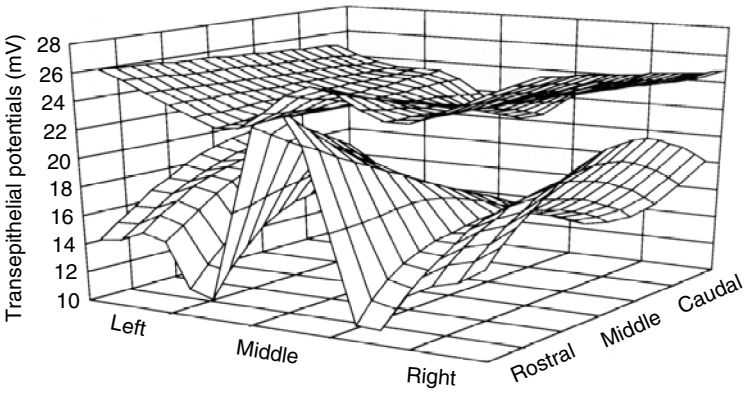

FIGURE 2.5
Summary of three-dimensional plot of TEPs at stage 15/16 (bottom) and stage 18/19 (top) axolotl embryos. The overall increase in the magnitude of TEPs at stage 18/19 is real, permitting these two views to be presented adjacent to each other. Note that only a hint of the characteristic voltage gradients beneath the ectoderm is evident at stage 18/19, and the potentials are not statistically different from one another. The embryo is essentially isopotential within the extracellular domain of the neural plate near the climax of neurulation. (Reproduced from Shi R.L and Borgens R.B. (1995) Dev. Dyn. *202*, 101–114, 1995. With permission.)

2.2.3 Fields Associated with the Neural Tube

The neural tube forms during development as a folding over of neural plate epithelium, inverting the normal polarity of this layer. The apical end of the neural plate becomes the inside of the tube so that transport of Na^+ occurs from the inside to the outside of the tube and the trans-tube potential is inside negative. This potential has been measured in both frog and axolotl to be as large as −90 mV (Hotary and Robinson, 1991; Shi and Borgens, 1994). Neuroblasts within the wall of the tube are therefore exposed to very large electric fields, since the wall is only about 50 μm thick and the 90 mV across this distance generates a field of roughly 1800 mV/mm. There is little doubt that such a large field will influence the migration and sprouting of these neuroblasts.

2.2.4 Fields Associated with Epithelial Wounds

As noted above, the earliest measurements of the electrical phenomena associated with wounds did not measure the electric field itself but rather the current flowing out of the wound. More modern techniques have also been used to study this wound current. The leakage current that is driven out of epithelia in low-resistance regions has been measured using the vibrating probe technique (Jaffe and Nuccitelli, 1974) in several systems. One of the earliest such measurements was a current as large as 100 $\mu A/cm^2$ leaving the stumps of regenerating newt limbs (Borgens et al., 1977). Similar measurements have also been made on fingertip amputation currents in humans (Illingworth and Barker, 1980), where up to 30 $\mu A/cm^2$ was detected leaving the accidentally amputated stump for about 3 wk. These currents will certainly generate electric fields just beneath the epidermis that will be proportional to the resistivity encountered in the tissue. The range of human tissue resistivity spans 200–1000 Ω cm (Faes et al., 1999), so these currents would be expected to generate an electric field within the tissue of about 10–100 mV/mm.

However, since this tissue resistivity can vary substantially as a function of cell density and tissue anatomy, it is always more reliable to measure these fields directly in the tissue rather than estimating them based on the transembryonic current density. This has been accomplished in four different wound types in skin and cornea. The classic approach to these measurements is to use KCl-filled glass microelectrodes to penetrate the outer epithelium and measure the voltage just beneath it in several positions along a line leading away from the wound. However, for skin measurements, another approach is more common. This method is to measure the potential gradient just beneath the stratum corneum on the surface of the epidermis, either with surface electrodes or by other means. The field generated by the current flowing between the upper surface of the epidermis and the stratum corneum is often larger than that generated below the epidermis because of the higher resistivity of that upper region. The range of field strengths measured in the four cases in the literature is surprisingly small, between 40 and 200 mV/mm (Table 2.1). The field direction is a function of position. Beneath and within the epidermis the field polarity has the negative pole at the wound center, and above the epidermis the wound current is flowing in the opposite direction so that the positive pole is at the wound (Figure 2.6).

These wound fields have some useful properties for signaling. First, they appear immediately upon wounding since the TEP is continuously present to drive current out of any low-resistance region as soon as it is formed. Second, the lateral electric field illustrated in Figure 2.6, that is generated by the wound current, will persist until the resistance increases as the wound heals. Thus, we have a signal that is immediate and persistent. These are ideal properties for a physiological signal to stimulate wound healing. If the epithelial cells forming the epidermis were able to detect such electric

TABLE 2.1

Endogenous Electric Fields Measured near Wounds

Species	Tissue	Wound Type	*E* Field (mV/mm)	Reference
Bovine	Cornea	Cut	42	Chiang et al., 1992; Sta Iglesia and Vanable, 1998
Notophthalmus viridescens	Digit	Digit tip amputation	40	McGinnis and Vanable, 1986; Chiang et al., 1989; Iglesia et al., 1996
N. viridescens	Limb stump	Amputation	7–50	McGinnis and Vanable, 1986
Guinea pig	Skin	Small cut	100–200	Barker et al., 1982

fields, they would be able to initiate wound healing immediately upon wounding. This is in fact the case, as discussed in the next section.

Measurements of endogenous electric fields near epithelial wounds have been made in three different systems. The first was a skin wound in the guinea pig (Barker et al., 1982). The transepidermal potential was measured in several locations lateral to a skin wound (Figure 2.7). At the wound itself, there is no epidermis, so the transcutaneous potential is zero, whereas about 1 mm away, the transcutaneous potential exhibited the normal value of 50–70 mV. The steepest voltage gradient was found immediately adjacent to the wound edge where values as high as 150 mV/mm were measured. The second direct measurement of the electric field near a wound was made in two regions of the newt limb. The electric field adjacent to an amputated digit was measured with microelectrodes and found to be about 40 mV/mm (McGinnis and Vanable, 1986; Chiang et al., 1989; Iglesia et al., 1996). This is very similar to the field near an amputated limb of the newt of 7–50 mV/mm (McGinnis and Vanable, 1986). The third direct measurement was made on the bovine cornea, and the magnitude of the electric field was 42 mV/mm (Chiang et al., 1992; Sta Iglesia and Vanable, 1998).

The fields in the cornea and the newt digit have been found to play a role in wound healing. When the field strength associated with the wound is modified, the rate of wound healing changes. The newt's wound healing rate can be optimized under normal

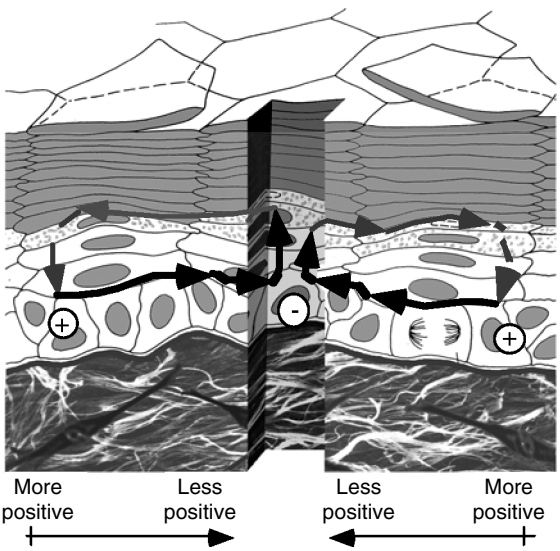

FIGURE 2.6

Generation of skin wound electric fields. Unbroken skin maintains a ''skin battery'' or TEP, generated by the apical influx of Na^+ and basolateral efflux of K^+. When there is a wound, the potential drives current flow through the newly formed low-resistance pathway, generating an electric field whose negative vector points toward the wound center at the lower portion of the epidermis and away from the wound on the upper portion below the stratum corneum.

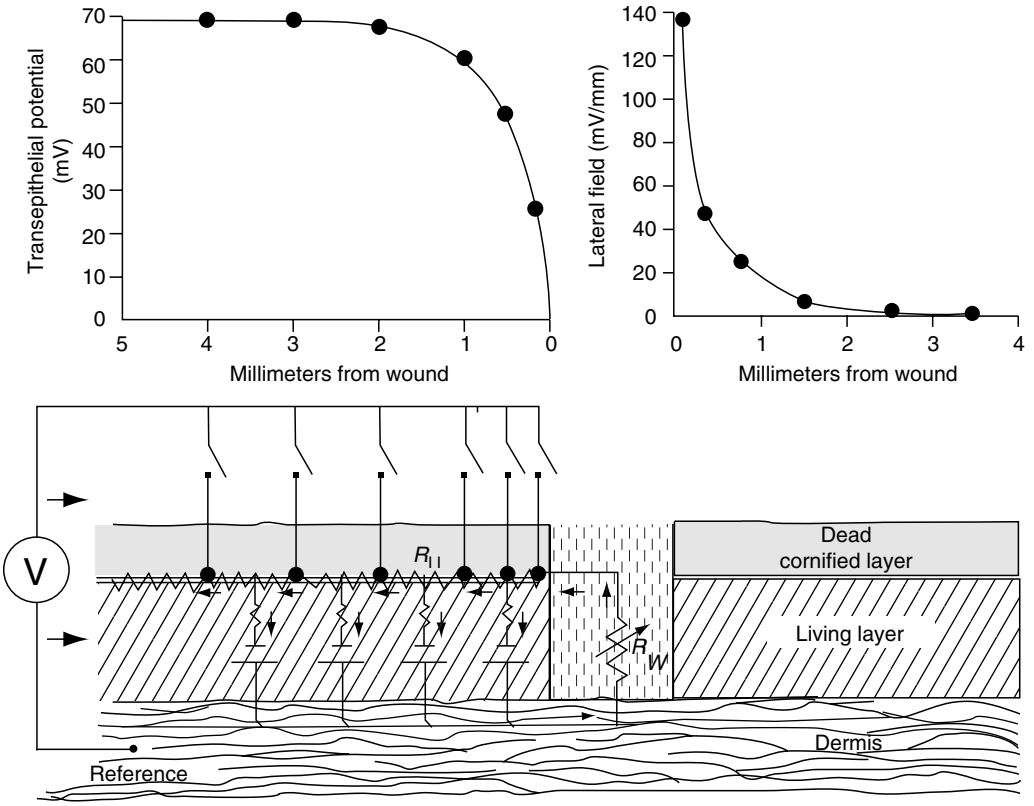

FIGURE 2.7
The electric field near a skin wound in a guinea pig. Bottom: diagram of the method used. A metal probe penetrated the stratum corneum to contact the epidermis at various distances from the wound site, and the surface voltage at each location was recorded with respect to the potential within the dermis. This voltage is the TEP and is plotted in the upper left of the figure. The voltage at the wound must be zero because the epidermal layer has been broken there, and far from that region, the TEP is 70 mV. The electric field at a given location is given by the voltage difference between sampling sites divided by the distance between those sites and is plotted on the upper right of the figure.

conditions but cannot be speeded up, removing the endogenous field does slow down the rate of wound healing by about 25%. However, the rate of bovine corneal wound healing can be enhanced by increasing the electric field strength. Epithelization was fastest in wounds with the field strength raised to 80 mV/mm, more than twice the normal field strength present in wounds maintained in Hanks' solution alone. Epithelization decreased, however, when the field strength was increased to 120 mV/mm. A similar pattern was also observed when the field's polarity was reversed. Decreasing the field strength by submersion of the lesions or by treating the lesions with the Na^+ channel blocker, benzamil, significantly retarded healing. In addition, an increase in the field strength of lesions treated with Na^+-depleted Hanks' solution, by the addition of DC, increased the rate of epithelization. These observations suggest that the endogenous electric field plays a role in the normal wound healing process.

More recent studies of rat cornea have reported a similar correlation between the wound healing rate and the electric field strength. The mammalian cornea exhibits an internally positive TEP of 30–40 mV. Na^+ and K^+ are transported out of the tear fluid and into the epithelium while Cl^- is transported in the opposite direction. A wound in this

epithelium exhibits the same current pattern as skin (Figure 2.6), and a laterally oriented electric field is generated by this wound current with the cathode at the wound site. Recent work from McCaig, Zhao, and colleagues has indicated a strong correlation between the rate of wound healing in the rat cornea and the electric field strength lateral to the wound (Zhao et al., 1996; Song et al., 2004). They have used drugs to either increase the trans-corneal potential or decrease it. Drugs that increased this voltage difference also increased the rate of wound healing, while drugs that reduced this voltage difference also slowed down the rate of wound healing. In addition, when current was injected to restore and amplify the endogenous electric field in bovine cornea, the wound healing rate increased (Sta Iglesia and Vanable, 1998). These data provide very strong support for the hypothesis that these electric fields near corneal wounds play an important role in influencing the healing of these wounds.

2.3 Measurements of Endogenous Intracellular Electric Fields

2.3.1 Nurse Cell Complex in Insects

In the silk moth oocyte-nurse cell complex or the ovarian follicle, the oocyte cytoplasm is about 10 mV more positive than that of the nurse cell cytoplasm despite their connection by a broad cytoplasmic bridge. Woodruff and Telfer have published several studies of this system in which they show that the polarized transport of fluorescently labeled proteins between nurse cells and oocyte depends on the charge of these proteins in a manner consistent with intercellular electrophoresis driven by the voltage gradient across the cytoplasmic bridge of the silk moth and other insects (Jaffe and Woodruff, 1979; Woodruff and Telfer, 1980; Woodruff and Cole, 1997; Cole and Woodruff, 2000). Since these nurse cell complexes arise from incomplete cell division they must be considered electrically as a single cell that is generating a significant voltage gradient across a small region.

2.3.2 Development of Left–Right Polarity in Chick and Frog

The most recent study of the role of electric fields in development utilized both frog and chick embryos. The generation of left–right asymmetry in these systems was found to depend on both functioning gap junctions and voltage difference between blastomeres in very early stages of development (Levin and Mercola, 1998, 1999; Levin et al., 2002). This work started with a pharmacological screen to identify drugs that interfered with the development of left–right patterning. The most effective drugs were the ones that interfered with K^+ and H^+ ion fluxes. Lansoprazole and chromanol 293B were the most effective and these block the H^+ pump and a specific K^+ channel (KvLQT-1), respectively. Next most effective was SCH28080 and omeprazole, which block the H^+/K^+-ATPase, followed by $BaCl_2$, which blocks all K^+ channels.

They further tested the hypothesis that these ion fluxes were important for left–right patterning by injecting mRNA for either the alpha or beta subunits of the H^+/K^+-ATPase or the K^+ channel into the frog egg. They found that heterotaxia was induced when either was injected but by far the largest increase, 37%, occurred when all three mRNAs were injected. This suggests that overexpression of these molecules, which can influence or perturb ion concentration gradients of K^+ or H^+, disrupted the normal left–right patterning of the embryo.

In order to learn more about the mechanism through which H^+/K^+-ATPase influenced patterning, they used *in situ* hybridization to show an asymmetrical distribution of the K^+/H^+-ATPase. It was concentrated in the right ventral blastomere of the 4-cell stage frog embryo. the addition of Both K^+ channels and K^+/H^+-ATPase should hyperpolarize cells making them more negative than their neighbors. This voltage difference between the blastomeres of the 4-cell stage embryo could be used to segregate low molecular weight determinants through gap junctions to achieve asymmetric gene expression. They further tested this hypothesis by measuring the membrane potential of cells near the primitive streak during early chick development. They used an anionic fluorescent dye, $DiBAC_4$, whose distribution depended on membrane potential to show that the early chick embryo exhibited a voltage gradient across the primitive streak. The left side of the primitive streak was 10–20 mV more positive than right side and this difference was inhibited by the K^+ channel blocker, $BaCl_2$, and the H^+/K^+-ATPase inhibitor, omeprazole. Since these drugs also partially inhibited the development of left–right patterning, the membrane potential difference appears to play a role in this aspect of development. This paper is the first to demonstrate a role for membrane potential differences between blastomeres in early vertebrate pattern formation.

2.4 Methods for Modifying Endogenous Electric Fields

Modifying endogenous fields within embryos or cells is really quite challenging. The only way to generate a relatively steady field in a conducting medium is to pass current through it. However, the outer membranes or epithelia surrounding the targets here make this very hard to accomplish. These structures have high resistance to current flow so that slowly varying fields placed outside the cell or embryo will not effectively penetrate to the inside but will mainly generate current flow around the outside of the cells or embryos. Because of this there have been precious few attempts to modify endogenous fields, but I will discuss some of them.

The only exception to this field penetration problem is the application of ultrashort pulses in the nanosecond domain that have risen times faster than the charging time of biological membranes (Schoenbach et al., 2004). These pulses penetrate beyond the plasma membrane into the interior of cells and tissues but are present only for very short times. It is conceivable that by combining millions of these short pulses per second, one could significantly modify the DC electric field within cells and tissues. This remains to be explored.

2.4.1 Passing Current between Electrodes

If two electrodes can be placed within a single cell or in different regions of an embryo, current can be passed between them and a well-defined electric field can be generated. However, this requires penetrating the outer membrane or epithelium and may damage this outer layer. The longer the field is applied, the more likely that some damage will occur due to vibrations or embryo movement. This approach has been used with some success in the regenerating tip of newt limbs (Chiang et al., 1991; Iglesia et al., 1996), where current was passed along the limb by inserting one electrode into a slit made at the knee and the current delivery electrode was placed distal to the wounded digit tip. The electric field at the newt limb could be manipulated in this way, and elimination of this field significantly slowed down the rate of wound healing.

2.4.2 Low-Resistance Shunts

One way to perturb the natural transembryonic current pattern is to place a low-resistance pathway or shunt into a resistive membrane or epithelium. The endogenous fields will drive current out through this shunt, and this new current flow will definitely perturb the endogenous field within the tissue. This technique was used with striking results by Robinson's group in the chick embryo as described above (Hotary and Robinson, 1994).

2.4.3 Placing Tissues in an External Electric Field

While DC electric fields cannot penetrate into the conducting cytoplasm of a cell or tissue, they have been found to perturb normal development at certain stages in amphibians (Metcalf and Borgens, 1994). In addition, there is a very extensive old literature in which the polarity of both development and regeneration could be strongly influenced by imposed DC electric fields (Jaffe and Nuccitelli, 1977; Levin, 2003). One interpretation of these observations is that the imposed field has its effective target along the exterior of the embryo via lateral electrophoresis of membrane glycoproteins.

The only external electric field that can penetrate into the interior of cells is the one that rises faster than the charges within the cell can redistribute (Schoenbach et al., 2004). Such a pulsed field could certainly modify internal electric fields for the extremely short duration of the pulse. Perhaps by using either a large field strength or multiple pulses, such brief pulsed fields might have a significant effect on endogenous fields. This relatively new area deserves future investigation.

2.5 Summary

All plasma membranes and epithelia generate voltage differences across themselves. These batteries are the power sources that drive ionic currents through cells, tissues, and organisms. These currents will generate internal electric fields as they traverse tissue, and such fields can do work through electrophoresis of charged molecules within and between cells as well as in the plane of the plasma membrane. Cases in which such fields have been measured include the following:

1. Two- to 4-day-old chick embryos generate a 20-mV/mm field near the posterior intestinal portal that is important for normal development of posterior structures.
2. Stage 14–21 amphibian embryos generate similar internal electric fields, and modifying these fields during neurulation but not gastrulation results in developmental abnormalities.
3. Neural tubes in amphibians generate an internally negative voltage difference of as much as 90 mV across the wall of the tube, and cells in this region are exposed to fields as large as 1800 mV/mm.
4. Mammalian skin wounds generate 150-mV/mm fields just below the stratum corneum, and corneal epidermal wounds exhibit fields of 40 mV/mm lateral to wounds.
5. The development of left–right asymmetry in frog and chick embryos utilizes an electric field between blastomeres that is generated by an asymmetrical distribution of the K^+/H^+-ATPase among the blastomeres.

In nearly all of these well-documented examples, the electric field plays a critical role in either the development of the organism or the wound healing and regeneration of adult structures. Because of this, imposed electric fields may be utilized to perturb or influence normal development. One intriguing possible perturbation is the use of imposed electric fields to enhance the rate of wound healing, particularly in cases where the normal healing process is slower than normal, as observed in chronic wounds.

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3

Dielectric Properties of Biological Materials

Camelia Gabriel

CONTENTS

3.1 Introduction

At some level of organization, all matter consists of charged entities held together by various atomic, molecular, and intermolecular forces. The effect of an externally applied electric field on the charge distribution is specific to the material; the dielectric properties are a measure of that effect; they are intrinsic properties of matter used to characterize nonmetallic materials. Biological matter has free and bound charges; an applied electric field will cause them to drift and displace, thus inducing conduction and polarization currents. Dielectric spectroscopy is the science that relates the dielectric properties to the underlying microscopic mechanisms of polarization and conduction. These dielectric phenomena are determined by and are informative about the structure and composition of the material. Consequently, knowledge of the dielectric properties is of practical importance in all fields of science where electromagnetic fields impinge or are used to probe or process matter. It is equally important in biomedical fields such as electrophysiology, where endogenous bioelectric sources provide signals that are sensed through various body tissues and are affected by their dielectric properties.

The past decade has seen a dramatic increase in the exposure of people to electromagnetic fields from wireless telecommunication devices and infrastructure. This situation sparked large research programs on the assessment and quantification of exposure of people and on the biological effects resulting from the exposure. Information on the dielectric properties of tissues is vital to these studies, for the computation of exposure metrics and the provision of a mechanistic explanation for biological effects. To satisfy the need of current research activity, this chapter will review the dielectric data for body tissue and the underlying mechanisms of interaction at the cellular, subcellular, and molecular levels. In doing so, we will draw on the authoritative article by Foster and Schwan (1996), published in the second edition of this book, which goes a long way toward establishing dielectric spectroscopy as a powerful tool for mechanistic studies.

Another area of scientific activity in the last decade revolved around the formulation of standard procedures for the experimental assessment of human exposure from electromagnetic sources, mostly telecommunication radio transceivers and their accessories. This created the need to formulate and measure the dielectric properties of tissue equivalent material and made dielectric measurement and the assessment of the associated uncertainty part of the compliance testing procedure. This chapter will deal with the fundamental issues that need to be established if dielectric measurement is to become a routine but accurate laboratory procedure.

It is not possible to review the dielectric properties and the polarization mechanisms in biological material without singling out the contribution to this field of Herman P. Schwan, whose name is associated with all the major findings over the past 50 years (Foster, 2002). Indeed, his 1957 review of the bulk electrical properties of cells and cell suspensions is one of the earliest and most studied texts on the subject. There are other reviews by Pethig (1979), Stuchly (1979), Schwan and Foster (1980), Pethig and Kell (1987), and Foster and Schwan (1989). The fundamental aspects and a more extensive treatment of the theoretical aspects of this subject can be found in books by Cole (1972), Grant et al. (1978), Schanne and Ceretti (1978), Pethig (1979), and more recently, Craig (1995), Roussy and Pearce (1995), and Grimnes and Martinsen (2000).

For most biological materials, the magnetic permeability is close to that of free space (i.e., diamagnetic), which implies that there is no direct interaction with the magnetic component of electromagnetic fields at low field strengths. However, this position is now changing following relatively recent reports of the presence of magnetite in human nervous tissue (see, e.g., Dobson and Grassi, 1996), which suggest that magnetite may provide a mechanism for direct interaction of external magnetic fields with the human central nervous system. The role of these strongly magnetic materials in organisms is only just beginning to be unraveled. This subject is elaborated in the second part of next chapter.

3.2 Dielectric Properties—Molecular Origin

From a historical perspective, the dielectric properties of materials were first observed experimentally by Faraday in the 1830s as a change in the capacity of an empty capacitor when a material is introduced inside it. Faraday introduced the term *specific inductive capacity* to describe the ratio of the capacities of the filled and empty capacitor. This quantity is now known as the permittivity and is denoted by ε. It is a fundamental property of nonmetallic or dielectric materials. Under quasistatic conditions, the capacitance C_0 of a perfect capacitor of area A and plate separation d changes to $C > C_0$:

$$C = \varepsilon\varepsilon_0 = \varepsilon\frac{\varepsilon_0 A}{d} \tag{3.1}$$

where ε is the relative permittivity of the material (dimensionless), ε_0 is the permittivity of free space (8.8542×10^{-12} F/m), and the product $\varepsilon\varepsilon_0$ is the absolute permittivity. The increase in capacity is due to the additional charge density induced by the field in the material. The field is said to have polarized the medium; polarizability or the ability of the material to polarize is the main determinant of its dielectric properties.

This section will start with the fundamental concepts of the interaction of homogenous matter with static fields and proceed, in steps, to heterogenous mixtures and their dynamic response to time-varying fields leading to the dielectric properties of tissues.

3.2.1 Quasi-Static Response

Considering the simple case of a monomolecular material, three main interaction mechanisms are possible: electronic, atomic, and molecular polarization. Electronic polarization is the shift of electrons, in the direction of the field, from their equilibrium position with respect to the positive nuclei. Atomic polarization is the relative displacement of

atoms or atom groups relative to each other. The orientation of permanent or induced molecular dipoles, when present, is known as molecular polarization. The total polarizability α_T is the sum of the contribution of, in this case, all three processes, termed α_e, α_a, and α_d.

In view of the relative importance of molecular orientation processes in defining the total polarization ($\alpha_e + \alpha_a < \alpha_d$) and hence the dielectric properties, it is usual to differentiate between the polar and nonpolar materials when these properties are considered.

For ideal nonpolar materials, the relationship $\varepsilon = n^2$, where n is the optical refractive index, holds true. When a dielectric material becomes polarized by the application of an external electric field E, the dipole moment of the constituent molecules is given by

$$\overline{m} = \alpha_T \overline{E}_l \tag{3.2}$$

where E_l is the local field acting on the molecules. The dipole moment per unit volume of the material P increases the total displacement flux density D, defined from the relationship $D = \varepsilon_0 E$ in vacuum and $D = \varepsilon_0 \varepsilon E$ in a medium of relative permittivity ε. The latter expression may also be written as

$$D = \varepsilon_0 E + P \tag{3.3}$$

The dependence of P on E can take several forms, the simplest and most common being a scalar proportionality:

$$P = \varepsilon_0 \chi E \tag{3.4}$$

where $\chi = \varepsilon - 1$ is the relative dielectric susceptibility. This simple relationship is valid for a perfect isotropic dielectric, at low or moderate field intensities and at static or quasi-static field frequencies.

If the material contains N dipoles per unit volume, then

$$P = N\alpha_T E_l \tag{3.5}$$

and

$$\varepsilon - 1 = \frac{N\alpha_T}{\varepsilon_0} \frac{E_l}{E} \tag{3.6}$$

The molecular description of the permittivity requires that the relationship between the microscopic and the macroscopic field intensities be known. In most cases, there is no exact solution to this problem, only more or less good approximations that hold within the confines of the assumptions and simplifications made, as will be briefly illustrated for typical classes of materials.

3.2.2 Permittivity of Low-Pressure Gases

At low pressures the molecules are far apart from each other, and their interaction with each other may be assumed to be negligible in comparison with the macroscopic field intensity E. Under these conditions $E_l \approx E$ and

$$\varepsilon - 1 = \frac{N\alpha_T}{\varepsilon_0} \tag{3.7}$$

The relative permittivity of a nonpolar gas is very close to 1, typically of the order of 1.0001 at atmospheric pressure.

3.2.3 Permittivity of Liquids and Dense Gases

When the intermolecular interactions are such that $E_l \neq E$, the local field must be estimated. One approach is to consider a spherical region inside the dielectric that is large compared to the size of a molecule; the field inside it is estimated for nonpolar materials to be

$$E_l = \left(\frac{\varepsilon + 2}{3}\right) E \tag{3.8}$$

which yields

$$\frac{3(\varepsilon - 1)}{\varepsilon + 2} = \frac{N}{\varepsilon_0}\alpha_T \tag{3.9}$$

The above expression is known as the Claussius–Mossoti–Lorentz formulation. It is not always valid, such as when the density of the material corresponds to $N = 3\ \varepsilon_0/\alpha_T$. An alternative formulation, valid when the molecules are polarizable point dipoles of permanent moment μ, was provided by Onsager:

$$\frac{(\varepsilon - n^2)(2\varepsilon + n^2)}{\varepsilon(n^2 + 2)^2} = \frac{N\mu^2}{9kT\varepsilon_0} \tag{3.10}$$

where k is the Boltzman constant and T is the absolute temperature.

Debye separated out the contribution to the total polarization of the permanent dipole from those associated with electronic and atomic displacements and arrived at the following relationship

$$\frac{\varepsilon - 1}{\varepsilon + 2} = \frac{N}{3\varepsilon_0}(\alpha + \mu^2/3kT) \tag{3.11}$$

While Onsager and Debye used semistatistical techniques to estimate the local field, others like Kirkwood, and later Fröhlich, used statistical methods to obtain a rigorous expression of the permittivity after taking local interactions into consideration and obtained

$$\frac{(\varepsilon - 1)(2\varepsilon + 1)}{3\varepsilon} = \frac{N}{\varepsilon_0}(\alpha + g\mu^2/3kT) \tag{3.12}$$

This is Kirkwood's equation for permittivity in which g is known as the Kirkwood correlation parameter, introduced to account for the effect of local ordering in the material. Fröhlich's theory gives

$$\frac{(\varepsilon - n^2)(2\varepsilon + n^2)}{\varepsilon(n^2 + 2)^2} = \frac{Ng\mu^2}{9kT\varepsilon_0} \tag{3.13}$$

which, except for the correlation parameter g, is identical to Onsager's equation.

This brief outline of the dielectric theory gives an idea of the nature of the electric field interaction problems and of the various techniques used to partially solve them under static field conditions. The solutions hold for slow time-varying fields as long as there is a quasistatic state. References to the original work by Debye (1929), Kirkwood (1936), Onsager (1936), and Fröhlich (1955) are given in Böttcher and Bordewijk (1978) and other well-known texts (Hill et al., 1969; Jonscher, 1983).

3.3 Time and Frequency Dependence of the Dielectric Response

Much of the interest in the dielectric properties of biological materials is concerned with their response to time-varying electric fields. This can be explained by the same macroscopic variables used for the quasi-static state except for the introduction of a time dependence for the excitation and response. The general discussion will assume sinusoidal fields and linear and isotropic responses, nonsinusoidal fields and material anisotropy, and nonlinearity being special cases.

3.3.1 Time-Dependent Polarization—Impulse Response—Kramers–Krönig Relations

The following relationship holds irrespective of the polarization mechanism:

$$P(t) = D(t) - \varepsilon_0 E(t) \tag{3.14}$$

For an ideal dielectric material with no free charge, the polarization follows the pulse with a delay determined by the time constant of the polarization mechanism. Assuming a rate process, which is that the rate of polarization is proportional to the constantly decreasing number of unpolarized units, the simplest expression for the polarization is obtained from the solution of the first-order differential rate equation with constant coefficients and time constant τ, giving

$$P(t) = P(1 - \mathrm{e}^{-t/\tau}) \tag{3.15}$$

The decay of polarization is also an exponential function

$$P(t) = \mathrm{e}^{-t/\tau} \tag{3.16}$$

For a linear system, the response to a unit-step electric field is the impulse response $f(t)$ of the system. The response of the system to a time-dependent field can be obtained from summation in a convolution integral of the impulses corresponding to a sequence of elements making up the electric field. For a harmonic field and a causal, time-independent system, the Fourier transform exists and yields

$$P(\omega) = \varepsilon_0 \chi(\omega) E(\omega) \tag{3.17}$$

indicating that the dielectric susceptibility $\chi(\omega)$ is the Fourier transform of $f(t)$. In general, the susceptibility is a complex function reflecting the fact that it informs on the magnitude and phase of the polarization with respect to the polarizing field

$$\chi(\omega) = \chi' - \mathrm{j}\chi'' \tag{3.18}$$

The real and imaginary parts of $\chi(\omega)$ can be obtained from the separate parts of the Fourier transform:

$$\begin{aligned}\chi'(\omega) &= \int_{-\infty}^{+\infty} f(t)\cos(\omega t)\,\mathrm{d}t = \int_{0}^{+\infty} f(t)\cos(\omega t)\,\mathrm{d}t \\ \chi''(\omega) &= \int_{-\infty}^{+\infty} f(t)\sin(\omega t)\,\mathrm{d}t = \int_{0}^{+\infty} f(t)\sin(\omega t)\,\mathrm{d}t\end{aligned} \tag{3.19}$$

The limit of integration can be changed from $-\infty$ to 0 since $f(t)$ is causal.

The impulse response $f(t)$ defines the dielectric response, and conversely, knowledge of the complex susceptibility allows the determination of the impulse response by carrying out the reverse transformation, which gives $f(t)$ in terms of either $\chi'(\omega)$ or $\chi''(\omega)$:

$$\begin{aligned}f(t) &= (2/\pi)\int_{0}^{+\infty} \chi'(\omega)\cos(\omega t)\,\mathrm{d}\omega \\ f(t) &= (2/\pi)\int_{0}^{+\infty} \chi''(\omega)\sin(\omega t)\,\mathrm{d}\omega\end{aligned} \tag{3.20}$$

Eliminating $f(t)$ from the above equations gives an expression of $\chi'(\omega)$ in terms of $\chi''(\omega)$ and vice versa. Thus, there is a relationship between the real and imaginary parts of the complex susceptibility of any material, such that knowledge of either enables the other to be calculated. The expressions of real and imaginary parts of the susceptibility or permittivity in terms of each other are known as the Kramers–Krönig relations and have been derived as

$$\begin{aligned}\chi'(\omega) &= \chi'(\infty) + \frac{2}{\pi}\int_{0}^{\infty} \frac{u\chi''(u) - \omega\chi''(\omega)}{u^2 - \omega^2}\,\mathrm{d}u \\ \chi''(\omega) &= \frac{2}{\pi}\int_{0}^{\infty} \frac{\chi'(u) - \chi'(\omega)}{u^2 - \omega^2}\,\mathrm{d}u\end{aligned} \tag{3.21}$$

where u is a variable of integration. Recalling the relationship between relative dielectric susceptibility and relative permittivity $\chi = \varepsilon - 1$, the permittivity is a complex function given by

$$\hat{\varepsilon}(\omega) = \varepsilon'(\omega) - \mathrm{j}\varepsilon''(\omega) = (1 + \chi'(\omega) - \mathrm{j}\chi''(\omega)) \tag{3.22}$$

Thus, the Kramers–Krönig relations relate ε' to the complete spectrum of ε'' and vice versa. A clear account of their derivation can be found in Jonscher (1983).

3.3.2 Permittivity of a Polar Substance—The Debye Equation

When a step field E is applied to a polar dielectric material, the electronic and atomic polarizations are established almost instantaneously compared to the time scale of the

molecular orientation; the total polarization reaches a steady state as a first-order process characterized by the time constant of the dipolar rotation. When the field is removed, the process is reversed; electronic and atomic polarizations subside first, followed by a relatively slow decay in dipolar polarization (Figure 3.1). The time constant τ depends on the physical process, in this case the rotational dynamics of the dipole determined by the size, shape, and intermolecular relations of the molecules. If P_∞ and P_0 are the instantaneous and steady-state polarization, respectively, then the total polarization for a first-order process characterized by a time constant τ is

$$P = P_\infty + (P_0 - P_\infty)(1 - \mathrm{e}^{-t/\tau}) \tag{3.23}$$

In time-varying fields the permittivity is a complex function originating from the magnitude and phase shift of the polarization with respect to the polarizing field:

$$\hat{\varepsilon} = \varepsilon' - \mathrm{j}\varepsilon'' = \varepsilon' - \mathrm{j}\sigma/\omega\varepsilon_0 \tag{3.24}$$

The real part ε' is a measure of the induced polarization per unit field and the imaginary part ε'' is the out-of-phase loss factor associated with it. The loss factor can also be represented by a conductivity term $\sigma = \omega\varepsilon_0\varepsilon''$ where ω is the angular frequency. The SI unit of conductivity is siemens per meter (S/m).

The frequency response of the first-order system is obtained from the Laplace transformation, which provides the relationship known as the Debye equation:

$$\hat{\varepsilon} = \varepsilon_\infty + \frac{(\varepsilon_0 - \varepsilon_\infty)}{1 + \mathrm{j}\omega\tau} = \varepsilon' - \mathrm{j}\varepsilon'' \tag{3.25}$$

The limiting values of the permittivity, ε_s and ε_∞, are known as static and infinite permittivity, respectively. The relaxation time τ corresponds to a relaxation frequency $f_\mathrm{r} = 1/2\pi\tau$. For a highly associated liquid such as water, the static permittivity can be expressed in terms of molecular parameters in accordance with the discussions in the previous section as

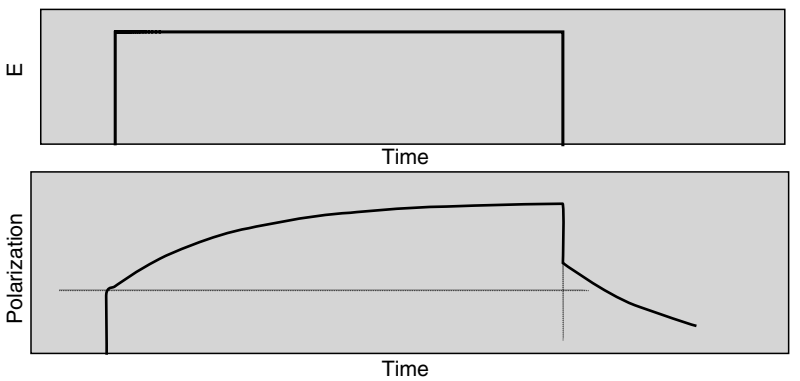

FIGURE 3.1
Schematic graph of dielectric response of a polar material expressed as polarization in the time domain in response to the step onset and removal of a polarizing electric field E. The nearly instantaneous rise in polarization, indicated by the horizontal dotted line, is P_∞; the vertical dotted line marks the instant and equivalent drop in polarization occurs when the field is removed.

$$\varepsilon_s = \varepsilon_\infty + \frac{Ng\mu^2}{2kT\varepsilon_0} \tag{3.26}$$

The relaxation time may be identified with the time constant of the molecular polarization and expressed in terms of molecular parameters. If η is the viscosity, then for a spherical molecule of radius a

$$\tau = 4\pi a^3 \eta / kT \tag{3.27}$$

For most polar materials, though not for water, ε_∞ corresponds to the optical permittivity and is equal to the square of optical refractive index n of the medium:

$$\varepsilon_\infty = n^2 \tag{3.28}$$

The dielectric properties of polar molecules vary with temperature; in general, both ε_s and τ decrease with increasing temperature.

As with the charge density and polarization, the time dependence of the current density J and σ, the current density per unit field, also follows a first-order law such that

$$J/E = \sigma_\infty + (\sigma_s - \sigma_\infty)(1 - e^{-t/\tau}) \tag{3.29}$$

This transforms into the conductivity equivalent of the Debye equation:

$$\hat{\sigma} = \sigma_\infty + \frac{(\sigma_s - \sigma_\infty)}{1 + j\omega\tau} \tag{3.30}$$

Figure 3.2 shows the variation in the permittivity, loss factor, and conductivity with frequency for a single time constant relaxation; such behavior pertains to an idealized monomolecular polar substance with no residual frequency-independent conductivity, that is $\sigma_s = 0$. The best, if not the only, example of such material is pure water as will be discussed later.

At the relaxation frequency, the permittivity is halfway between its limiting values and the loss factor at its highest. In the case of a single time constant as described in Figure 3.2, the conductivity is halfway between its limiting values at the relaxation frequency.

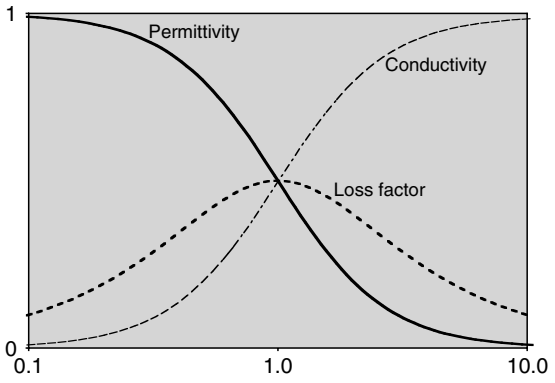

FIGURE 3.2
Normalized permittivity $(\varepsilon' - \varepsilon_\infty)/(\varepsilon_s - \varepsilon_\infty)$, loss factor $\varepsilon''/(\varepsilon_s - \varepsilon_\infty)$, and conductivity $\omega\varepsilon_0\,\varepsilon''/(\varepsilon_s - \varepsilon_\infty)$ for a single time constant relaxation plotted against f/f_r.

3.3.3 Nonpolar Molecules

The permittivity of nonpolar materials is virtually constant throughout the frequency range. In general, the temperature dependence is not significant. The static and optical values of the permittivity are almost identical, hence the Maxwell relation $\varepsilon = n^2$ holds true throughout the frequency and temperature range.

3.4 Observed Responses of Real Systems—Conduction—Multiple Relaxations—The Universal Law

In the previous section we described the expected behavior of idealized materials; we now need to deal with the observed responses of real systems. Few materials exhibit single relaxation time dispersions as in the Debye model; real materials depart from this ideal behavior to a greater or lesser extent depending on the complexity of the underlying mechanisms. To describe these responses we need to introduce the concepts of multiple dispersions and distribution of relaxation time. Moreover, biological materials exhibit conduction as well as polarization mechanisms; this needs to be taken into consideration in describing their dielectric response.

3.4.1 Conduction

The Debye expression does not include the effect of conduction currents as would arise from, for example, the drift of free ions in static fields. If σ_s is the static conductivity, the Debye expression becomes

$$\hat{\varepsilon} = \varepsilon_\infty + \frac{(\varepsilon_s - \varepsilon_\infty)}{1 - j\omega\tau} - \frac{j\sigma_s}{\omega\varepsilon_0} \tag{3.31}$$

In terms of real and imaginary parts we have

$$\begin{aligned} \varepsilon' &= \varepsilon_\infty + \frac{(\varepsilon_s - \varepsilon_\infty)}{1 + (\omega\tau)^2} \\ \varepsilon'' &= \frac{\sigma_s}{\omega\varepsilon_0} + \frac{(\varepsilon_s - \varepsilon_\infty)\omega\tau}{1 + (\omega\tau)^2} \end{aligned} \tag{3.32}$$

The total conductivity σ is given by

$$\sigma = \omega\varepsilon_0\varepsilon'' = \sigma_s + \frac{(\varepsilon_s - \varepsilon_\infty)\varepsilon_0\omega^2\tau}{1 + (\omega\tau)^2} \tag{3.33}$$

The total conductivity is thus made of two terms corresponding to the residual static conductivity and polarization losses. In practice, it is only possible to measure the total conductivity of a material; σ_s is obtained from data analysis or by measurement at frequencies corresponding to $\omega\tau \ll 1$ where the dipolar contribution to the total conductivity is negligible.

3.4.2 Multiple Relaxation Models—Distribution of Relaxation Times—Fractional Power Law Behavior

The occurrence of multiple interaction processes or the presence of more than one molecular conformational state or type of polar molecule may cause the dielectric behavior of a substance to exhibit multiple relaxation time dispersions. Deviation from Debye behavior may also indicate a polarization process whose kinetics are not first order or the presence of a complex intermolecular interaction. Models are needed to analyze the dielectric spectra of complex systems to unravel the underlying interaction mechanisms.

The simplest case is that of a dielectric response arising from multiple first-order processes; in this case the dielectric response will consist of multiple Debye terms to correspond to the polarization processes such that

$$\hat{\varepsilon} = \varepsilon_\infty + \frac{\Delta\varepsilon_1}{1 - j\omega\tau_1} + \frac{\Delta\varepsilon_2}{1 - j\omega\tau_2} + \cdots \tag{3.34}$$

where $\Delta\varepsilon_n$ corresponds to the limits of the dispersion characterized by time constant τ_n. If the relaxation times are well separated such that $\tau_1 \ll \tau_2 \ll \tau_3 \ll \cdots$, a plot of the dielectric properties as a function of frequency will exhibit clearly resolved dispersion regions.

If, as is quite often the case, the relaxation times are not well separated, the material will exhibit a broad dispersion encompassing all the relaxation times. In the limit of a continuous distribution of relaxation times, the multiple Debye expression would be

$$\hat{\varepsilon} = \varepsilon_\infty + (\varepsilon_s - \varepsilon_\infty) \int_0^\infty \frac{\rho(\tau)\, d\tau}{1 - j\omega\tau} \tag{3.35}$$

where

$$\int_0^\infty \rho(\tau)\, d\tau = 1 \tag{3.36}$$

The above equations can be used to represent all dielectric dispersion data, provided an appropriate distribution function $\rho(\tau)$ is available. Conversely, it should also be possible, at least in principle, to invert dielectric relaxation spectra to determine $\rho(\tau)$ directly; however, this is not easily achievable in practice. More commonly, one has to assume a distribution to describe the frequency dependence of the dielectric properties observed experimentally. The choice of distribution function should depend on the cause of the multiple dispersions in the material. For example, one can assume a Gaussian distribution as is known to occur for other physical characteristics (Figure 3.3) would be

$$\rho(t/\tau) = \frac{b}{\sqrt{\pi}} e^{-b^2[\ln(t/\tau)]^2} \tag{3.37}$$

where τ is the mean relaxation time. The shape of the Gaussian function depends on the parameter b; it reduces to the delta function when b tends to infinity and becomes very broad when b decreases; the area under the curve remains the same as required by the normalization condition. Incorporated into the expression for complex permittivity, it produces an expression that cannot be solved analytically, which makes it impractical for experimental data analysis.

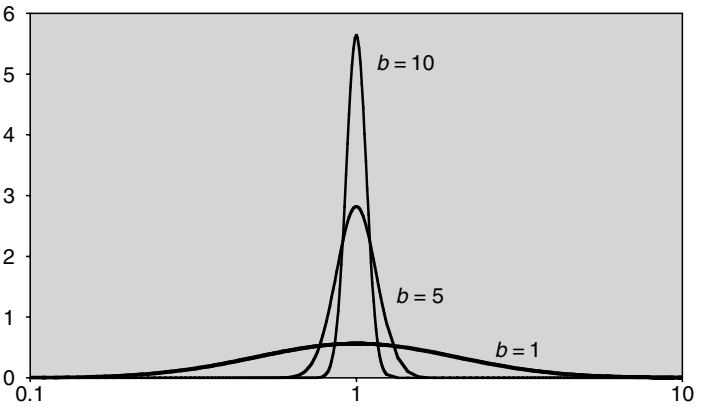

FIGURE 3.3
Gaussian distribution function as a function of t/τ.

Numerous empirical distribution functions or models have been proposed to model the experimental data without elaboration of the underlying mechanisms. One of the most commonly used models, a modified version of the Debye expression, was proposed in 1941 by Cole and Cole and is widely known as the Cole–Cole model:

$$\hat{\varepsilon} = \varepsilon_\infty + \frac{(\varepsilon_s - \varepsilon_\infty)}{1 - (j\omega\tau)^{1-\alpha}} = \varepsilon' - j\varepsilon'' \tag{3.38}$$

In it, α is a distribution parameter in the range $1 > \alpha \geq 0$; for $\alpha = 0$, the model reverts to the Debye equation. The real and imaginary parts are

$$\begin{aligned} \varepsilon' &= \varepsilon_\infty + \frac{(\varepsilon_s - \varepsilon_\infty)[1 - (\omega\tau)^{1-\alpha} \sin(\alpha\pi/2)]}{1 + (\omega\tau)^{2(1-\alpha)} + 2(\omega\tau)^{1-\alpha} \sin(\alpha\pi/2)} \\ \varepsilon'' &= \frac{(\varepsilon_s - \varepsilon_\infty)(\omega\tau)^{1-\alpha} \cos(\alpha\pi/2)}{1 + (\omega\tau)^{2(1-\alpha)} + 2(\omega\tau)^{1-\alpha} \sin(\alpha\pi/2)} \end{aligned} \tag{3.39}$$

Eliminating $\omega\,\tau$ from the above equations gives

$$\left(\varepsilon' - \frac{(\varepsilon_s + \varepsilon_\infty)}{2}\right)^2 + \left(\varepsilon'' + \frac{(\varepsilon_s + \varepsilon_\infty)}{2} \cot\frac{(1-\alpha)\pi}{2}\right)^2 = \left(\frac{\varepsilon_s - \varepsilon_\infty}{2} \operatorname{cosec}\frac{(1-\alpha)\pi}{2}\right)^2 \tag{3.40}$$

indicating that a plot of ε' against ε'' is a semicircle with its center below the real axis. For $\alpha = 0$, the Debye equivalent of the above equation is

$$\left(\varepsilon' - \frac{(\varepsilon_s + \varepsilon_\infty)}{2}\right)^2 + \varepsilon''^2 = \left(\frac{\varepsilon_s - \varepsilon_\infty}{2}\right)^2 \tag{3.41}$$

which indicates that ε' against ε'' is a semicircle with its center on the real axis (Figure 3.4); these semicircle plots are known as Cole–Coles.

The distribution function that corresponds to the Cole–Cole model is

$$\rho(t/\tau) = \frac{1}{2\pi} \frac{\sin(\alpha\pi)}{\cos h[(1-\alpha)\ln(t/\tau)] - \cos(\alpha\pi)} \tag{3.42}$$

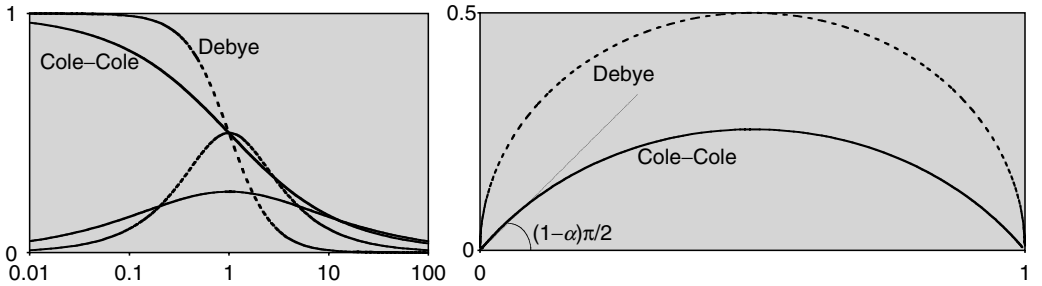

FIGURE 3.4
Left: Frequency dependence of normalized permittivity $(\varepsilon' - \varepsilon_\infty)/(\varepsilon_s - \varepsilon_\infty)$ and loss factor $\varepsilon''/(\varepsilon_s - \varepsilon_\infty)$ against frequency, normalized to the relaxation frequency, for a Debye and Cole–Cole with $\alpha = 0.4$. Right: Plot of normalized permittivity against loss factor showing a semicircle with its center on the real axis in the case of the Debye and an arc of a semicircle with its center below the real axis in the case of the Cole–Cole; the apex of the arc corresponds to the mean relaxation frequency.

Here again, τ is the mean relaxation time. As with the Gaussian, this distribution is logarithmically symmetrical about t/τ (Figure 3.5).

In 1951, Davidson and Cole proposed another variant of the Debye equation in which an exponent β is applied to the whole denominator:

$$\hat{\varepsilon} = \varepsilon_\infty + \frac{(\varepsilon_s - \varepsilon_\infty)}{(1 - j\omega\tau)^\beta} \tag{3.43}$$

which gives

$$\begin{aligned} \varepsilon' &= \varepsilon_\infty + (\varepsilon_s - \varepsilon_\infty)\cos(\beta\phi)(\cos\phi)^\beta \\ \varepsilon'' &= (\varepsilon_s - \varepsilon_\infty)\sin(\beta\phi)(\cos\phi)^\beta \end{aligned} \tag{3.44}$$

where $\phi = \arctan(\omega\tau)$. The corresponding distribution of relaxation times is

$$\rho(t/\tau) = \frac{1}{\pi}\left(\frac{t}{\tau - t}\right)^\beta \sin(\pi\beta) \tag{3.45}$$

When $\beta = 1$, the model reverts to the Debye equation. A plot of the real and imaginary parts of the model presents a skewed arc, similar to the Debye plot at low-frequencies, where it intercepts the abscissa at $\pi/2$, but at high frequencies the tangent to the arc is $\beta\pi/2$ (Figure 3.6).

The distribution function is shown graphically in Figure 3.7. It has a singularity at $t/\tau = 1$ and returns zero at $t > \tau$.

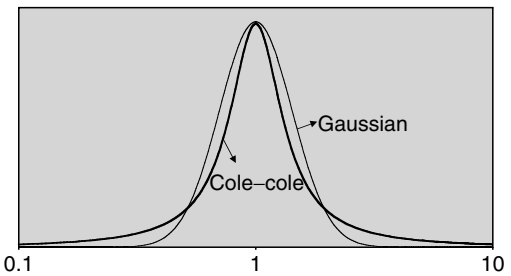

FIGURE 3.5
Gaussian distribution with $b = 2$ and Cole–Cole distribution with $\alpha = 0.09$ as a function of t/τ.

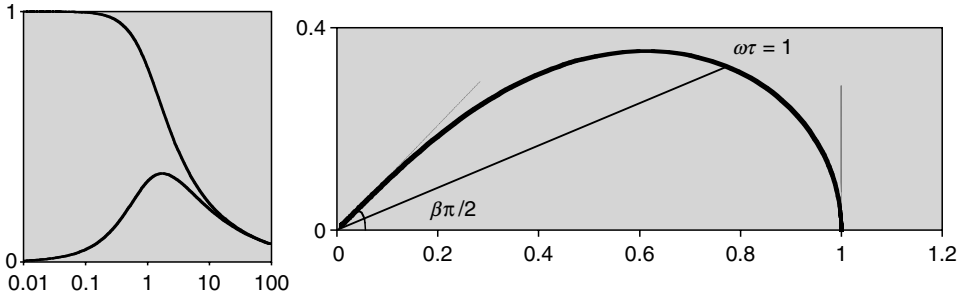

FIGURE 3.6
Left: Frequency dependence of normalized permittivity $(\varepsilon' - \varepsilon_\infty)/(\varepsilon_s - \varepsilon_\infty)$ and loss factor $\varepsilon''/(\varepsilon_s - \varepsilon_\infty)$ for a Cole–Davidson model with $\beta = 0.5$. Right: Plot of normalized loss factor against permittivity showing the characteristic Cole–Davidson skewed arc where the maximum in ε'' does not correspond with $\omega\tau = 1$; this point is found at the interception of the bisector of the high-frequency limiting angle with the data plot.

Another expression, sometimes used to model dielectric data, is the Havriliak–Negami relation (Havriliak and Negami, 1966). It combines the variations introduced in both the Cole–Cole and the Cole–Davidson models, giving

$$\hat{\varepsilon} = \varepsilon_\infty + \frac{(\varepsilon_s - \varepsilon_\infty)}{(1 - (j\omega\tau)^{(1-\alpha)})^\beta} \tag{3.46}$$

with real and imaginary parts:

$$\begin{aligned} \varepsilon' &= \varepsilon_\infty + \frac{(\varepsilon_s - \varepsilon_\infty)\cos(\beta\phi)}{1 + 2(\omega\tau)^{(1-\alpha)}\sin(\alpha\pi/2) + (\omega\tau)^{2(1-\alpha))^{\beta/2}}} \\ \varepsilon'' &= \frac{(\varepsilon_s - \varepsilon_\infty)\sin(\beta\phi)}{1 + 2(\omega\tau)^{(1-\alpha)}\sin(\alpha\pi/2) + (\omega\tau)^{2(1-\alpha))^{\beta/2}}} \end{aligned} \tag{3.47}$$

in which $\phi = \arctan\{[(\omega\tau)^{(1-\alpha)}\cos(\alpha\pi/2)]/[1 + (\omega\tau)^{(1-\alpha)}\sin(\alpha\pi/2)]\}$ and the corresponding distribution of relaxation times is

$$\rho(t/\tau) = \frac{1}{\pi}\frac{(t/\tau)^{\beta(1-\alpha)}\sin(\beta\theta)}{(t/\tau)^{2(1-\alpha)} + 2(t/\tau)^{(1-\alpha)}\cos(\pi(1-\alpha)) + 1)^{(\beta/2)}} \tag{3.48}$$

where $\theta = \arctan\{[(\sin(1-\alpha)\pi)/((t/\tau) + \cos(1-\alpha)\pi)]\}$.

The Cole–Cole plot of the Havriliak–Negami model is an asymmetric curve intercepting the real axis at different angles at high and low-frequencies (Figure 3.8). The distribution of relaxation times is also asymmetric (Figure 3.9).

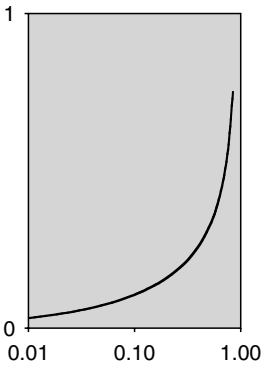

FIGURE 3.7
Cole–Davidson distribution with $\beta = 0.5$ as a function of t/τ.

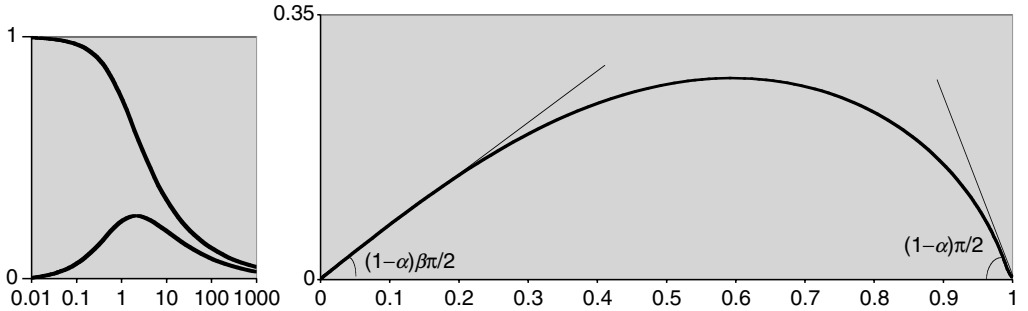

FIGURE 3.8
Left: frequency dependence of normalized permittivity $(\varepsilon' - \varepsilon_\infty)/(\varepsilon_s - \varepsilon_\infty)$ and loss factor $\varepsilon''/(\varepsilon_s - \varepsilon_\infty)$ for a Havriliak–Negami model with $\alpha = 0.2$ and $\beta = 0.5$. Right: Cole–Cole plot of the same data. As with the Cole-Davidson plot, the $\omega\tau = 1$ point is found at the interception of the bisector of the high-frequency limiting angle with the data plot.

Havriliak–Negami expressions revert to their Cole–Cole, Cole–Davidson, and Debye equivalents at the limiting values of β, α, and α and β, respectively. In principle, this should be the model of choice for dielectric data analysis. In practice, it is not widely used to describe the dielectric properties of biological material, as will be discussed later. It is important to recall that these empirical distribution functions lack mechanistic justification; however, they do serve a useful purpose in enabling the parametrization of the experimental data, albeit with very limited clarification of the underlying mechanisms.

Another limitation of this type of analysis is the possibility of obscuring multirelaxation processes, particularly the presence of a small amplitude dispersion following in the high-frequency tail end of a much larger principal one. This point is well illustrated by Wei and Sridhar (1993); they point out that a graphical representation of the parameter $\sigma'' = \omega\varepsilon_0(\varepsilon' - \varepsilon_\infty)$ versus $\sigma' = \omega\varepsilon_0\varepsilon''$ provides a more sensitive visualization of multirelaxation processes.

The Debye model and its many variations, including those described in this section, have been widely used over more than half a century primarily because they lend themselves to simple curve-fitting procedures. In particular, the Cole–Cole model is

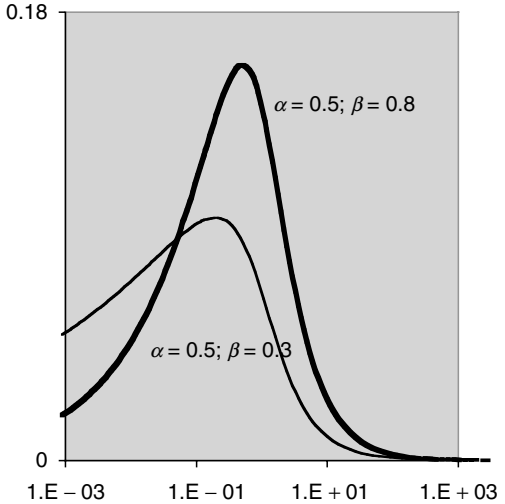

FIGURE 3.9
Havriliak–Negami distribution as a function of t/τ showing the effect of β for a given value of α.

used almost as a matter of course in the analysis of the dielectric properties of biological materials. Mathematically, at the limit of high frequencies, the Cole–Cole function simplifies to a fractional power law, that is, both ε' and ε'' are proportional to $(\omega\tau)^{(\alpha\ -1)}$. This fractional power law behavior is at the basis of what is known as the universal law of dielectric phenomena developed by Jonscher, Hill, and Dissado (Jonscher, 1983) for the analysis of the frequency dependence of dielectric data.

3.4.3 Universal Law of Dielectric Relaxation

Jonscher and his collaborators (Hill and Jonscher, 1983; Dissado and Hill, 1989) collated and analyzed extensive dielectric data obtained from numerous sources, pertaining to a wide range of materials, measured over a broad range of temperatures and frequencies. Their aim was to observe how dielectrics behave rather than presume a model for their frequency dependence; they studied the data on a log–log scale to better recognize the presence of a power law dependence, if present. Figure 3.10 shows plots for Debye and non-Debye responses where ω_p is the loss peak radial frequency.

Very few materials exhibit a pure Debye behavior where, at frequencies in excess of ω_p, the logarithmic slopes for $\varepsilon'(\omega)$ and $\varepsilon''(\omega)$ are -2 and -1, respectively, which is a Kramers–Krönig compatible result. However, for most materials a power law dependence of the type ω^{n-1}, with $n \neq 0$, applies for both $\varepsilon'(\omega)$ and $\varepsilon''(\omega)$. This is in compliance with the Kramers–Krönig relations, which require that at frequencies exceeding ω_p, both parameters follow the same frequency dependence, making the ratio $\varepsilon''(\omega)/\varepsilon'(\omega)$ frequency independent. Under such conditions, the ratio of energy dissipated to energy stored per radian of sinusoidal excitation is constant. The universal law can be summarized by the following frequency dependencies for the normalized complex permittivity:

$$\text{for } \omega < \omega_p, \quad \varepsilon''(\omega) \approx \omega^m \quad \text{and} \quad \varepsilon'(\omega) \approx 1 - \varepsilon''(\omega) \tag{3.49}$$

$$\text{for } \omega > \omega_p, \quad \varepsilon''(\omega) \approx \omega^{n-1} \quad \text{and} \quad \varepsilon'(\omega) \approx \varepsilon''(\omega) \approx \omega^{n-1} \tag{3.50}$$

Observation of the experimental data showed that ω_p is temperature dependent and follows an Arrhenius function:

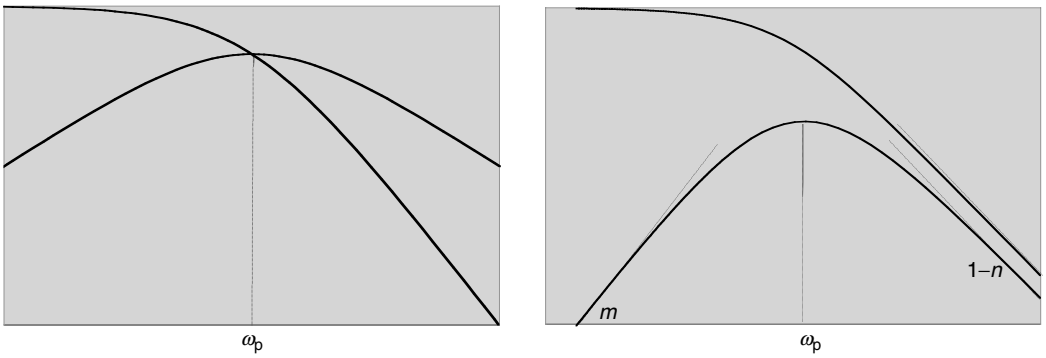

FIGURE 3.10
Log–log plot of the normalized permittivity and loss factor against frequency for a Debye-type behavior (left) and a non-Debye response (right).

$$\omega_{\mathrm{p}} = A\mathrm{e}^{-W/kT} \tag{3.51}$$

and the functional form for $\varepsilon''(\omega)$ is

$$\varepsilon''(\omega) = \frac{A}{(\omega/\omega_{\mathrm{p}})^{1-n} + (\omega_{\mathrm{p}}/\omega)^{\mathrm{m}}} \tag{3.52}$$

The values for $\varepsilon'(\omega)$ can then be determined numerically from the Kramer–Krönig relations.

Although the features of the dielectric spectra of most materials can be described using this approach, there is no theoretical justification for it. This makes it yet another empirical model, albeit a very general and mathematically elegant one.

3.4.4 Combined Response Model

A model that combines features from Debye-type and universal dielectric response behavior was proposed by Raicu (1999). In the course of modeling broad dielectric dispersions, as is often observed in the dielectric spectrum of biological materials, Raicu found that neither approach was good enough over a wide frequency range. He proposed the following very general function

$$\hat{\boldsymbol{\varepsilon}} = \boldsymbol{\varepsilon}_{\infty} + \frac{\Delta}{[(\mathrm{j}\omega\tau)^{\alpha} + (\mathrm{j}\omega\tau)^{1-\beta}]^{\gamma}} \tag{3.53}$$

where α, β, and γ are real constants in the range [0,1], τ is the characteristic relaxation time, and Δ is a dimensional constant, which becomes the dielectric increment $(\varepsilon_{\mathrm{s}} - \varepsilon_{\infty})$ when $\alpha = 0$, and the above expression reverts to the Havriliak–Negami model, which further reduces to the Debye, Cole–Cole, or Cole–Davison models with an appropriate choice of the α, β, and γ parameters. For $\gamma = 1$, it reverts to Jonsher's universal response model; in the special case where $\gamma = 1$ and $\alpha = 1 - \beta$, it becomes

$$\hat{\boldsymbol{\varepsilon}} = \boldsymbol{\varepsilon}_{\infty} + \left(\mathrm{j}\frac{\omega}{s}\right)^{\beta-1} \tag{3.54}$$

which is known as the constant phase angle model (Dissado, 1990). In this expression S is a scaling factor given by $S = (\Delta/2)^{1/(1-\beta)}\tau^{-1}$. The above expression was successfully used to model the dielectric spectrum of a biological material over five frequency decades from 10^3 Hz to 10^8 Hz.

3.5 Dielectric Properties of Biological Materials—Main Components

Tissue is a heterogenous material containing water, dissolved organic molecules, macromolecules, ions, and insoluble matter. The constituents are highly organized in cellular and subcellular structures forming macroscopic elements and soft and hard tissues. The presence of ions plays an important role in the interaction with an electric field, providing means for ionic conduction and polarization effects. Ionic charge drift creates conduction currents and also initiates polarization mechanisms through charge accumulation at

structural interfaces, which occur at various organizational levels. Their dielectric properties will thus reflect contributions to the polarization from both structure and composition. In this section, the contribution of each of the components will be determined individually and then collectively, leading to the formulation of models for the dielectric response of biological tissue.

3.5.1 Water

Water is a constituent of all living things; it is the environment in which body electrolytes and biomolecules reside and interact. Knowledge of its properties must precede the study of the more complex system. Many of the physical properties peculiar to water are due to its molecular asymmetry, polar nature, and ability to hydrogen bond, which are all interrelated. Water is described as an associated liquid because of its intermolecular hydrogen bonding. One practical reason for emphasizing the study of water in this chapter is its increasing use as a reference liquid, that is, a material of well-known dielectric properties. Consequently, it is often used as a standard for the calibration and testing of dielectric measuring procedures.

The dielectric properties of water are among the most studied and reported in the literature. Over the past decades, many experimental studies have been carried out to determine the dielectric properties of water over wide frequency and temperature ranges. These include Haggis et al. (1952), Lane and Saxton (1952), Hastead and El Sabeh (1953), Grant et al. (1957), Grant and Shack (1967), Grant and Sheppard (1974), Schwan et al. (1976), Grant et al. (1981), Hastead et al. (1985), Kaatze (1986, 1988), Buckmaster (1990), and Buchner et al. (1998). A comprehensive list of references and a historical overview of the subject can be found in Ellison et al. (1996). Other notable reviews were carried out by Kaatze (1989) and Liebe et al. (1991).

Data up to 100 GHz exhibit a near-perfect Debye dispersion with fairly well-defined parameters. Table 3.1 gives the Debye parameters for water at 20°C from three relatively recent reviews. Kaatze (1989) used a Debye expression to model his own extensive experimental data covering −4°C to 60°C and 1 to 57 GHz in addition to what he considered to be credible data from other sources.

Liebe et al. (1991) gathered extensive static and high-frequency data. For frequencies up to 100 GHz and temperatures from 0°C to 30°C, the data were a very good fit to the Debye function. However, including data at higher frequency somewhat reduced the goodness of the fit, suggesting the possible presence of a much smaller secondary dispersion in the hundreds of gigahertz range. The next logical step was then to use a two-Debye model. This proved a good fit to all experimental data up to 1 THz, thus confirming the presence of a small, high-frequency dispersion, probably due to some subtle molecular mechanism.

TABLE 3.1

Debye Parameters for Pure Water at 20°C

Review	ε_s	τ (ps)	ε_∞
Kaatze (1989)	80.2	9.47	5.2
Liebe et al. (1991)	80.1	9.35–9.39	5.3–5.4
Buchner et al. (1998)	80.2	9.32–9.52	5.9–6.0

Notes: For Liebe et al. (1991), τ and ε_∞ values are those of the single-Debye model (<100 GHz) and of the principal dispersion in the two-Debye model (up to 1 THz). Buchner et al. (1998) provide upper and lower bounds for τ and ε_∞ of the principal relaxation of a two-Debye model.

This secondary dispersion, centered around 670 GHz, brought down the high-frequency permittivity from 5.4 to 3.3 and made practically no impact on the characteristics of the principal dispersion, which were almost unchanged (Table 3.1). Liebe et al. (1991) extended the model to the far infrared (30 THz) by accounting for two near-infrared resonance absorption terms.

The most recent and comprehensive analysis of the dielectric properties of water is provided by Ellison et al. (1996), who critically reviewed the literature spanning the late 19th and most of the 20th centuries. With respect to the static permittivity, they obtained a function $\varepsilon_s = a\,e^{-b}$ with $a = 87.85306$ and $b = 0.00456992$, which predicts the value of ε_s at a given temperature to well within the limits of experimental accuracy for the range $-35^\circ C < t < 100^\circ C$. All high-frequency data (up to 1 THz) that met their selection criteria are tabulated. They stopped short of formulating models for the frequency dependence of the data; instead, they invited comments from the scientific community prior to the determination of what would probably be the ultimate model and spectral parameters for the dielectric properties of pure water, a finding that will greatly benefit this field of study. Already, other researchers have used this extensive survey. For example, Buchner et al. (1998) reported values for τ and ε_∞ of the principal water dispersion (Table 3.1) by fitting a two-Debye model to combined experimental data from Ellison et al. (1996) and other, more recent, studies (Barthel et al., 1995).

It is evident from Table 3.1 that the static permittivity and the relaxation time are fairly well-defined, less so the infinite permittivity. Fortunately, this parameter has little impact on the dielectric data in the gigahertz range because its value is only a small percentage of the permittivity in that frequency range. This relatively large uncertainty highlights the fact that even this most studied, pure substance is not a perfect reference liquid and that much remains to be done in the characterization of the dielectric properties of water at terahertz frequencies. Figure 3.11 is a plot of the dielectric properties of water at 20° tabulated by Ellison et al. (1996).

In biological materials, water is a solvent for salts, protein, nucleic acids, and smaller molecules. It is therefore important to study the effect of solutes on its dielectric response.

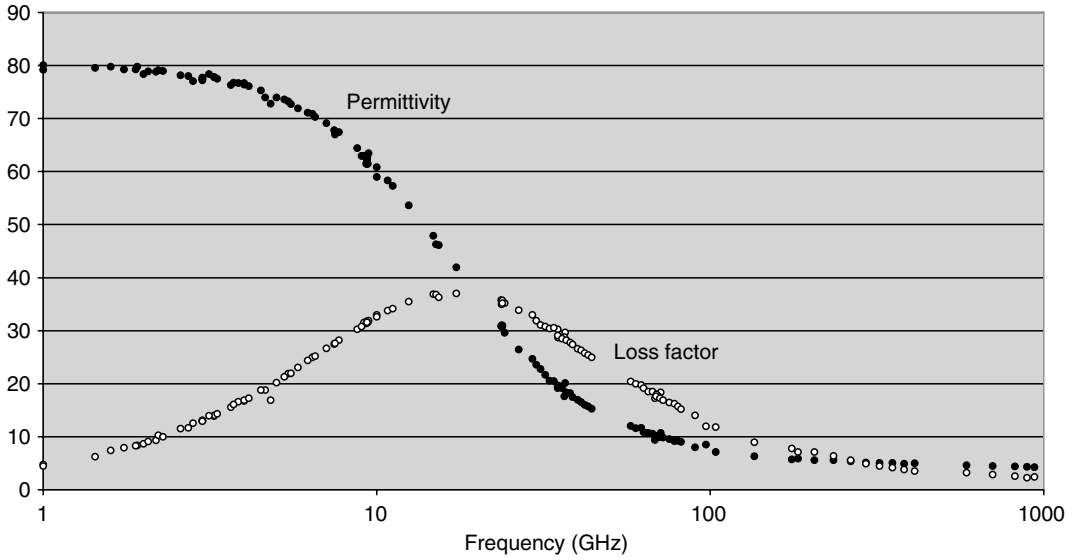

FIGURE 3.11
Experimental data from numerous sources reviewed and tabulated by Ellison et al. (1996).

3.5.2 Carbohydrates

In quantitative terms carbohydrates are not major constituents of animal cells; they are present at the surface of the cell membrane and are known to play a role in cellular communications. They are responsible for the gel consistency that gives certain body fluids such as vitreous humor and synovial fluid cushioning or lubricating properties. They are important constituents of certain tissues such as cartilage, tendon, and ligament. In terms of molecular structure, they vary in complexity and molecular size; they have in common the presence of one or more hydroxyl groups and the ability to hydrogen bond with each other or with water molecules. In aqueous solution they modify the principal dispersion of water to an extent that depends on the nature and concentration of the organic radical. In general, the dispersion is likely to be broader than a Debye, the static permittivity lower, and the relaxation time longer than for pure water, as observed and reported by Bateman and Gabriel (1987).

3.5.3 Proteins and Other Macromolecules

Protein constitutes the bulk of the organic matter in the body. Proteins are described as biopolymers, each molecule being a sequence of amino acids folded into a specific three-dimensional structure enclosing its hydrophobic sites within it. The surface has polar, hydrophilic groups with an affinity to bind water molecules from its surrounding aqueous environment. Part of the function of a protein resides in its structure; if the structure unfolds the protein is said to be denatured and is no longer functional. A good model for a globular protein in solution is that of a cluster of organic matter surrounded by a layer of strongly bound water; the solvent is referred to as free water to differentiate it from bound water. The size of the cluster depends on the molecular weight of the protein, which is typically of the order of tens or hundreds of thousands, that is, significantly larger than a water molecule. In an aqueous environment, most biological macromolecules including proteins act like polar molecules with permanent or induced dipole moment the magnitude of which depends on the molecular structure, configuration, and size.

Dielectric spectroscopy is therefore an important tool in the study of these molecular properties (Bateman et al., 1990, 1992). Typically, the dielectric dispersion of a protein will be in the megahertz frequency range, corresponding to a time constant of the order of microseconds. The dielectric spectrum of an aqueous globular protein solution will have two dispersion regions corresponding to the polarization of the protein and water molecules; the larger the protein the more clearly defined they will be. Conventionally, they are referred to as β and γ dispersions, respectively (Figure 3.12). Figure 3.12 shows a conceptual spectrum of a binary, protein–water system. In practice, to maintain the conformational stability of the biological molecules, inorganic ions, in the form of dissolved salts, must also be present. Table 3.2 has actual data, gathered from the literature, on the magnitude of the dielectric increment and the relaxation time for proteins of different shapes, sizes, and dipole moments. Many authors have reported the presence of a small dispersion that is attributed to bound water, described as molecules that are more or less strongly bound or otherwise affected by the presence of organic matter. When present, the spectral region of the bound water is termed δ dispersion. The book by Grant et al. (1978) is a good introduction to this important topic.

Larger biopolymers such as DNA, whose molecular weight may be of the order of several million, have more complex dielectric spectra with dispersions extending from kilohertz to megahertz. The elucidation of the polarization mechanisms responsible for

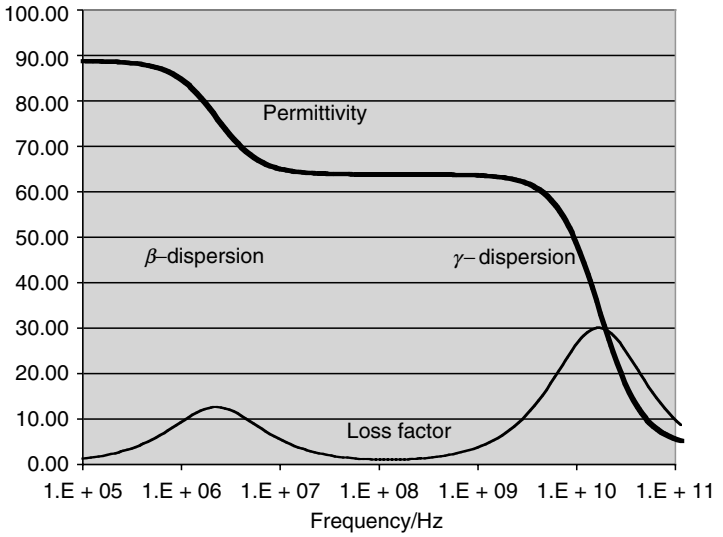

FIGURE 3.12
Conceptual representation of the dielectric spectrum of an aqueous protein solution. In practice, the two dispersions may overlap. The nearest to this picture is the complex permittivity spectrum of an aqueous solution of 1,2-dimyristoyl-L-3-phosphatidycholine reported by Kaatze and Giese (1980).

the dielectric spectrum of aqueous DNA solution is an area of active research. A good introduction to the subject is the book on biopolymers by Takashima (1989).

There is more than just academic interest in the study of biopolymers. Advances in nanotechnology are such that biological macromolecules are being considered as possible nanoscale electronic devices for fast information processing and transfer, a quest that will keep theoreticians and experimentalists busy for a long time.

3.5.4 Electrolytes

Electrolytes in the form of sodium, potassium, calcium, magnesium, chloride, and other ions play an important role in the function of biological systems. Many vital processes depend on a subtle balance being established between the concentration of electrolytes

TABLE 3.2

Dielectric Parameters of Various Proteins at 25°C

Protein	Mol wt. ($\times 10^3$)	$\Delta\varepsilon$	μ (D)	$\tau \times 10^8$ (s)	a/b
Myoglobin	17	0.15	170	2.9	—
β-Lactoglobulin (in 0.25 M glycine)	40	1.51	730	15, 5.1	4
Ovalbumin	44	0.10	250	18, 4.7	5
Horse carboxyhemoglobin	67	0.33	480	8.4	1.6
Horse serum albumin	70	0.17	380	36, 7.5	6
Horse serum pseudoglobulin	142	1.08	1100	250, 28	9

Notes: a/b is the axial ratio that determines the shape of the molecule. Where the shape deviates significantly from the spherical, two relaxation times are observed. The dielectric increment is $\Delta\varepsilon$, the dipole moment μ is given in Debye unit (1 D $= 3.33 \times 10^{-30}$ cm)
Source: From Foster KR, Schwan HP. 1989. *Crit Rev Biomed Eng* 17(1): 25–104. With permission.

inside and outside the cell. The cell membrane is, to a great extent, impermeable to the passive exchange of ions but allows directed movement under physiological control. In terms of dielectric properties, electrolytes have two effects. The direct effect, already mentioned, is the production of ohmic currents and energy loss in the system. This has the effect of making the static conductivity finite with a value commensurate with the ionic concentration and mobility. There are also important indirect effects whereby ionic charges contribute to the polarization of a biological system. One is interfacial polarization, whereby charge accumulation occurs at interfaces that are impermeable to ions. Another polarization mechanism is the ionic diffusion in electrical double layers adjacent to charged surfaces. Conduction, interfacial, and ion diffusion phenomena contribute significantly to the dielectric spectra of tissue.

3.5.5 Dielectric Dispersions in Tissue

The dielectric spectrum of a biological tissue (spleen at 37°C) is given in Figure 3.13 as an example of the response of a high water content tissue. Three main dispersion regions are immediately obvious and are referred to as α, β, and γ dispersions. The dispersions are rather broad, indicating the possible overlap of discrete relaxations arising from the polarization mechanisms encountered in the complex biological environment. Ionic conductivity contributes significantly to the loss factor, obliterating its features, and it is more

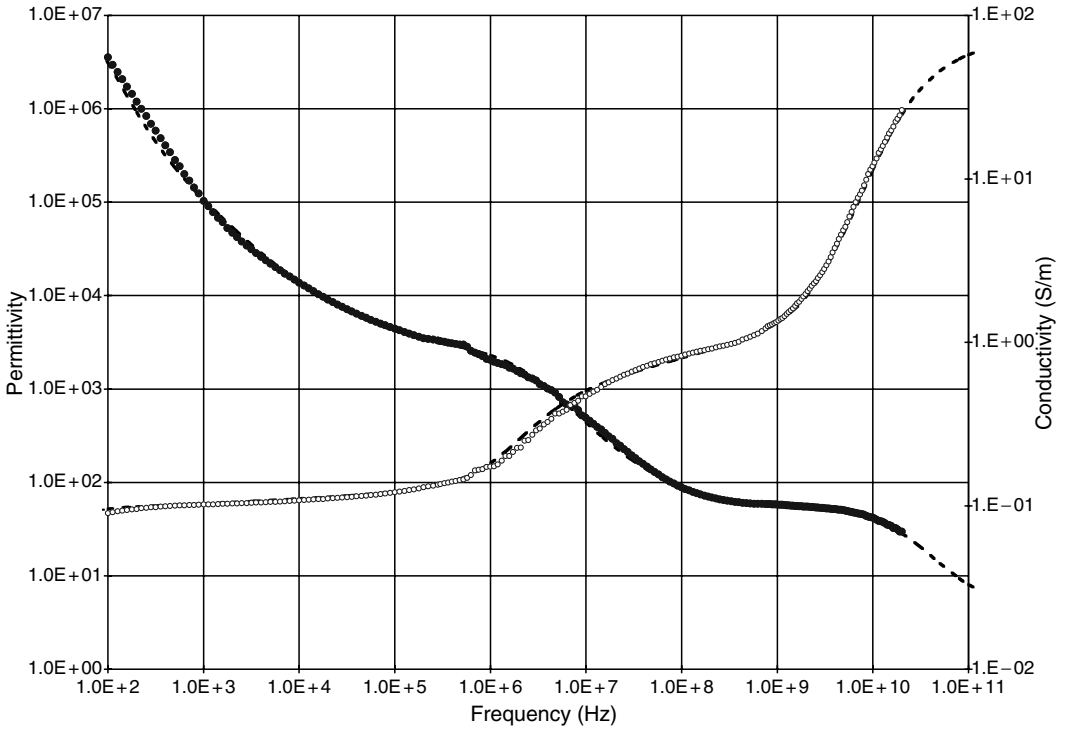

FIGURE 3.13
Dielectric spectrum of a high water content tissue (spleen at 37°C); experimental data are from Gabriel et al. (1996); dotted line is a best fit to a model of four Cole–Coles and a conductivity term.

informative to express the dielectric properties of tissues as permittivity and conductivity as in Figure 3.13.

3.5.5.1 α Dispersion

The α or low-frequency dispersion is characterized by very high permittivity values and can be ascribed, at least partially, to counterion diffusion effects. Such large dispersions are predicted by theories of ionic diffusion in heterogenous media. While it is not possible to model the complexity of a tissue, simpler mixture models predict dielectric increments of the right order of magnitude. Other mechanisms were postulated to contribute to the α dispersion; many relate to interactions in the vicinity of the cell membrane. The cell membrane is a complex, dynamic structure comprising a phospholipid bilayer. The lipid, hydrophobic ends of the phospholipids form a middle layer; the hydrophilic groups cover the inner and outer surfaces. Embedded in the bilayer are proteins, transport organelles, and ionic channels that operate under physiological control. The ionic balance between the intra- and extracellular media maintains a 60- to 70-mV potential difference between them of about 10 kV/mm across the membrane, assuming a 6- to 7-nm thickness. Membrane-related mechanisms that are thought to contribute to the α dispersion include the charging of intracellular membrane-bound organelles and a frequency dependence in the impedance of the cell membrane itself. An important reason for the uncertainty in the understanding of this dispersion is the paucity of error-free dielectric data in its frequency range. The α dispersion has a very large permittivity increment. The corresponding decrement in conductivity is small; this, however, does not contravene the principle of causality and the Kramers–Kronig relations, which predict a change in conductivity of about 0.005 S/m for a 10^6 increment in permittivity and relaxation frequency of 100 Hz.

3.5.5.2 β Dispersion

The β dispersion occurs at intermediate frequencies and originates mostly from the capacitive charging of the cellular membranes and those of membrane-bound intracellular bodies. This phenomenon, also known as interfacial polarization, has been studied theoretically and experimentally. It was established experimentally that damage to the cell membrane changes the features of the β dispersion. Numerous biomedical applications are based on the variation of the parameters of the β dispersion with pathological conditions involving changes in cell physiology and morphology. Tissue with directed, anisotropic cellular structure would exhibit an anisotropic dielectric response in the frequency range of the β dispersion.

Modeling the electrodynamics of a simplified tissue-like system, for example, suspensions of spherical inclusions in conductive media, has established theoretical grounds for the presence of the β dispersions. It enables the computation of an effective permittivity of similar order of magnitude to the β dispersion. For a system of concentric shells in conductive media (Hanai et al., 1988; Irimajiri et al., 1991), it predicts the presence of dielectric dispersions equal in number to the number of interfaces. These interfacial polarizations are boundary effects that occur in addition to other polarizations that may occur in the components of the system. The multiplicity of mehanisms goes a long way toward explaining why the β dispersions in tissue are rather broad.

3.5.5.3 γ Dispersion

The γ dispersion is due to the dipolar polarization of tissue water. At frequencies in excess of a few hundred megahertz, where the response of tissue water is the dominant

TABLE 3.3

Dielectric Parameters of Water Dispersion in Tissues Obtained by Analysis of Experimental Results at 37°C

Tissue	ε_s	τ (ps)	α	σ (S/m)
Bone (cortex)	14.9	13.8	0.26	0.092
Bone (section)	22.1	14.4	0.22	0.208
Cartilage	43.6	12.8	0.27	0.58
Cornea	53.0	8.72	0.13	1.05
Lens (cortex)	52.1	9.18	0.11	0.72
Lens (nucleus)	38.1	11.3	0.20	0.33
Retina	67.3	7.25	0.05	1.42
Brain (gray)	55.5	7.76	0.12	1.03
Brain (white)	37.0	8.04	0.24	0.47
Cerebellum	50.2	8.52	0.09	0.89
Dura	49.2	9.63	0.14	0.77
Brain stem	34.6	8.45	0.20	0.47
Tongue (*in vivo*)	57.7	9.12	0.08	0.63
Aqueous humor	74.2	6.81	0.01	1.83
Water	74.1	6.2	0.0	>0.0001

Source: From Gabriel et al. (1996c).

mechanism, the complex permittivity may be expressed as Cole–Cole plus a conductivity term to simulate the dipolar dispersion of water and the contribution of the electrolytes; thus,

$$\hat{\varepsilon}(\omega) = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_\infty}{1 + (j\omega\tau)^{1-\alpha}} + \frac{\sigma}{j\omega\varepsilon_0}$$

where σ is the conductivity due to ionic currents and to the lower-frequency polarization mechanisms. Table 3.3 gives the parameters of the γ dispersion of tissues modeled to the above expression. The water content of the tissues considered ranges from >95% for vitreous humor and >85% for retina to <20% for cortical bone. The correlation between ε_s and tissue water content is an obvious and expected result. The value of the distribution parameter α is significant for most tissues and negligible for body fluids (as for aqueous humor, for example). The mean relaxation time τ is generally longer than the value for water, indicating a restriction in the rotational ability of at least some of the tissue water molecules. The lengthening of the relaxation time of water in biological material is a well-studied hypothesis; the effect is common to most organic solutes, is known to increase with solute concentration (Grant et al., 1981; Bateman et al., 1990), and has previously been observed in tissues (Gabriel et al., 1983).

3.5.5.4 δ Dispersion

Tissues and other biological materials may exhibit dispersions other than the three main ones. The δ dispersion, identified in some protein solutions between the β and γ, dispersions may also occur in tissue in the hundreds of megahertz range; when present, its magnitude is small compared to the adjacent ones. Possible mechanisms include the dipolar relaxation of bound water, relaxation of small dipolar segments or side chains of biological molecules, and counterion diffusion along small regions of the charged surface. Under these conditions it is difficult to isolate and, in view of the multiplicity of possible mechanisms, difficult to interpret. It is often treated as the tail end of the β dispersion or a broadening of the γ dispersion.

3.5.6 Effective Complex Permittivity of a Heterogenous System

Where adequate experimental data are available, the complex permittivity of a tissue can be quite adequately modeled with four Cole–Coles and a static conductivity term:

$$\hat{\varepsilon}(\omega) = \varepsilon_\infty + \sum_{n=1}^{4} \frac{\Delta\varepsilon_n}{1 + (\mathrm{j}\omega\tau_n)^{(1-\alpha_n)}} + \sigma_\mathrm{s}/\mathrm{j}\omega\varepsilon_0 \tag{3.55}$$

This is a descriptive model, imparting no definite information on the polarization mechanisms; the measured dielectric properties represent the bulk response of the tissue. Assigning effective parameters to a heterogenous medium is equivalent to treating it as homogenous where these parameters are concerned; in this case, its structural components are much finer than the wavelength of the field probing it.

The derivation of a general formula for the effective permittivity of a system in terms of those for its constituents is based on the theory of the transport properties of mixtures (Reynolds and Hough, 1957). For example, in the case of a binary mixture where a medium with permittivity ε_1 has inclusions of permittivity ε_2 and assuming that v_1 andv_2 are their respective volume fractions such that $v_1 + v_2 = 1$, then the average electric displacement D is given by

$$D = v_1 D_1 + v_2 D \tag{3.56}$$

and the average electric field is given by

$$E = v_1 E_1 + v_2 E_2 \tag{3.57}$$

The effective permittivity ε of the mixture is given by

$$D = \varepsilon\varepsilon_0 E \tag{3.58}$$

and for each component, $D_1 = \varepsilon_1\varepsilon_0 E_1$ and $D_2 = \varepsilon_2\varepsilon_0 E_2$. Equation 3.56 and Equation 3.57 give

$$\varepsilon = \varepsilon_1 v_1 f_1 + \varepsilon_2 v_2 f_2 \tag{3.59}$$

where $v_1 f_1 + v_2 f_2 = 1, f_1 = E_1/E$, and $f_2 = E_2/E$, which gives two general formulations for the effective permittivity of the mixture:

$$\varepsilon = \varepsilon_1 + (\varepsilon_2 - \varepsilon_1) v_2 f_2 \tag{3.60}$$

or

$$(\varepsilon - \varepsilon_1) v_1 f_1 + (\varepsilon - \varepsilon_2) v_2 f_2 = 0 \tag{3.61}$$

The theoretical problem that needs to be resolved for specific mixtures boils down to the determination of the field ratios f_2 or f_2 and f_1. Theoretically, the two formulations are equivalent but, when approximations have to be made for the values of the field ratios, this is no longer true. Most of the published mixture equations differ from one another in the approximations considered appropriate. As for which of the two formulations to use as a starting point, it would seem reasonable to use Equation 3.60 for the case of sparse inclusions in a continuous medium and Equation 3.61 when the volume fractions of the

two components are comparable. In the general case, the dielectric properties (in Equation 3.60 and Equation 3.61) are complex. However, under static or quasistatic conditions, the mixture equations hold for either permittivity or conductivity.

Maxwell (1891) was the first to characterize the field ratios for a system of sparse spherical inclusions in a homogenous medium under static field conditions and obtained:

$$\frac{\sigma - \sigma_1}{\sigma + 2\sigma_1} = \nu_2 \frac{\sigma_2 - \sigma_1}{\sigma_2 + 2\sigma_1} \tag{3.62}$$

where the subscripts 1 and 2 refer to the suspending medium and inclusions, respectively. In terms of permittivity, Equation 3.62 is known as the Rayleigh formula; in its complex form it is attributed to Wagner and commonly known as the Maxwell–Wagner equation. Other well-known mixture equations for spherical inclusions include:

Böttcher equation:

$$\frac{\varepsilon - \varepsilon_1}{3\varepsilon} = \nu_2 \frac{\varepsilon_2 - \varepsilon_1}{\varepsilon_2 + 2\varepsilon_1} \tag{3.63}$$

Bruggeman equation:

$$\left(\frac{\varepsilon - \varepsilon_1}{\varepsilon_2 - \varepsilon_1}\right)^3 + (1 - \nu_2)\frac{\varepsilon}{\varepsilon_1} = 1 \tag{3.64}$$

Looyenga equation:

$$\varepsilon^{1/3} = \nu_1 \varepsilon_1^{1/3} + \nu_2 \varepsilon_2^{1/3} \tag{3.65}$$

To first-order approximation, the above mixture equations revert to the same expression irrespective of the formulation of the problem and of the technique used to solve it. This is because the conditions of infinite dilution and the spherical shape enable an almost exact solution to the field ratio to be obtained.

Other formulations exist for different shape inclusions such as oblate and prolate spheroids. The subject has been reviewed by, among others, Van Beek (1967), Hanai (1968), Dukhin (1971), and more recently, Greffe and Grosse (1992), Sihvola and Lindell (1992), and Tinga (1992).

It is possible to extend mixture equations to multiple inclusions by using an iterative procedure (Tamasanis, 1992). For example, if $\varepsilon(\varepsilon_1, \varepsilon_2, \nu_2)$ is the effective permittivity of a binary mixture of background of permittivity ε_1, inclusion of permittivity ε_2, and volume fraction v_2, then a mixture with two types of inclusions identified with subscripts 2 and 3, respectively, can be described as a binary mixture of background permittivity $\varepsilon(\varepsilon_1, \varepsilon_2, v_2/1 - v_3)$ and inclusion of permittivity ε_3 and volume fraction v_3. The effective permittivity of such a mixture will be

$$\varepsilon(\varepsilon_1;\, \varepsilon_2,\, v_2;\, \varepsilon_3,\, v_3) \approx \varepsilon\left[\varepsilon\left(\varepsilon_1;\, \varepsilon_2,\, \frac{v_2}{1 - v_3}\right);\, \varepsilon_3,\, v_3\right] \tag{3.66}$$

The contributions of the different types of inclusion are added recursively in order of increasing density.

Where the assumptions used in their derivation can be approximated in the tissue model, mixture equations can be used to analyze the dielectric properties of biological materials in terms of their constituents. A few examples are given here to illustrate their application.

If the ionic conductivities of the suspending phase and that of a protein solution are known, say, by measurement at a frequency below the protein β dispersion, and if an assumption is made about the conductivity of the protein molecules, an appropriate mixture equation can then be used to determine the volume fraction of the inclusions, which, in this case, is the hydrated protein. In turn, this enables the amount of bound water to be calculated given that the fraction of anhydrous protein is known. Bull and Breese (1969) followed this approach and calculated the bound water for a variety of proteins. They evaluated the water fraction to be 0.6 g/g of protein. Pauly and Schwan (1966), following a similar procedure, estimated the conductivity of the human erythrocyte to be 0.518 S/m at 25°C, compared to the value of 1.45 S/m calculated from the known ionic composition of the cell. They attributed the difference partly to excluded volume by the protein-bound water and partly to decreased ionic mobility due to hydrodynamic effects.

Bound water in biological systems including tissue was estimated by applying mixture equations in the near-plateau region between the β and γ dispersions of the permittivity spectrum. Assuming the tissue to be a suspension of hydrated organic matter in an electrolyte solution that is little affected by the presence of the organic matter, the measured permittivity at 1 GHz is a reasonable estimate of the effective static permittivity. Knowledge of the permittivity of the suspending medium and an estimate of the permittivity of the organic matter enables the volume fraction of the inclusion to be calculated. Comparison with the known organic content provides an estimate of bound water (e.g., Grant et al., 1984; Kaatze, 1990; Schaefer et al., 2003).

3.6 Dielectric Relaxation Mechanisms in Heterogenous Media

The description of a material as heterogenous is a matter of scale; in the context of dielectric relaxation, it refers to electrical heterogeneity or the presence of electrical boundaries or interfaces. Boundary conditions at and around the interfaces gives rise to dielectric dispersions quite apart from dipolar-type dispersions that occur in the surrounding media. In biological materials, cellular membranes provide such interfaces; their presence is associated with two major dispersion regions in the dielectric spectra of tissues, namely, α and β dispersions originating mainly from interfacial polarization and ionic diffusion effects. The main mechanisms giving rise to these phenomena will be briefly discussed in this section.

3.6.1 Interfacial Polarization

Interfacial polarization is due to the charging of interfaces between conducting media and is an important mechanism of interaction in biological material. The basic principles of this phenomenon are best illustrated in simple models first before discussing their occurrence in biological materials.

3.6.1.1 Interface between Two Media

The simplest model is that of an interface between two media, for example, two slabs of thickness d_1 and d_2 in contact with each other with their interface perpendicular to an external electric field (Figure 3.14a). If the static permittivity and conductivity of the two materials are ε_1, σ_1 and ε_2, σ_2, respectively, the boundary condition on the electric field component normal to the interface gives

$$E_1\varepsilon_1 = E_2\varepsilon_2 \tag{3.67}$$

If the current densities j_1 and j_2 are equal, there will be no charge accumulation at the interface; this, however, is hardly ever the case. The ratio of current densities at the interface is

$$j_1/j_2 = \sigma_1 E_1/\sigma_2 E_2 = \sigma_1\varepsilon_2/\sigma_2\varepsilon_1 \tag{3.68}$$

Therefore, if $\sigma_1\,\varepsilon_2 \neq \sigma_1\,\varepsilon_2$, the interface will be charged at a rate that is proportional to the difference between j_1 and j_2.

The effective permittivity ε and conductivity σ of the system are calculated from its effective capacitance. With the field across the interface, this is equivalent to capacitances in series combination; thus,

$$\frac{d_1 + d_2}{\varepsilon - \mathrm{j}\sigma/\omega\varepsilon_0} = \frac{d_1}{\varepsilon_1 - \mathrm{j}\sigma_1/\omega\varepsilon_0} + \frac{d_2}{\varepsilon_2 - \mathrm{j}\sigma_2/\omega\varepsilon_0} \tag{3.69}$$

This can be rearranged into a Debye type expression with a relaxation time of

$$\tau = \varepsilon_0 \frac{\varepsilon_1 d_2 + \varepsilon_2 d_1}{\sigma_1 d_2 + \sigma_2 d_1} \tag{3.70}$$

and limiting values for low and high frequencies

$$\varepsilon_s = \frac{(\varepsilon_2\sigma_1 - \varepsilon_1\sigma_2)^2 (d_1 + d_2) d_1 d_2}{(\varepsilon_1 d_2 + \varepsilon_2 d_1)(\sigma_1 d_2 + \sigma_2 d_1)^2} + \varepsilon_\infty \tag{3.71}$$

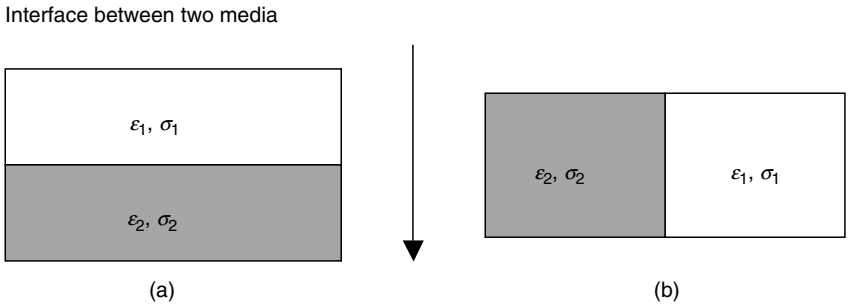

FIGURE 3.14
Two-media system; the arrow gives the direction of the electric field: (a) interface at right angle to the field and (b) interface along the field.

$$\sigma_s = (d_1 + d_2)\frac{\sigma_1\sigma_2}{\sigma_1 d_2 + \sigma_2 d_1} \tag{3.72}$$

$$\varepsilon_\infty = \frac{(d_1 + d_2)\varepsilon_1\varepsilon_1}{(\varepsilon_1 d_2 + \varepsilon_2 d_1)} \tag{3.73}$$

The polarization of the effective capacitance occurs in addition to any polarization process within the constituent phase, in which case the dielectric spectrum of the composite system will reflect the multiple dispersions.

If the field is along the interface (Figure 3.14b), no interfacial dispersion is observed, the effective permittivity is $\hat{\varepsilon} = (\hat{\varepsilon}_1 + \hat{\varepsilon}_2)/2$.

3.6.1.2 Suspension of Spheroids

The simplest system in this category is a dilute suspension of spherical inclusions in a continuum. Its effective complex permittivity is given by the formulation known as the Maxwell–Wagner equation, where the subscripts 1 and 2 refer to the suspending medium and inclusions, respectively:

$$\frac{\hat{\varepsilon} - \hat{\varepsilon}_1}{\hat{\varepsilon} + 2\hat{\varepsilon}_1} = v_2 \frac{\hat{\varepsilon}_2 - \hat{\varepsilon}_1}{\hat{\varepsilon}_2 + 2\hat{\varepsilon}_1} \tag{3.74}$$

This equation can be rearranged in the form of a dispersion equation with the following parameters:

$$\begin{aligned}
\varepsilon_\infty &= \varepsilon_2 \frac{2\varepsilon_2 + \varepsilon_1 - 2v_2(\varepsilon_2 - \varepsilon_1)}{2\varepsilon_2 + \varepsilon_1 + v_2(\varepsilon_2 - \varepsilon_1)} \\
\varepsilon_s - \varepsilon_\infty &= \frac{9(\varepsilon_2\sigma_1 - \varepsilon_1\sigma_2)^2 v_2(1 - v_2)}{[2\varepsilon_2 + \varepsilon_1 + v_2(\varepsilon_2 - \varepsilon_1)][2\sigma_2 + \sigma_2 + v_2(\sigma_2 - \sigma_1)]^2} \\
\sigma_s &= \sigma_2 \frac{2\sigma_s + \sigma_2 - 2v_2(\sigma_2 - \sigma_1)}{2\sigma_2 + \sigma_2 + v_2(\sigma_2 - \sigma_1)} \\
\sigma_s - \sigma_\infty &= \frac{9(\sigma_2\varepsilon_1 - \sigma_1\varepsilon_2)^2 v_2(1 - v_2)}{[2\sigma_2 + \sigma_1 + v_2(\sigma_2 - \sigma_1)][2\varepsilon_2 + \varepsilon_2 + v_2(\varepsilon_2 - \varepsilon_1)]^2} \\
\tau &= \varepsilon_0 \frac{2\varepsilon_2 + \varepsilon_1 - v_2(\varepsilon_2 - \varepsilon_1)}{2\sigma_2 + \sigma_2 + v_2(\sigma_2 - \sigma_1)}
\end{aligned} \tag{3.75}$$

The dispersion will occur when $\sigma_1\varepsilon_2 \neq \sigma_1\varepsilon_2$, which is practically always the case. The magnitude of the dispersion depends on the differences in dielectric parameters between the two phases.

In the context of mixture theory, sparse means $v_2 \leq 0.2$; to model the effective permittivity of more concentrated suspensions, it is necessary to take into consideration interparticle interactions. This becomes a very complex model; there are no rigorous solutions even for the relatively simple case of identical spherical inclusions. The Bruggeman–Hanai Equation 3.64 was formulated taking account of some interaction between particles and is therefore better suited than the Maxell–Wagner equation to model more concentrated suspension. In its complex form, it can be shown to predict the occurrence of a dispersion with the following limiting parameters:

$$\left(\frac{\varepsilon_\infty - \varepsilon_2}{\varepsilon_1 - \varepsilon_2}\right)\left(\frac{\varepsilon_1}{\varepsilon_s}\right)^{1/3} = 1 - v_2$$

$$\varepsilon_s\left(\frac{3}{\varepsilon_s - \sigma_2} - \frac{1}{\sigma_s}\right) = 3\left(\frac{\varepsilon_1 - \varepsilon_2}{\sigma_1 - \sigma_2} + \frac{\varepsilon_2}{\sigma_s - \sigma_2}\right) - \frac{\varepsilon_2}{\sigma_2}$$

$$\left(\frac{\varepsilon_s - \sigma_2}{\sigma_1 - \sigma_2}\right)\left(\frac{\sigma_1}{\sigma_s}\right)^{1/3} = 1 - v_2$$

$$\sigma_\infty\left(\frac{3}{\varepsilon_\infty - \varepsilon_2} - \frac{1}{\varepsilon_\infty}\right) = 3\left(\frac{\sigma_1 - \sigma_2}{\varepsilon_1 - \varepsilon_2} + \frac{\sigma_2}{\varepsilon_\infty - \varepsilon_2}\right) - \frac{\sigma_1}{\varepsilon_1} \tag{3.76}$$

In these expressions ε_s, ε_∞, σ_∞ are the limiting values of the corresponding parameters. The dispersion is characterized by a distribution of relaxation times.

The validity of the model has been verified experimentally for mixtures of known composition and geometry (Hanai et al., 1982; Ishikawa et al., 1982). The dispersion is broader than a single time constant because of the interactions between particles. Moreover, if the components of the heterogenous system exhibit molecular dielectric dispersion of their own, then these intrinsic dispersions will also appear, together with the interfacial dispersion, in the complete frequency spectrum of the system.

Fricke (1955), Sihvola and Kong (1988), Sihvola and Lindell (1992), and many others have extended the model to the more general case of a suspension of spheroids with any combination of axial ratios. Ultimately, the outcome is equivalent to introducing a parameter to account for the shape. The Maxwell–Wagner equation becomes

$$\frac{\hat{\varepsilon} - \hat{\varepsilon}_1}{\hat{\varepsilon} + F\hat{\varepsilon}_1} = v_2 \frac{\hat{\varepsilon}_2 - \hat{\varepsilon}_1}{\hat{\varepsilon}_2 + F\hat{\varepsilon}_1} \tag{3.77}$$

where F is the shape factor, equal to 2 for spheres, which reverts to Equation 3.74. In cases where the shape of the inclusion is not known, limiting values for the effective permittivity can be obtained using the shape factors in the extreme cases of infinitely long thin rods and infinitely thin circular disks.

An interesting case is that of ellipsoids with their axes aligned in the same direction. The permittivity would be different depending on the direction of the field; the mixture would be electrically anisotropic and the effective permittivity is represented by a tensor.

Another case of practical interest is that of layered spherical inclusions. This situation is required when modeling cellular structures surrounded by a membrane of finite thickness. Solutions for the effective permittivity of this model were provided by many researchers in this field (e.g., Schwan, 1957; Zhang et al., 1983; Grosse, 1988). These authors applied two mixture models, once to the concentric bodies, thus obtaining an effective permittivity for the inclusions, and then treating the mixture as a suspension of homogenous spheres. The parameters of the dispersion could be expressed in terms of the physical dimensions and electrical characteristics of the cell and cell membrane; simplified versions of these expressions are reported by Foster and Schwan (1989). Sihvola (1989) and Irimajiri et al. (1991), among others, extended the treatment to several concentric shells by using a recursive technique. These complex models are more relevant to the study of biological systems and to the understanding of the interactions at the cellular level. They are not sufficiently developed for the quantitative characterization of the interfacial polarization in biological systems, but do provide an insight into the factors that determine its characteristics. An example from the recent literature is the modeling of the dielectric response of heart tissue by Schaefer et al. (2002). The model is a function of the cell shape, electrical cell coupling and

polarization of cell membranes, and intracellular structure. It describes heart cells and subcellular organelles as rotational ellipsoids filled with electrolyte enclosed by an isolating membrane and is capable of reproducing the main features of the dielectric spectrum of heart tissue.

In recent years, statistical methods using probabilistic descriptions of the physical mixture in terms of a spatial density function have been developed to provide realistic bounds for the effective permittivity of mixtures. This approach, developed by, among others, Bergman (1978) and Milton (2002), provides an analytic integral representation of the effective permittivity $\hat{\boldsymbol{\varepsilon}}$ of an arbitrary binary mixture in terms of a spatial density function $g(x)$:

$$\frac{\hat{\boldsymbol{\varepsilon}} - \hat{\boldsymbol{\varepsilon}}_1}{\hat{\boldsymbol{\varepsilon}}_1} = \int_0^1 \frac{g(x)\,\mathrm{d}x}{x + \hat{\boldsymbol{\varepsilon}}_1/\hat{\boldsymbol{\varepsilon}}_2 - \hat{\boldsymbol{\varepsilon}}_1}$$

where, as before, the subscripts 1 and 2 refer to continuum and dispersed phases, respectively, and the integration is over all possible positions. Depending on the choice of distribution function $g(x)$, it is possible for the above equation to revert to some of the well-known binary mixture equations. Recursive application is possible; modeling biological systems remains challenging.

A new tool for the study of mixtures, including biological materials, has evolved with the development of increasingly powerful numerical modeling packages for the propagation of electromagnetic fields in complex structures from full solutions of Maxwell's equations. With structures being defined at the nanoscale, the characterization of fields within cells and subcellular structures appears to be within reach (Gimsa and Wachner, 1998, 1999, 2001a,b; Bianco et al., 2000; Sebastian et al., 2001; Munoz et al., 2003).

3.6.2 Counterion Polarization Effects

Another important polarization phenomenon in electrically biological materials originates from ionic diffusion effects near charged surfaces and the formation of counterion or electric double layers. The distribution of ions in the vicinity of charged interfaces is subject to concentration and electric field gradients; an equilibrium is reached with the ions continuously distributed over the volume of the electrolyte solution. The time constant associated with this mechanism is longer than that of the Maxwell–Wagner effect, it is of the form L^2/D, where L is the length over which diffusion occurs and D is a diffusion coefficient (Schwarz, 1962).

Counterion phenomena are difficult to analyze rigorously; they involve coupled electrodynamic and hydrodynamic mechanisms. The theories are complex, but good reviews are available as an introduction to the subject (Dukhin, 1971; Dukhin and Shilov, 1974; Fixman, 1980, 1983; Mandel and Odijk, 1984). Relatively simple models that provide exact solutions have been proposed (Grosse and Foster, 1987; Grosse, 1988), whereby coupled differential equations for the ion concentrations and current densities are obtained for a macroscopic sphere of radius a in an ionic medium. Their solution yields a broad, asymmetrical, low-frequency dispersion. The time constant of this dispersion is a^2/D, where D is the diffusion coefficient of ions in the bulk electrolyte.

To visualize the effect, consider the motion of an ion in the bulk electrolyte near the particle, it will be conducted away or excluded depending on whether its sign is the same or opposite that of the ions in the counterion layer. Thus, for an ion in the electrolyte, the particle acts either as a good conductor or as an insulator depending on its charge

compared to that of the counterion. A cloud of charge accumulates within a Debye length of the charged surface; for physiological saline (0.15 N NaCl) the Debye length is very small, <1 nm, resulting in a very large induced capacitance and hence a large permittivity dispersion.

3.7 Dielectric Properties of Tissue—State-of-Knowledge

Research into the dielectric properties of biological materials and their variation with frequency has been ongoing for most of the past century. Early studies went a long way toward understanding and establishing the principles of interaction and the corresponding features of the highly frequency-dependent spectrum of a tissue. In the last few decades, the research was driven, above all, by the need to establish a credible database of dielectric properties of all body tissues for use in electromagnetic dosimetry studies, where the object is to quantify the exposure of people to external electromagnetic fields from knowledge of the effective internal fields and currents induced in them. In these studies, tissues are characterized by their measured dielectric properties. In the last decade, most dosimetric studies drew on data published in the scientific literature in 1996 and made widely available on the Internet thereafter (Gabriel et al., 1996; Gabriel and Gabriel, 1997).

3.7.1 1996 Database

The backbone of the 1996 database is a large experimental study providing data pertaining, almost exclusively, to excised animal tissue at 37°C. For most tissues, the characterization was over a wide frequency range, 10 Hz to 20 GHz, using three previously established experimental setups with overlapping frequency ranges. The following are some of its characteristics:

- The data are presented in the context of a review covering all relevant publications in the preceding half-century. By and large, the experimental data were well within the confines of corresponding values from the literature.
- The data showed good internal consistency, that is, good agreement between data obtained with different experimental setups in a common frequency range.
- Finally, an element of great practical importance, the dielectric spectra were parametrized using a multidispersion model consisting of four Cole–Cole terms and one ionic conductivity term. For each tissue, the parameters of the model enable the reconstruction of its spectrum, a procedure that could easily be incorporated in numerical studies to provide dielectric data that are broadly in line with the vast body of literature on the subject.
- The fact that the complex permittivity data could be fitted to Cole–Cole dispersions implies that they also agree with the Kramers–Kronig relation in accordance with the principle of causality for a linear system. This imparts another level of consistency to the data.

Examples are given here to illustrate the extent of the available data in the literature for certain tissues at certain frequencies in contrast to the scarcity of data elsewhere

(Figure 3.15 through Figure 3.17). No attempt is made at a quantitative or mechanistic analysis.

While useful, the 1996 database has several limitations, as pointed out by its authors:

- Most measurements were carried out on excised tissue, while data pertaining to live tissue would have been more relevant in bioelectromagnetics studies.
- For most tissues, the predictions of the model can be used with confidence for frequencies above 1 MHz because of the availability of supporting data in the literature.
- At lower frequencies, where the literature values are scarce and have larger than average uncertainties, the model should be used with caution in the knowledge that it provides a ''best estimate'' based on the then available knowledge. This is particularly important for tissues where there are no data to support its predictions.
- Electrode polarization, an inevitable source of error at low-frequencies, was not totally accounted for. It affects the data at frequencies below 100 Hz.
- Because of the geometry of the sampling probe, it was not possible to orient the field along and across directed structure to demonstrate the anisotropy of the dielectric properties.

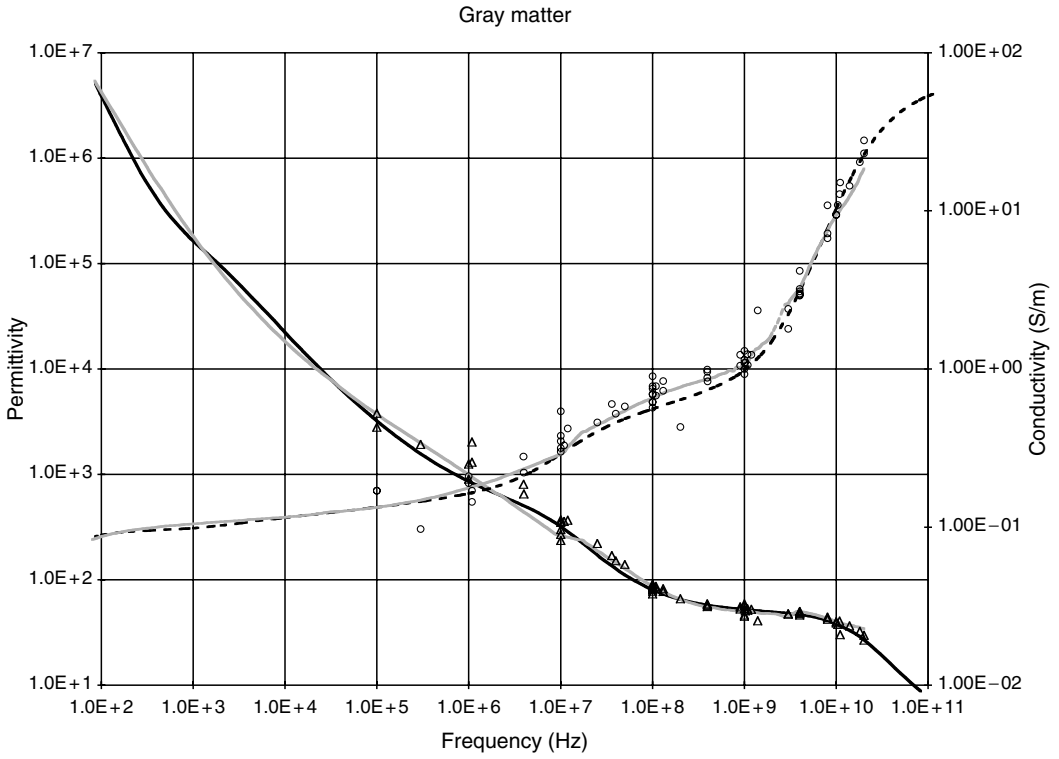

FIGURE 3.15
Permittivity and conductivity of gray matter at 37°C; gray lines are experimental data from Gabriel et al. (1996), triangles and circles are permittivity and conductivity values from the pre-1996 literature, black solid and dashed lines are the predictions of the model.

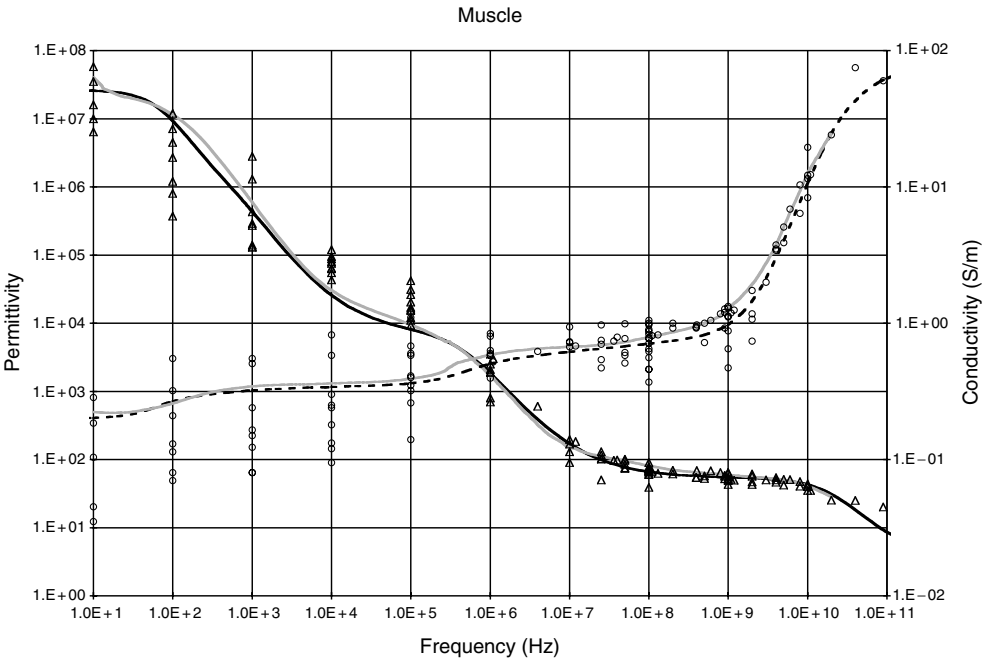

FIGURE 3.16
Permittivity and conductivity of skeletal muscle at 37°C; legend as in Figure 3.15. The very wide spectrum of data below 1 MHz is, at least partially, due to the anisotropy in the dielectric properties of muscle tissue. The literature data pertain to measurement along and across the muscle fibers and to measurements where the direction was not specified.

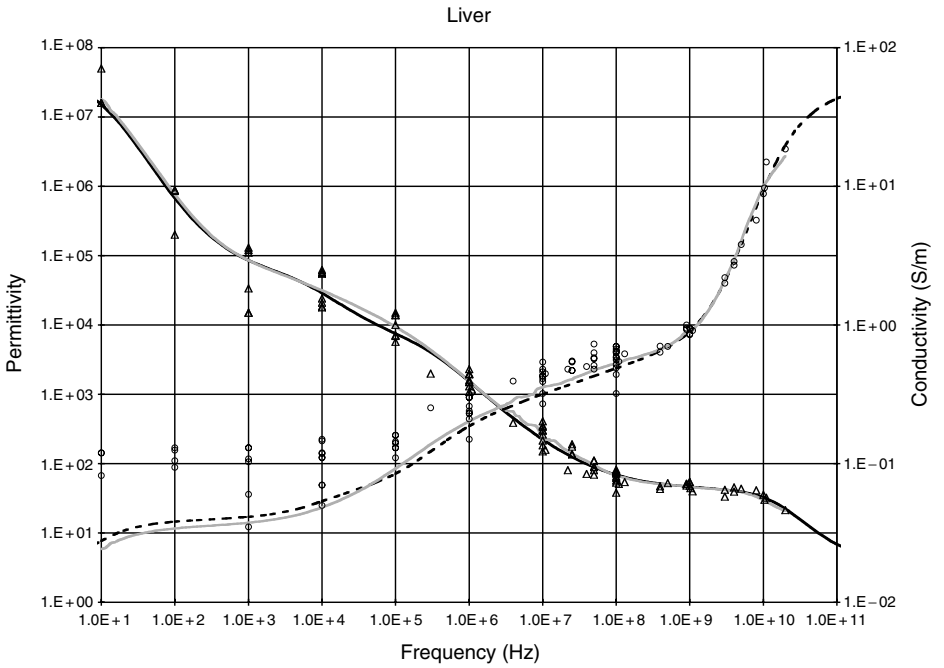

FIGURE 3.17
Permittivity and conductivity of liver tissue at 37°C; legend as in Figure 3.15. Liver tissue exhibits no significant anisotropy in its dielectric properties, but as with all tissue, the characteristics of the β dispersion and the static conductivity are sensitive to the viability and time after death when the measurements were made.

Evidently, much remains to be done, in particular with respect to reducing the uncertainty in the data and filling in the gaps identified. Ten years on, the recent literature is reviewed to update the state-of-knowledge on the subject.

3.7.2 Literature After 1996—A Brief Review

The review is carried out per tissue type or thematic underline. In some cases, data from recent studies are compared with the model in the 1996 database and with data from a recent study, where the dielectric properties of over 40 tissues were characterized *in vivo* and *in vitro* in the frequency range 10^2 to 10^4 MHz (Peyman et al., 2005).

3.7.2.1 Brain Tissue: Gray and White Matter

At microwave frequencies, three studies reported new data for brain tissue (Bao et al., 1997; Schmid et al., 2003a,b). Data tabulated by the authors are given in Figure 3.18. Data by Peyman et al. (2005) are in reasonable agreement with the database, while data by Bao and coworkers and Schmid and coworkers are higher for both permittivity and conductivity.

It is important to find a reason as to why carefully conducted studies, using adaptations of a conceptually similar experimental procedure, are still coming up with different results. In terms of explanation we note the handling of the sample by Bao et al., in which the whole brain is excised, immersed in saline, temperature regulated, and measured while immersed. The authors give good reasons for following this procedure.

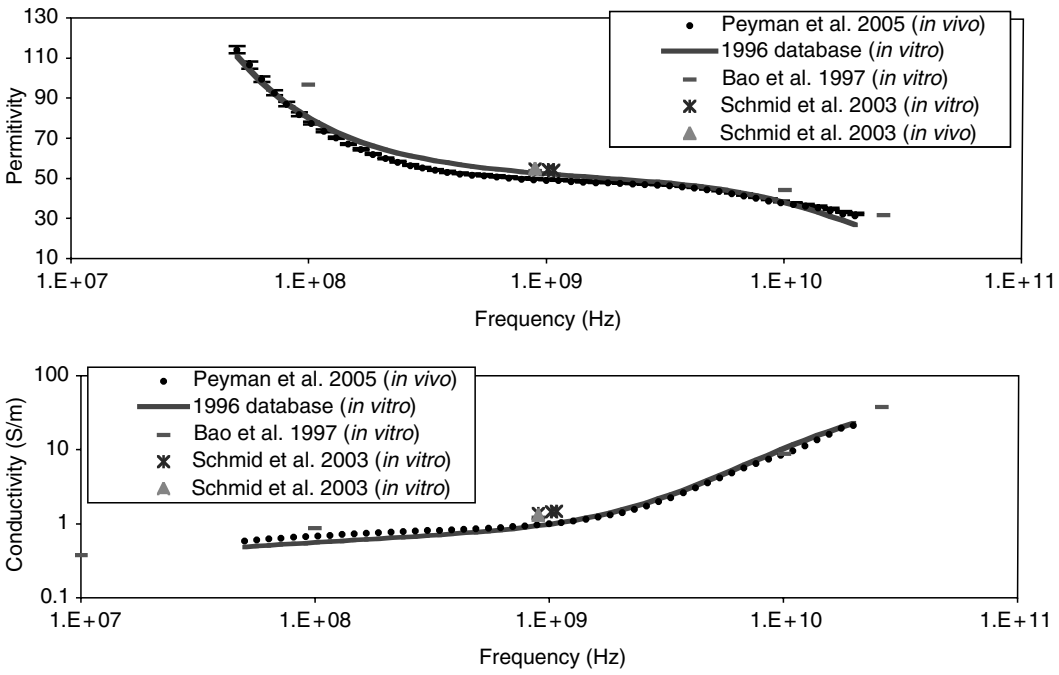

FIGURE 3.18
Dielectric properties of gray matter at 37°C. Data from recent studies compared to the prediction of the 1996 database.

It is inevitable, however, that one should expect their data to fall on the high side of average because of the presence of saline. Schmid et al. published data on porcine (*in vivo*) and human gray matter (*in vitro*). Their porcine gray matter data were obtained under conditions designed for the study of variation with time over a period spanning the time of death and beyond. Presumably, this is why their measurements were carried out over a narrow frequency range with the measurement probe held in position for the duration of the experiment (150 min). One might speculate that the amount of pressure used to maintain constant contact between the probe and the live brain could cause local oozing of fluid and higher conductivity values.

Conjecture apart, these data are valuable additions to the literature, but one must be cautious not to generalize on the basis of such limited data that measurement *in vitro* underestimates the dielectric properties of living tissues at microwave frequencies. Differences between tissue properties obtained *in vivo* and *in vitro* are to be expected at lower frequencies, in the range of α and β dispersions, in view of the sensitivity of their causal mechanism to the physiological state of the tissue. Differences between *in vivo* and *in vitro* data are much less likely in the frequency range of the γ dispersion, where water content is the most important determinant factor, and as recently reported by Stauffer et al. (2003), for liver tissue, and by Peyman et al. (2005), for many tissues including gray matter. Measurements *in vivo* are fraught with difficulties. For example, Burdette et al. (1986) measured the gray matter, *in vivo*, through the pia matter and directly beneath it. Of the two sets of data obtained, one is similar to that of Schmid et al., and the other is significantly lower.

In their human study, Schmid et al. measured the dielectric properties of gray matter in the frequency range of 800 MHz to 2450 MHz on 20 human brains immediately after excision. The measurements were carried out at room temperature in the range 18°C to 25°C and extrapolated to 37°C using experimentally determined thermal coefficients. Nevertheless, the dielectric properties at 900 MHz were in very good agreement with their data for porcine gray matter *in vivo*. It is understandably frustrating to realize that the bounds of uncertainty remain high when comparing data from different laboratories, even for those tissues that have been widely measured and reported.

Latikka et al. (2001) reported conductivity values at 50 kHz for gray matter (0.28 S/m), white matter (0.25 S/m), cerebrospinal fluid (1.25 S/m), and tumors (0.1 S/m to 0.43 S/m). They used a monopolar needle electrode during brain surgery on nine patients who had deep brain tumors. The technique is not geared toward making directed measurement and detecting anisotropy in the electrical properties, although those are anticipated on theoretical grounds and are known to be present in the hertz to kilohertz frequency range (Nicholson, 1965; Ranck et al., 1965; Yeldin et al., 1974; Nicholson and Freeman, 1975). Observed differences in the conductivity along and across the cellular structure were factors between 2 and 10 depending on the tissue. Clearly, this is an area of importance to electrophysiology, among other applications; it is also an area where data are scarce.

Peyman et al. (2001) reported variation in the dielectric properties of rat brain tissue as a function of age, at microwave frequencies. Their data pertained to the whole brain. The observed variation was ascribed, at least partially, to the change in the ratio of gray to white matter, which is known to occur throughout the developmental stage. In a recent study on porcine tissues (Peyman et al., 2005), they were able investigate gray and white matter separately. In this case, no variations were observed in the dielectric spectrum of gray matter, while statistically significant variations were observed in the dielectric spectrum of white matter (Figure 3.19). The observed variations are probably related to the process of myelination, which begins at birth and lasts to maturation. Similar variations were observed in the dielectric properties of the spinal cord.

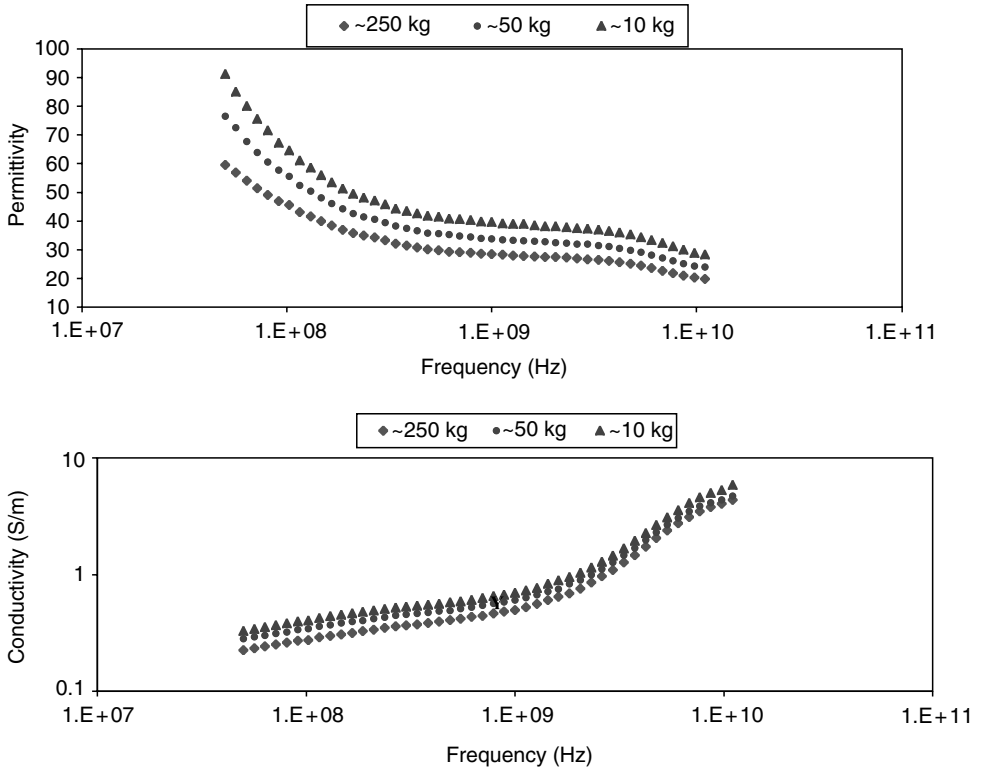

FIGURE 3.19
Permittivity and conductivity of white matter as a function of animal growth. The measurements were made *in vitro* at 37°C. The lowest permittivity and conductivity spectra pertain to a fully grown, 250-kg sow, the highest to a 10-kg piglet. (Data are from Peyman A, Holden S, Gabriel C. 2005. Dielectric Properties of Biological Tissues at Microwave Frequencies. Final technical report, MTHR Department of Health, U.K.)

3.7.2.2 Liver

Dielectric data for liver tissue were reported in several studies carried out under different conditions for a variety of reasons. For example, Riedel et al. (2003) developed a contact-free inductive measurement procedure and demonstrated the system by carrying out conductivity measurements on liver tissue between 50 and 400 kHz as a function of time after death. Stauffer et al. (2003) characterized the dielectric properties of normal and cancerous liver tissue in the frequency range of 0.3 to 3 GHz and reported higher permittivity and conductivity for tumor tissue. Chin and Sherar (2001) observed irreversible changes in the dielectric properties of liver tissue at 915 MHz because of excessive heating causing protein denaturation. Haemmerich et al. (2002) reported changes in the electrical resistivity of liver tissue during induced ischemia and postmortem. They observed increases in resistivity *in vivo* during occlusion. They analyzed the data in terms of intra- and extracellular resistance and cell membrane capacitance.

Valuable contributions by Raicu et al. (1998a,b) have provided data for rat liver tissue, measured *in vivo*, in the frequency range of 10^2 to 10^8 Hz. This is an eventful part of the dielectric spectrum of a tissue where contributions from interfacial and counterion interaction mechanisms occur. The measured data were corrected for electrode polarization and found to be in reasonable agreement with some previous studies (Surowiec et al., 1986; Foster and Schwan, 1996; Gabriel et al., 1996c). As expected, the data obtained traced a broad dielectric dispersion curve over the range of 10^3 to 10^8 Hz, suggestive of the

involvement of widely distributed relaxation times. In the second of their 1998 papers, they provide a mechanistic analysis. A simple application of the Maxwell–Wagner interfacial polarization theory could not fully explain the observed dielectric behavior, especially at frequencies below 1 MHz. The Bruggeman–Hanai-type effective medium theory (EMT) was better, but not perfect, at simulating the observation at low-frequencies. A better simulation of the effective permittivity was obtained when second-order corrections, for possible dipole–dipole interaction (DDI) effects, were introduced to the classical EMT for a concentrated suspension of particles. Application of the new EMT-DDI model enabled reasonable estimates to be made of the following: effective size and shape of hepatic cell; specific capacitance for the plasma, nuclear, and mitochondrial membranes associated with the hepatocyte; and cytosolic as well as nucleoplasmic conductivities of physiological interest.

3.7.2.3 Muscle

Muscle tissues, be it skeletal, myocardial, lingual, or other, exhibit large anisotropy in their electrical properties. This is to be expected from the tissue structure and was observed at frequencies below 1 MHz (Epstein and Foster, 1983; Fallert et al., 1993). The static conductivity value measured along the muscle fiber may be up to an order of magnitude higher than when measured across. The α dispersion is more prominent and the β dispersion less defined in the longitudinal direction in accordance with the predictions of effective permittivity modeling of elongated structures. For example, Semenov et al. (2002) evaluated anisotropy of the myocardium using a cellular model of the myocardial tissue and concluded that at frequencies lower than 10 MHz, myocardial dielectric properties are highly anisotropic (up to a factor of 10). Reliable, low-frequency data are very scarce, and there is a wide range in what is available in the literature, partly due to the fact that many authors do not specify the measurement orientation. The situation is not helped by the fact that the apparent anisotropy depends on the measurement procedure, in particular the interelectrode distance in relation to the size of the muscle fiber. Some of the problems associated with obtaining good data at frequencies below 1 MHz have been described by Tsai et al. (2000, 2002) in the context of their *in vivo* measurement of swine myocardial resistivity. In their study, they report changes in the myocardial resistivity as a function of time after death. The postmortem resistivity at 1, 10, and 100 Hz increased to about three times their original *in vivo* value and at 500 kHz and 1 MHz increased less than 15%, 6 h after death.

Most recent studies on the electrical properties of muscle tissue focused on the differences between normal and ischemic or hypoxic tissue. One of the drivers is to investigate the possibility of using *in situ* impedance measurements to map the histological changes in tissue *in vivo*. There is also potential for noninvasive imaging provided that the electrical characteristics of both normal and scar tissue are well-defined. Miyauchi et al. (1999) and Schaefer et al. (1999) observed changes in the α and β dispersions of normal and ischemic skeletal muscle. Ischemia in myocardial muscle is a matter of clinical importance in the assessment of myocardial infarction and has been the subject of many dielectric investigations. Schwartzman et al. (1999) investigated the properties of the border zone, which were found to be intermediate between healthy and infarcted tissue in the case of chronically infarcted ventricular myocardium. Semenov et al. (2002) observed the dielectric properties of canine myocardium during acute ischemia and hypoxia to explore the potential of these observations for the clinical assessment of myocardial tissue using electrical impedance and microwave tomography. One of the problems identified is the need to know and take into consideration the tissue electrical anisotropy.

3.7.2.4 *Skin*

Skin is the interface of the body with environmental agents including electromagnetic fields; knowledge of its dielectric properties is of importance in the assessment of human exposure and in numerous biomedical applications. Data from *in vivo* measurements are now available, obtained using noninvasive, open-ended coaxial probes (Gabriel et al., 1996c; Gabriel, 1997; Raicu et al., 2000). However, the interpretation of such topical measurements as effective permittivity of the skin is far from straightforward. Lahtinen et al. (1997) and Alanen et al. (1998) advocate an analysis based on a quasistatic approximation of the fringing field of the probe penetrating a layered structure. Gabriel (1997) drew attention to the effect on the dielectric spectrum of the degree of hydration of the stratum corneum (Figure 3.20), which also affects penetration of the field into the tissue. Joining the discussion, Raicu et al. (2000) carried out *in vivo* measurements on dry skin and on skin moistened with physiological saline, in the frequency range of 100 Hz to 100 MHz. They analyzed the data using the dispersion model comprising a Debye-type and ''universal'' responses (Equation 3.53) and a conductivity term. Comparing the parameters of the model for dry and saline-moistened skin, they noted a fivefold increase in the dispersion magnitude. One possible explanation they provide is that the ''effective penetration depth'' increases and contributions from the innermost skin layers become evident. This statement appears paradoxical; in fact, it is due to the reduction in the layering effect; when moistened, the skin appears more homogenous and behaves like a high water content tissue.

Raicu et al. (2000) further speculate that an interfacial polarization originating from the stratum corneum–epidermis interface occurs in the case of dry skin, as suggested by Alanen et al. (1999), but not in that of the saline-moistened skin. In support of this argument, they refer to the change in one of the distribution parameters, β, which decreases from 0.152 to 0.076 after the skin is hydrated with aqueous NaCl solution. It therefore appears that topical measurement on dry (normal) skin *in vivo* may not be proportionately representative of the inner layers. On the other hand, the use of an aqueous coupling agent that is likely to hydrate the stratum corneum affects the results of the measurements. In practice, the use of a coupling agent gives more reproducible results and leads to better agreement between data from the recent literature, as is evident in Figure 3.21 through Figure 3.23, which contain such data (Gabriel, 1997; Ghodgaonkar et al., 2000; Raicu et al., 2000; Sunaga et al., 2002; Hwang et al., 2003; Petaja et al., 2003) and collectively cover the frequency range of 100 Hz to 100 GHz.

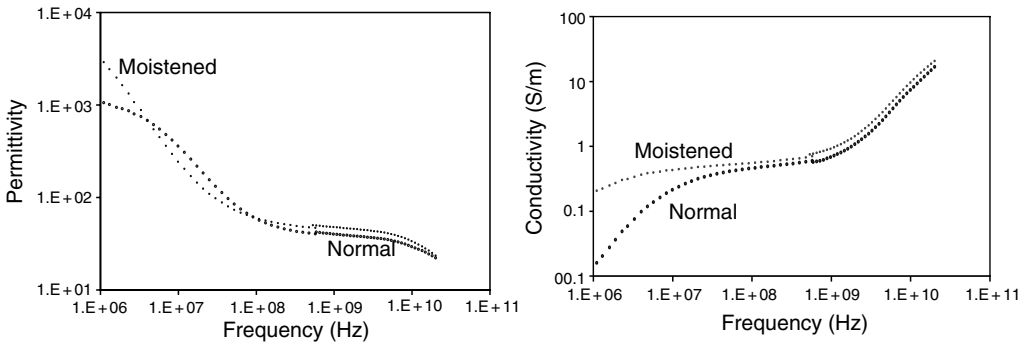

FIGURE 3.20
Permittivity and conductivity of skin (ventral forearm) illustrating the effect of moistening the skin on the dielectric spectra (Gabriel, 1996).

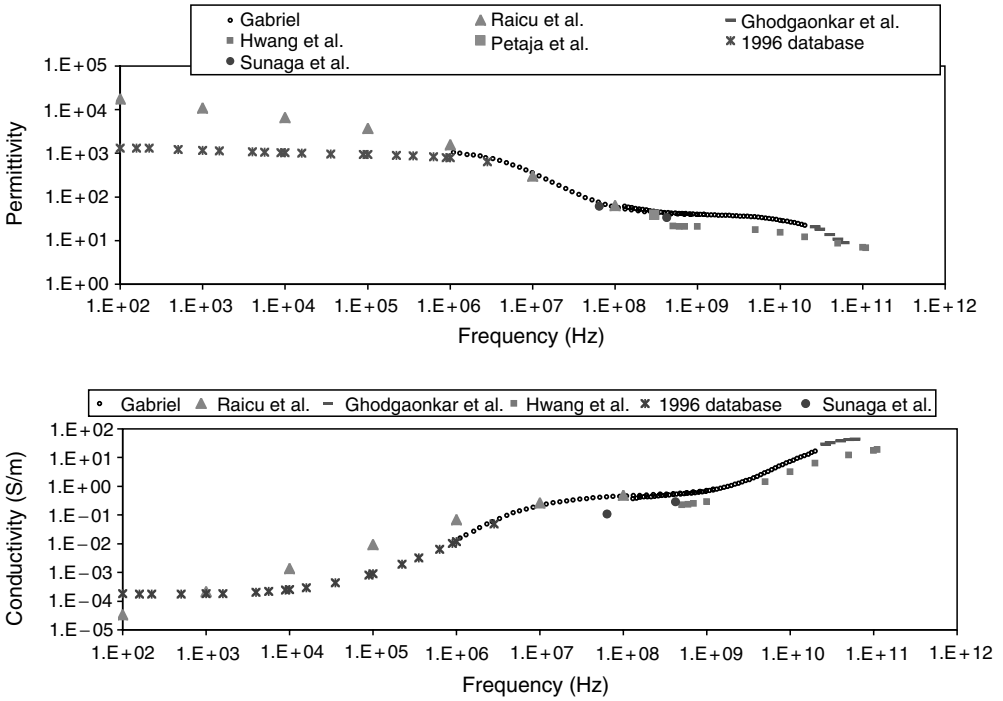

FIGURE 3.21
Permittivity and conductivity of skin (different parts of the body, excluding palms and soles). No moistening or contact gel was used. Different measurement techniques were used including open-ended coaxial probes of vastly different sizes.

The dielectric properties of skin have been widely investigated as monitors of various pathological conditions. Hayashi et al. (2005) investigated the dielectric properties of human skin *in vivo* at frequencies up to 10 GHz to monitor the progress of the healing process of skin burns using water content as the determinant factor. Their measurement technique, time domain spectroscopy and open-ended probe, is similar to that used by

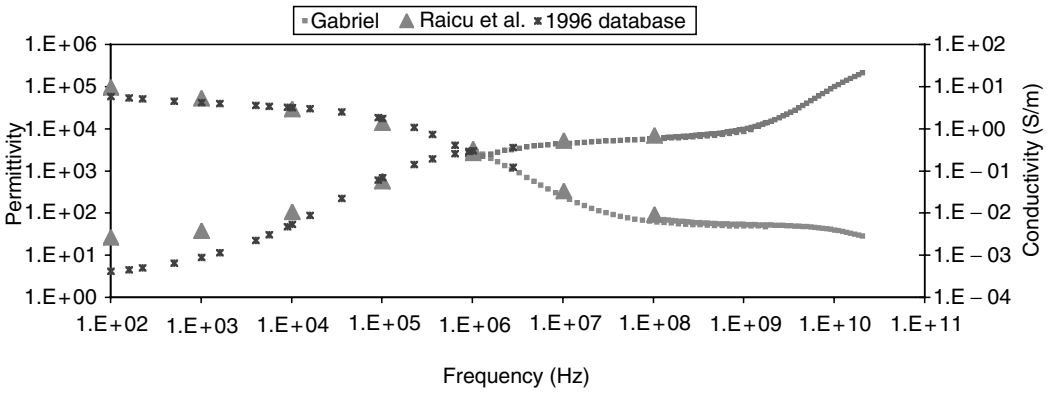

FIGURE 3.22
Permittivity and conductivity of skin (Raicu et al.: back of neck, moistened with physiological saline; Gabriel and database: ventral forearm, moistened with water). Open-ended coaxial probes of vastly different sizes were used.

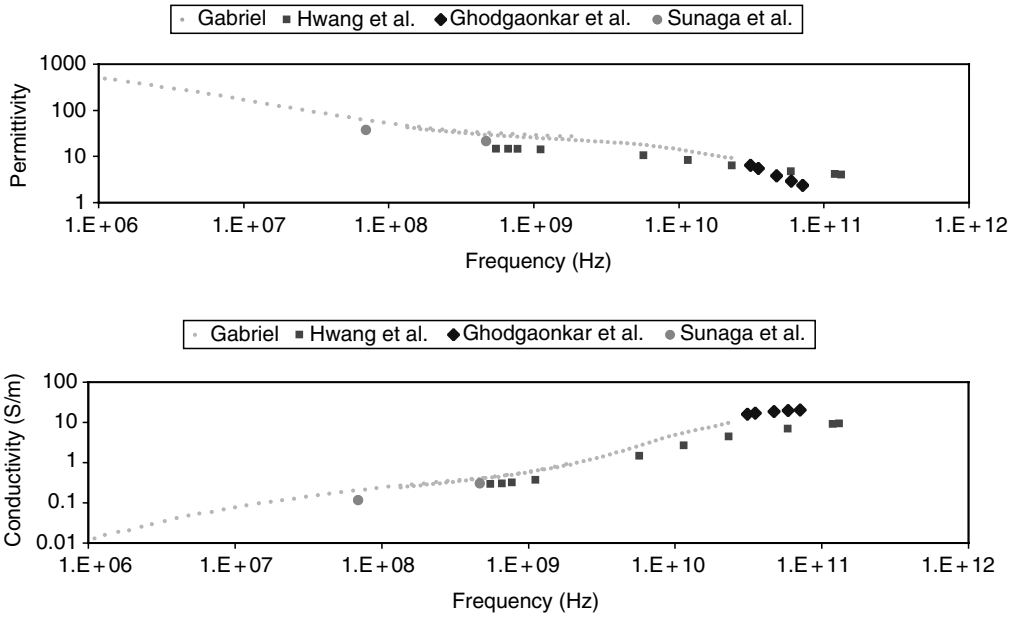

FIGURE 3.23
Permittivity and conductivity of palm, from recent studies.

Gabriel et al. (1997), who reported the dielectric spectra of normal and wounded tissue and ascribed the differences to water content.

Petaja et al. (2003) attempted to correlate the dielectric properties of skin at 300 MHz to body fluid changes after cardiac surgery and report limited success. Sunaga et al. (2002) investigated the variability in the dielectric properties of human skin of healthy volunteers, collagen disease patients, and dialysis patients over the frequency range of 1 to 450 MHz. No significant difference was detected in the dielectric properties among the three groups; some regional (abdomen, thigh, and forearm) dependence was observed. Marzec et al. (1999) measured the conductance and susceptance of soles and calves in leg skin from healthy controls and patients with ischemia in the frequency range of 100 Hz to 100 kHz. Ischemia was found to have no effect on the admittance at frequencies lower than 10 kHz, where the effect of the stratum corneum is dominant. Observed differences at frequencies in excess of 10 kHz are ascribed to ischemia in the underlying skin tissue.

Lindholm-Sethson et al. (1998) investigated the potential of using noninvasive skin impedance spectroscopy for the early detection of diabetic changes. They implemented a multivariate data analysis procedure to demonstrate how a regression model between the skin impedance and other diagnostic data for diabetic and control groups can be developed into a novel diagnostic tool for the early discovery of possible complications in diabetic patients. Statistical procedures are increasingly being applied to correlate dielectric parameters to structural or compositional elements of biological material, particularly in cases where there is a physical mechanism underpinning the effect that is obscured by noisy data (Kent et al., 2002).

The use of dielectric spectroscopy to monitor damage to the skin caused by ionizing radiation is an active field of research aiming at monitoring the side effects of clinical radiotherapy objectively and quantitatively. It appears that the changes to the skin during

the acute stage cause both permittivity and conductivity to decrease (Tamura et al., 1994; Nuutinen et al., 1998), while the reverse happens when radiation-induced fibrosis finally sets in (Lahtinen et al., 1999). The initial decrease in permittivity, which also means a decrease in skin water, may be due to damage to skin capillaries resulting in swelling of the cytoplasm, with narrowing or occlusion of capillaries and a reduction in the effective microcirculation of the skin. In the long term, an increase in collagen and collagen-bound water is a likely explanation for the observed increase in the permittivity in line with a clinical indicator of subcutaneous fibrosis (Nuntineu, 1998).

3.7.2.5 Bone

Peyman et al. (2001) observed variation in the dielectric properties of rat skull bone as a function of developmental stage from neonate to 70 days old. They reported lower permittivity and conductivity values across the spectrum (100 MHz to 20 GHz). Similar results were recently reported for porcine skull, cortical bone, and bone marrow (Peyman et al., 2005).

3.7.2.6 Dielectric Properties of Cancerous Tissue

The pathological differences between normal and cancerous cells affect their composition and morphology and shape their dielectric spectrum. Interest in this field of study is driven by biomedical applications where such differences can be exploited for the treatment or diagnosis of cancer. Most of the clinical applications are based on hyperthermia, whereby electromagnetic energy is preferentially applied to the cancerous tissue, usually as an adjunct to radiotherapy. Electromagnetic hyperthermia was an active field of study in the 1980s, and it remains the domain of specialist medical centers. In contrast, there is a growing interest in applications geared toward the detection of cancerous regions using three-dimensional microwave tomography procedures and signal analysis (Hagness et al., 1998, 1999; Bulyshev et al., 2001; Wersebe et al., 2002). In cases where the suspect region is accessible for dielectric measurements, the procedure relies on the characterization and comparative analysis of the dielectric spectrum (Walker et al., 2000). The ultimate goal is to detect changes at the precancerous stage prior to their visibility by x-rays and to the emergence of serious clinical symptoms.

There is evidence that tumors have higher water content than the corresponding normal tissue; for certain types of tumor, such as breast carcinoma surrounded by fatty tissue, the difference could be considerable. In terms of dielectric properties, one would expect cancerous tissue to have higher permittivity and conductivity at microwave frequencies compared to normal tissue, as observed and reported by Schepps and Foster (1980), Foster and Schepps (1981), Rogers et al. (1983), and more recently, Stauffer et al. (2003).

Morphological changes affect the dielectric properties in the frequency range of the β dispersion and can be quite significant (Smith et al., 1986). Walker et al. (2000) used a finite element analysis to model the differences in impedivity between normal and precancerous cervical cells in the frequency range of 100 Hz to 10 MHz. Their results showed significant differences at frequencies lower than 10 kHz, basically in line with measurements carried out *in situ* with a four-electrode pencil probe. Polevaya et al. (1999) used time domain dielectric spectroscopy to study the differences between normal and malignant white blood cells. They used a Maxwell–Wagner mixture formulation and a double-shell cell model to determine differences in cellular and nuclear membrane characteristics between normal and malignant cells. Their detailed analysis reflects on some functional differences between membranes and provides some insight into the etiology of cancer.

The use of the electrical characteristics of tissue to understand, image, or treat cancerous tissue relies on the availability of good representative data across the spectrum but particularly in the frequency range of the β dispersion, where the changes are specific to the cellular transformation as well as the water content.

3.7.2.7 Conductivity of Tissue at Low-Frequency

There are limited, reliable dielectric data for body tissue at frequencies below 100 kHz. Some of the reasons relate to the dependence of the dielectric properties on the physiological state, degree of perfusion, time after death, and other biological parameters. There are also experimental difficulties, in particular electrode polarization, which is a major source of systematic error at frequencies below 100 Hz, even when precautions are taken to minimize its effects. Based on typical tissue dielectric data and a simple model for the electrode polarization, it is possible to estimate that it affects the permittivity more than the conductivity and that for body tissue, the conductive rather than the capacitive component dominates its electrical admittance (Schwan, 1992). For this reason, at extremely low-frequencies, the conductivity of tissue is considered real rather than complex, and the body is modeled as a resistive network the parameters of which are determined by the conductivity of the various tissues.

The conductivity of body tissue can be estimated by modeling on a cellular scale and applying appropriate mixture equations. Using this approach, Peters et al. (2001) evaluated the effective conductivity of several tissues such as cerebral cortex, liver, and blood. Such studies help to place upper and lower bounds on the conductivity values based on cellular parameters and knowledge of the conductivity of the phases.

Faes et al. (1999) carried out a meta-analysis of review studies (Geddes and Baker, 1967; Stuchly and Stuchly, 1980; Duck, 1990; Gabriel et al., 1996a,b) of tissue conductivity in the frequency range 100 Hz to 10 MHz. To make relative comparisons between different tissues, they calculated the mean and 95% confidence interval. They found large confidence intervals such that the conductivities of most high water content tissues (skeletal and cardiac muscle, kidney, liver, lung, and spleen) were not statistically different from one another at that level of significance. In contrast, blood has higher conductivity, while bone and fat have demonstrably lower conductivities. The insignificance of differences in high water content tissues could, of course, imply an equality of their conductivities, but it could also point at a large source of experimental variation that obscures real differences.

The conductivity of the body, or body parts, can be obtained by volume averaging using anatomical models and individual tissue conductivity as in Table 3.4, where the conductivity of the whole and the various parts of the body is given based on tissue conductivity in Gabriel (2000) and a voxel anatomical human model (Dimbylow, 1996).

At 50 Hz, the calculated conductivity values are comparable to the commonly used estimate of 0.2 S/m for the effective permittivity of a homogenous body model. When dielectric data become available, it would become imperative to reexamine the whole

TABLE 3.4

Conductivity (in S/m) of the Whole and Parts of the Body Obtained by Volume Averaging

Frequency	Whole Body	Head	Torso	Arm	Leg	Neck
50 Hz	0.22	0.25	0.22	0.19	0.20	—
10 kHz	0.28	0.28	0.26	—	0.24	0.22
100 kHz	0.29	0.30	0.33	—	0.24	0.24

Source: From Gabriel (2000).

question of whether or not there is sufficient justification for neglecting the contribution of the capacitive element of the body's electrical properties.

3.7.2.8 Nonlinear Dielectric Properties

The polarization mechanisms discussed so far occur from interactions with weak fields eliciting linear responses. At high field strength, nonlinear molecular and cellular polarization phenomena are predicted on theoretical grounds, on the basis of induced dipolar properties and classical electrodynamics. The threshold for initiating such effects is system and frequency dependent. As a general rule, as the frequency increases, so does the field level required to cause an effect. In general, at frequencies below the manifestation of the β dispersion, field strengths of the order of 10^6 V/m may be capable of initiating polarization mechanisms that affect the cellular function; higher fields may cause dielectric breakdown within the membrane, ultimately leading to cell destruction.

Under controlled conditions, high field strength, nonlinear effects are the focus of numerous applications in biotechnology. For example, dielectrophoresis, or the motion of particles caused by electrical polarization effects in nonuniform fields, is used to separate and manipulate cells. For a review of this subject, see Pethig (1996). Another nonlinear phenomenon, electroporation, is a consequence of the electrical breakdown of biological membranes, resulting in the formation of pores and a significant increase in the membrane permeability to external ions and molecules. Under controlled conditions, electroporation could be reversible and used to advantage in therapeutic, drug delivery applications. The basic principles can be found in mechanistic studies by Plickett and Weaver (1996), Prausnitz et al. (1999), and many others.

The hypothesis that weak fields may trigger nonlinear effects in cells has been investigated in theory and practice (Weaver and Astumian, 1990; Woodward and Kell, 1990). The generation of harmonics is one aspect that can be used to monitor their occurrence (Woodward and Kell, 1990); it also means that the dielectric properties are nonlinear, responding to harmonics as well as to the fundamental frequency. The study of harmonics is a subtle and clever tool; it has yet to prove its effectiveness in monitoring physiological responses to weak fields.

More recently, Balzano (2002) proposed to use a similar approach to test whether biological cells exhibit nonlinear responses to weak fields, at microwave frequencies. His idea hinges on the possibility of detecting a microwave signal at 1.8 GHz (second harmonic of 900 MHz) as weak as one microwave photon per cell per second. An experimental project based on this hypothesis is currently under way (see MTHR Web site: http://www.mthr.org.uk/research_projects/HO_funded_projects_excell.htm, accessed August 5, 2005). It will help to clarify the issue of nonlinear dielectric properties.

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4

Magnetic Properties of Biological Material

Jon Dobson

CONTENTS

4.1 Introduction

Magnetism arises from the movement of electrical charges, such as the oscillation of electrons in a conducting wire, the flow of ions in an organism or the orbital, and spin motions of electrons in an atom. Since all materials contain moving subatomic particles (electrons and protons), all materials are, in some sense, ''magnetic.'' In order to understand more about the role of magnetic materials in organisms, it is first necessary to examine what is meant by the various types of magnetic behavior of materials.

The magnetic properties of materials are dominated by the electron spin motion. In quantum mechanical terms, electrons may assume two possible spin states: spin $+1/2$ or spin $-1/2$. These may also be referred to as ''spin up'' and ''spin down.'' The Pauli exclusion principle states that no two electrons may occupy the same energy state in an atom. This means that no two electrons may have the same set of values for the quantum numbers as they would then be indistinguishable. As electrons are added, they fill up each possible state in a given shell before filling the shell associated with the next higher energy state. The filling of the shells is governed by Schrödinger's wave equation and the quantum numbers.

Electrons are added to subshells in parallel spin configurations first according to Hund's rule. If all electrons are paired, there is no ''spin'' magnetic moment. These materials are still magnetic though, because of the electron's orbital motion. In most materials of biological origin, however, electron spin motion is cancelled, allowing electron orbital motion to dominate.

The spin structure of the transition series elements (iron in particular) is most important for the magnetic properties of biological materials. This is due to the presence of uncompensated spins in the 3d orbital, which gives rise to a spin magnetic moment. The spin moment is much stronger than the orbital moment and is aligned parallel to an applied field.

All materials, including biological materials, fall into one of the three categories of magnetic materials based on the spin and orbital motion of electrons: (1) diamagnetic, (2) paramagnetic, and (3) ferromagnetic.

4.2 Diamagnetic Materials

Diamagnets are materials in which all electron spins are paired (i.e., there are no uncompensated spins). Therefore, the magnetic properties of diamagnets are determined by the electron orbital motion.

According to Faraday's law, in the presence of an applied magnetic field there is an electric field induced that is acting on the orbiting electron. The induced electric field produces a torque on the electron, which gives the electron extra angular momentum. This extra angular momentum produces a magnetic moment, the sign of which is negative (i.e., antiparallel to the induced or applied magnetic field). Therefore, diamagnetic materials are repelled in magnetic fields (they have weak, negative magnetic susceptibility).

4.3 Paramagnetic Materials

Paramagnetic materials are those in which individual atoms, ions, or molecules have some number of uncompensated spins and thus a permanent net spin magnetic moment. As we have stated before, the spin moment is much larger than the orbital moment, so we would therefore expect that the behavior of paramagnetic materials when placed in a magnetic field will be governed by the behavior of the spin magnetic moments. This is indeed the case.

When paramagnetic substances are placed in an external magnetic field, the uncompensated spin moments tend to align, to some degree, parallel to the applied field direction (Figure 4.1). The magnetic energies involved in this alignment are relatively

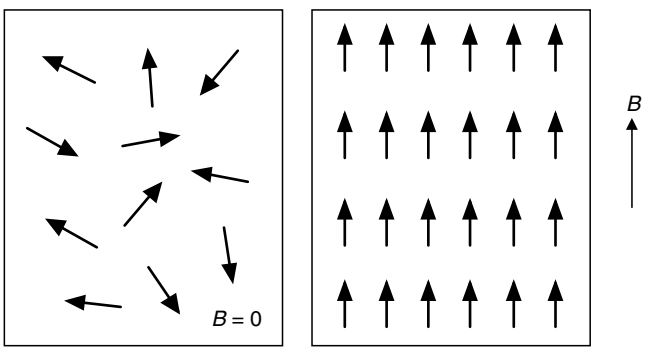

FIGURE 4.1
Orientation of spins in a paramagnet in the absence of a magnetic field ($B = 0$; left) and in the presence of a strong magnetic field (right)

small, and the energy associated with thermal agitation tends to work against the alignment, having a randomizing effect. The degree of alignment of the uncompensated spins with the applied magnetic field depends, therefore, on the strength of the field (the stronger the field, the greater the degree of alignment up to very high fields) and the temperature (the hotter the material, the lower the degree of alignment in the same applied field).

Since the spin moments in paramagnetic materials align with the applied field in this classical model, they add to it, so that the net effect is that these materials are attracted to a magnetic field (and they have a positive magnetic susceptibility). The linear temperature dependence of the magnetic susceptibility in paramagnetic materials was worked out by Pierre Curie and is known as Curie's law:

$$M/H = \chi = C/T$$

where M is the magnetization, H is the applied magnetic field, χ is the magnetic susceptibility, T is the temperature, and C is the Curie constant and is related to the magnetic properties of the material.

In paramagnetic materials, the individual dipole spin moments of the ions may be thought of as noninteracting (in other words, the magnetic moment of one atom has no effect on its neighboring atoms in the material). Because of the noninteraction of the magnetic moments, this fairly weak effect (paramagnetism) is lost upon removal of the external field. Therefore, when a paramagnetic material is not in an external magnetic field, the net magnetic moment in the material is zero because of the randomizing effects of thermal agitation.

4.4 Ferromagnetic Materials

As in paramagnets, in ferromagnetic materials, there are also uncompensated spins; however, these spins are coupled, giving rise to strong magnetic effects. Ferromagnetism may be thought of as a ''group phenomenon,'' where groups of spin moments act in concert, whereas paramagnetism may be thought of as an ''individual phenomenon,'' where the moment of one atom has little or no effect on the moment of neighboring atoms.

In ferromagnetic materials, as in paramagnets, the magnetic susceptibility is positive, and these materials acquire a positive magnetization when placed in an applied field because of alignment of the spin moments in the material with the field. Unlike paramagnets, however, the net magnetization is not lost upon removal of the field (as long as the material is below a certain temperature, which will be discussed in a moment), and the induced moment in the material may be very strong (Figure 4.2). This is to say that ferromagnetic materials exhibit ''hysteresis.''

The mechanism responsible for coupling of the spin magnetic moments in neighboring atoms in a material is due to quantum mechanical phenomena and is governed by the Pauli exclusion principle. The uncompensated spins in individual atoms of a ferromagnetic material may couple either directly (direct exchange) or through an intermediate anion—usually oxygen (superexchange). In ferromagnetic materials, this gives rise to a net magnetic moment because of the coupling of spins in a preferred orientation. Keep in mind that this coupling is quantum mechanical in nature and not purely due to magnetic forces acting between uncompensated spins in neighboring atoms.

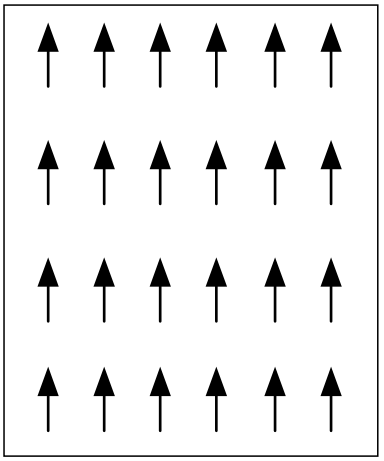

FIGURE 4.2
In ferromagnets, all spins are coupled and aligned, even in the absence of an applied field. This is the origin of remanent magnetization (i.e., hysteresis) in materials.

There are also special cases of ferromagnetism in which neighboring spins are coupled, but not necessarily in the same direction. We will examine two of these cases, antiferromagnetism and ferrimagnetism, as they are important to biological materials, though there are others.

4.4.1 Antiferromagnetism

For some ferromagnetic materials, the exchange coupling between neighboring lattice elements is such that the spins are aligned opposite to each other. This is called antiferromagnetism, and the exchange coupling arises from super exchange according to the Pauli exclusion principle and Hund's rule (Figure 4.3).

In this case the spin moments will still align themselves to an external applied field, only some will be parallel to the applied field and those exchange coupled to them will be antiparallel. This would normally give rise to a material with no net magnetic moment if for every spin up, it was coupled to a spin down. This is not, however, always the case. In some materials, there is a canted antiferromagnetic spin structure (Figure 4.3) or lattice defects and frustrated surface spins (in very fine particles), which can give rise to a net moment in the absence of an applied field.

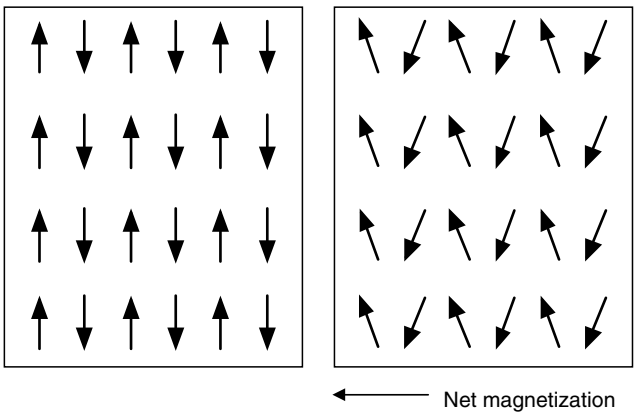

FIGURE 4.3
Pure antiferromagnetic behavior in which spins are coupled antiparallel to each other (left) and an antiferromagnet with a canted spin structure that gives rise to a net magnetization even in the absence of an applied field (right).

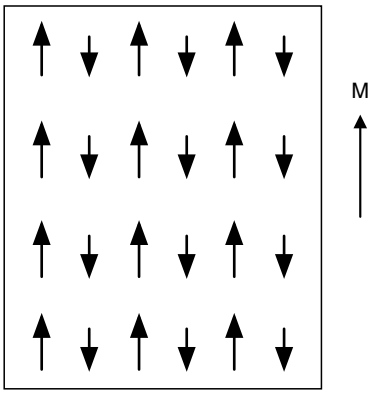

FIGURE 4.4
Electron spin configuration for a ferrimagnet. M = magnetization.

4.4.2 Ferrimagnetism

In addition to antiferromagnetic materials, it is also possible for the neighboring lattice subunits to have unequal numbers of uncompensated electrons coupled antiparallel to each other. This is the case for magnetite (Fe_3O_4), which contains both Fe^{2+} and Fe^{3+} in its lattice structure. The unequal distribution of the two neighboring iron ions gives rise to a net moment (again, even in the absence of an applied field) since one sublattice will have a magnetic moment of greater magnitude than the other, as shown in Figure 4.4. This type of material is called ferrimagnetic.

4.4.3 Temperature Dependence of Ferromagnetism

Since ferromagnetism results from the interaction of atomic moments in materials, there is an exchange energy associated with coupling of the spin moments. At room temperature, this exchange energy is much greater than the energy due to randomizing thermal effects (kT). If thermal energy exceeds the spin coupling (exchange) energy, the coupling breaks down, and the material behaves as a paramagnet. This temperature is dependent on the material and is called the Curie temperature (or, in the case of antiferromagnetic materials, the Néel temperature) (Figure 4.5).

Finally, materials that are superparamagnetic are generally very small (on the order of nanometers), and the electron spins may be coupled either parallel (ferromagnet) or

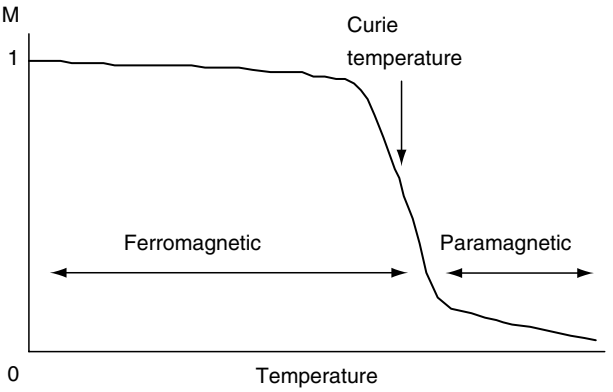

FIGURE 4.5
Magnetization as a function of temperature for a ferromagnet. Above the Curie temperature, spin coupling breaks down, and the material behaves as a paramagnet.

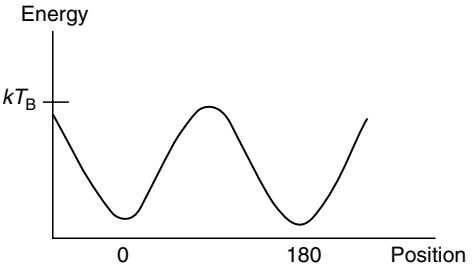

FIGURE 4.6
Schematic of the energy barriers in a superparamagnet. If thermal energy is above a given temperature—the blocking temperature (T_B)—the spins will be able to very rapidly flip between 0° and 180° along the easy axis of magnetization. If the particle becomes larger or the temperature is lowered, the height of the energy barrier constrains the orientation of the electron spins to one or the other of the easy axis energy wells.

antiparallel (ferri- or antiferromagnet). In the case of these materials, however, thermal considerations are dominant. Superparamagnetic materials are named as such because thermal energy causes them to behave—even though this is a special class of ferromagnetism—like a paramagnet. The difference is that, because of coupling of the spin moments, thermal energy causes the spins to flip rapidly as a group rather than individually, as is the case for paramagnetism. On a macroscopic level, the behavior of the two is very similar, except at low temperatures when the thermal energy is sufficiently reduced.

If the superparamagnetic particles are placed in an applied field, the energy of the field will cause the spins to align themselves parallel to it, just as with a normal ferromagnet or paramagnet (the degree of alignment depending on the strength of the field and the temperature—as with paramagnets). If the field is taken away, thermal fluctuation causes a ''relaxation'' of the spins, and they begin to flip rapidly between parallel and antiparallel orientations along the easy axis of magnetization (determined by magnetocrystalline or shape anisotropy). This has the effect of causing the material to appear paramagnetic when the magnetization is examined on timescales longer than the flipping frequency (generally $\sim 10^{-9}$ s). The remanent magnetization (which is the magnetization left in the material after removal of the field) decays with time according to the equation:

$$\tau = f_0 \exp\left(\frac{\nu M_s H_c}{2kT}\right)$$

where τ = relaxation time, f_0 = lattice vibration frequency, ν = grain volume, M_s = spontaneous magnetization, H_c = coercivity, k = Boltzmann's constant, and T = temperature.

The relaxation time depends on the height of the energy barrier—which is a function of grain volume and the magnetic properties of the material—and the amount of thermal energy (kT) required to overcome it (Figure 4.6). Using this equation, it is possible to calculate grain volumes above which the magnetization becomes stable or ''blocked'' (i.e., decays over very long periods of time at a given temperature).

4.5 Biological Magnets

For most biological materials, the magnetic permeability is close to that of free space (i.e., diamagnetic), which implies that there is no direct interaction with the magnetic component of electromagnetic fields at low field strengths. However, this is not the case for all biological materials.

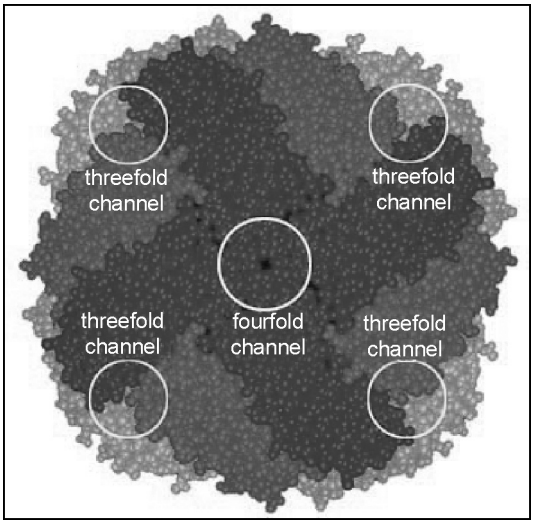

FIGURE 4.7 (See color insert following page 380.) Model of the ferritin protein showing the peptide subunits and iron transport channels. (From www.chemistry.wustl.edu/~edudev/LabTutorials/Ferritin/FerritinTutorial.html. With permission.)

Most magnetic (paramagnetic and ferromagnetic) materials in organisms are compounds of iron—and in particular, iron oxides. Virtually all organisms require iron to function normally. This is mainly due to its redox activity, which allows it to play an important role in energetic biochemical reactions. In organisms, iron is stored as the mineral ferrihydrite ($5Fe_2O_3 \cdot 9H_2O$) within the iron storage protein ferritin. It consists of a 12-nm hollow spherical protein shell made up of 24 subunits (Figure 4.7). The core of ferritin protein is 8 nm in diameter, and it can hold up to 4500 iron atoms in the form of ferrihydrite. Iron is transported into and out of the core through three- and fourfold channels in the shell. During transport, highly toxic Fe(II) is oxidized to Fe(III) for storage as ferrihydrite (Harrison and Arosio, 1996). The specific iron biochemistry of ferritin is complex and is not completely understood (e.g., Yang et al., 1998; Zhao et al., 2001).

Ferrihydrite is a superparamagnetic antiferromagnet at body temperature, and as such, its magnetic properties are potentially important for understanding the environmental consequences of electromagnetic field exposure, including exposure to strong fields within magnetic resonance imaging (MRI) scanners. In fact, the development of pulse sequences for MRI of ferritin is leading to novel ways of assessing iron concentrations in the liver and examining iron associated with neurodegenerative disorders such as Alzheimer's and Parkinson's diseases (Clarke and St. Pierre, 2000; Bartzokis et al., 2004; St. Pierre et al., 2004, 2005). These techniques rely on the magnetic fields generated by ferritin to produce contrast in ferrihydrite-rich tissue in much the same way as synthetic superparamagnetic iron oxide contrast agents do (for a review, see Pankhurst et al., 2003).

In addition to ferrihydrite in ferritin, in 1992 Joseph Kirschvink's group at the California Institute of Technology discovered that biogenic magnetite is produced in the human brain (Kirschvink et al., 1992). Later work demonstrated that this magnetic iron biomineral is present in several organs in the human body, including the heart, liver, and spleen (Schultheiss-Grassi et al., 1997).

Magnetite (Fe_3O_4)—a ferromagnetic iron oxide—is also known as lodestone and is a mineral more commonly associated with sedimentary rocks and volcanics. However, it is also found in many organisms. Probably, the most well-known example is the magnetotactic bacterium. These bacteria use chains of single-domain, biogenic magnetite arranged in chains in order to sense the geomagnetic field and use it for navigation—much like a

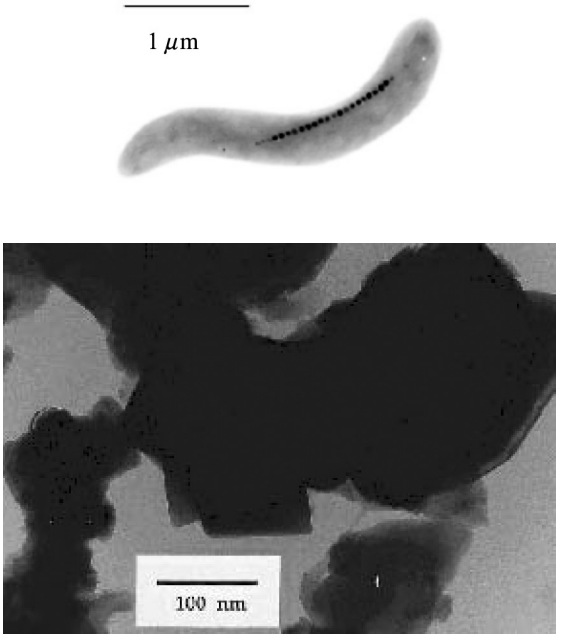

FIGURE 4.8
Transmission electron micrograph of the magnetotactic bacterium MS-1 (top). (From www.calpoly.edu/~rfrankel/mtbphoto.html) Biogenic magnetite extracted from the human hippocampus (bottom). (From Schultheiss-Grassi, PP, R Wessiken, and J Dobson (1999) *Biochim. Biophys. Acta* 1426: 212–216. With permission.)

compass needle (Blakemore, 1975) (Figure 4.8). Although the mechanism by which these organisms produce perfect magnetite crystals is not well understood, it has recently been shown that the process appears to be mediated by specific proteins (Arakaki et al., 2003). Since Blakemore's early discovery, magnetite has been found in a wide variety of animals from bacteria to humans, and in some cases, as with magnetotactic bacteria, it appears to be used for navigation (e.g., Walker and Bitterman, 1989; Walker et al., 1997; Wiltschko and Wiltschko, 2002; for a review, see Kirschvink and Hagadorn, 2000).

Although by 1992, magnetite was known to occur in many organisms, the discovery of biogenic magnetite in the human brain proved controversial. Further work in this area confirmed and extended Krischvink's results, examining not only the occurrence of magnetite in the brain but also its potential role in neurophysiological processes (Dunn et al., 1995; Dobson and Grassi, 1996; Schultheiss-Grassi and Dobson, 1999; Dobson 2001, 2002, 2004; Hautot et al., 2003; Collingwood et al., 2005) (Figure 4.8).

One area of research where the presence of biogenic magnetite in the brain may provide answers to some controversial questions is in the examination of potential mechanisms for the interaction of environmental electromagnetic fields with humans. Two theoretical models have been proposed to demonstrate how biogenic magnetite could act as a transducer of both low-frequency magnetic fields and radio frequency (RF) fields emitted from mobile phones and base stations (Kirschvink, 1992, 1996; Dobson and St. Pierre, 1996). These models rely on the fact that magnetite will couple strongly to the magnetic fields from electrical devices and, either through ferromagnetic resonance effects or through mechanical effects on membrane ion channels, can disrupt the normal functioning of cells in the brain.

Early tests of these models indicate that low-frequency, pulsed magnetic fields from mobile phones may have an influence on cellular activity (including cell death), whereas effects due to ferromagnetic resonance in RF fields are less clear (Cranfield et al., 2003a,b). In addition, magnetite contamination and the presence of biogenic magnetite in model organisms have also been highlighted as potential confounders that could influence the results of studies on the effects of environmental magnetic fields on organisms (Kobayashi and Kirschvink, 1995; Cranfield et al., 2004).

Although magnetite and ferrihydrite are two of the most ubiquitous magnetic materials in organisms, they are not the only ones. Greigite (Fe_7S_8) is a ferrimagnetic iron sulfide found in some iron-reducing bacteria (Posfai et al., 1998). It has a strong magnetic moment similar to magnetite and is thought to be produced as a by-product of iron reduction. Hematite (Fe_2O_3) and wüstite-like (FeO) iron phases also have recently been found within human ferritin (Quintana et al., 2004). And hemosiderin (FeOOH) is a goethite-like iron oxyhydroxide that is antiferromagnetic and is found primarily in pathogenic liver tissue (St. Pierre et al., 1998). In addition to these ferromagnetic materials, other ions and iron compounds, such as hemoglobin, are paramagnetic.

4.6 Magnetic Iron Compounds Related to Pathogenesis

Though iron is an important component of normally functioning organisms, in some cases, it can also be toxic. Because of its redox potential, Fe(II) generally has the potential to do more damage than oxidized Fe(III). For this reason, iron is primarily stored as Fe(III) within ferritin in organisms.

Disruption of the body's normal mechanisms for iron storage can lead to iron overload diseases such as hemochromatosis and β-thalassemia and the deposition of significant amounts of magnetic iron compounds (St. Pierre et al., 1998; Chua-anusorn et al., 2000). These diseases result in the formation of significant iron deposits, predominantly in the liver, which consist mainly of the iron biomineral hemosiderin (FeOOH). Hemosiderin is antiferromagnetic, but can occur as large particles in the body. As with ferrihydrite, both these antiferromagnets contain only Fe(III) and as such have a relatively weak magnetic moment primarily due to lattice defects and, for very fine particles, to frustrated spins on the particle's surface. As mentioned earlier, the presence of these magnetic iron compounds is being exploited for the development of noninvasive MRI monitoring of liver iron in order to track the effectiveness of chelating compounds that are used to treat these diseases (Clarke and St. Pierre, 2000; St. Pierre et al., 2004, 2005). In the brain, disruption of normal iron metabolism results from either disease or trauma and can often lead to pathogenesis (Beard et al., 1993). The accumulation of excess iron is known to induce epileptic activity, primarily as a result of intracranial bleeding due to head trauma. The model of iron-induced epilepsy was first introduced by Willmore et al. (1978), and the electrophysiological responses have been characterized in many studies since then (e.g., Ueda and Willmore, 2000; Engstrom et al., 2001). More recently, evidence shows that iron overload diseases may even predispose a person to epilepsy (Ikeda, 2001).

Although the initial seizure response to trauma and excess iron is relatively swift (Ueda et al., 1998), the long-term consequences of intracranial bleeding on the formation of various magnetic iron compounds in the brain are unclear. Little is known about the formation of iron compounds in the brain of epileptic patients, other than that there appears to be a relationship with an increase in iron (e.g., Willmore et al., 1978; Ueda and

Willmore, 2000; Engstrom et al., 2001). This increase may lead to increased iron loading in the ferritin core or the sequestration of free iron in another form, which could have significant consequences for disease progression. A preliminary correlation between magnetite particle packing geometry and epileptogenic tissue has been demonstrated; however, there is as yet no indication of an increase in magnetite biomineralization associated with temporal lobe epilepsy (Schultheiss-Grassi and Dobson, 1999).

The association of abnormal accumulations of iron with neurodegenerative disorders such as Alzheimer's, Parkinson's, and Huntington's diseases has been known for over 50 y (Goodman, 1953). Although this relationship has been studied extensively, it is not yet clear which iron compounds are present and what their role in these diseases is; however, evidence is mounting that there are likely synergistic mechanisms related to iron and amyloid-β (Aβ, the principal component of Alzheimer's plaques) and other disease-related proteins (e.g., Sayre et al., 2000; Rottkamp et al., 2001; Atamna and Frey, 2004]. Recent work seems to confirm that iron plays a role in disease progression as iron chelators appear to have neuroprotective effects in rat models of Parkinson's disease (Ben Shachar et al., 2004).

Various forms of iron may play a significant role in the biochemical processes that lead to the progression of neurodegenerative diseases. Although there is much speculation on that role, the primary mechanism is thought to be the result of oxidative stress—the generation of free radicals via the Fenton reaction (Connor and Menzies, 1995; Markesbery, 1997; Koppenol, 2001). Recently, Floor (2000) demonstrated the connection between high levels of iron in the basal ganglia and oxidative stress in Parkinson's patients. A disruption of iron metabolism and increased iron in the same region of the brain also has been implicated in Alzheimer's and Huntington's diseases (Bartzokis and Tishler, 2000). Furthermore, iron accumulation has been associated with microgliosis and correlated with increased damage to the CA1 region of the hippocampus via iron–zinc interactions in models of neurodegenerative diseases (Shoham and Youdim, 2000).

It should be noted, however, that some results have shown that the presence of oxidized nucleosides in neurons does not appear to be related to senile plaque material or neurofibrillary tangles in Alzheimer's (Nunomura et al., 1999). In some cases, free radical damage has even been reported to be reduced by Aβ deposition because of the inhibitory role of Aβ-related Zn^{2+} in H_2O_2-mediated toxicity (Cuajungco et al., 2000; Nunomura et al., 2000). More recently, it has been noted that in transgenic mouse models of Alzheimer's, neurogenesis was related to increased deposition of Aβ (Jankowsky et al., 2003). It has been postulated that this may be due to a possible neuroprotective role of Aβ in binding excess redox active iron, which is deposited because of the increased need for iron during neurogenesis (Dobson and Batich, 2004).

Recently, state-of-the-art superconducting quantum interference device (SQUID) magnetometry, nuclear forward scattering, and synchrotron x-ray fluorescence imaging have been employed to evaluate which specific iron compounds are present in these diseases and to map them to structures in the tissue (Hautot et al., 2003; Collingwood et al., 2005; Mikhailova et al., 2005). Early results of these studies indicate that several magnetic iron compounds are associated with these diseases—ferrihydrite (from ferritin), biogenic magnetite, α-iron, and hemosiderin. These results represent a major step toward our understanding of the origin and role of magnetic iron compounds in these diseases.

The role of the various magnetic materials in many organisms, particularly in humans, is only just beginning to be unraveled. After more than two decades of research on magnetic biominerals, it is clear that in many cases they play an important role in biological processes and may provide us with insights into mechanisms of interaction of environmental electromagnetic fields and organisms.

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5

Interaction of Direct Current and Extremely Low-Frequency Electric Fields with Biological Materials and Systems

Frank S. Barnes

CONTENTS

5.1 Introduction

The fact that electrical currents can affect the behavior of biological systems has been known for more than 2000 years. Electric shocks have been used to treat a wide variety of ailments since the eighteenth century. However, our knowledge of how these fields and the resulting currents influence biological systems is surprisingly incomplete. Electrical signals are clearly important in the control of biological processes and in carrying information from one part of the body to another. Nerve cells propagate electrical signals from sensors of pressure, temperature, light, sound, etc., to the brain and return control signals to muscles and other tissue. Yet, if we choose to stimulate these processes with external electrical inputs, we have a relatively limited understanding of how a given electrical signal will affect various biological organs; what the safe limits of exposure are (particularly overextended periods of time); and how electrical signals are carried across cell membranes, are propagated along nerves, or affect growth processes and cell division.

The purpose of this review is to bring together some of the physical concepts that underlie the interaction between electric fields and biological materials with the objective of providing background for determining safe levels of exposure and new applications for the use of electricity in therapy. This is the first step in a long chain of events that lead from externally applied electric field forces to significant biological changes. An objective of this chapter is to provide a background for some of the other chapters that cover both possible health effects and some therapeutic applications of electric and magnetic fields.

The approach that will be taken is to start with Maxwell's equations and couple them to the bulk electric and magnetic properties of the materials. These equations allow us to calculate the values of the electric and magnetic fields as a function of time and space given the values for the dielectric constant and the conductivity. The techniques for the solution of these equations for a wide variety of biological systems are covered in Chapter 10 in this volume by J. Lin and P. Bemardi and for imaging see Chapter 12 in this volume by W.T. Joines, O.H. Liu and G. Ybarra. From the solutions of these equations for the electric and magnetic fields, the conservation of energy, and charge, expressions can be obtained for the current density and other parameters of interest.

Next, the force equations are used to develop equations for the conductivity and the dielectric constant. This section is organized to begin at the lowest level of complexity by examining some of the forces that are exerted on charged particles in fluids, and it then proceeds to some of the effects of electric fields on chemical reaction rates and membranes. At the next level of complexity, some effects of externally applied electric fields on currents through membranes and membrane nonlinearities are described. Some effects of high-level fields and electroporation are described in Chapter 9 in *BMA* by Weaver and Chizmadzhev [112]. This is followed by a discussion of some long-term adaptive processes and secondary effects of current flow due to heating and by a description of a few effects on whole animals. This information is presented with the objective of specifying the general level or intensity of fields, currents, and temperatures where one can expect to observe a given class of biological responses. Much more data are presented in Chapter 3 in *BMA* by Anderson et al. [113]. The next section contains data on the levels of typical naturally occurring and man-made fields. This section also includes a comparison of some externally applied fields, fundamental noise levels, and signals generated in the body. J. Weaver and M. Bier present a more complete treatment of some of the noise sources in biological cells in Chapter 7 in this volume.

5.2 Maxwell's Equations and the Properties of Materials

Maxwell's equations can be written in both differential and integral form, and solutions to them under a variety of boundary conditions are extensively covered in Chapter 10 in this volume by James C. Lin and Paolo Bernardi. In differential form they are given by [1]

$$\vec{\nabla} \times \vec{H} = \vec{J} + \frac{\partial \vec{d}}{\partial t} \tag{5.1}$$

$$\vec{\nabla} \times \vec{E} = -\frac{\partial \vec{B}}{\partial t} \tag{5.2}$$

$$\vec{d} = \varepsilon_0 \vec{E} + \vec{p} \tag{5.3}$$

$$\vec{B} = \mu_0 \vec{H} + \vec{M}_B \tag{5.4}$$

where $\vec{H}$ is the magnetic field, $\vec{J}$ is the current density, $\vec{d}$ is the displacement vector, t is time, $\vec{E}$ is the electric field, $\vec{\nabla}$ is the partial differential operator, del, $\vec{B}$ is the magnetic flux density, ε_0 is the dielectric constant for free space, $\vec{p}$ is the electrical polarization per unit volume, μ_0 is the magnetic permeability in vacuum, and $\vec{M}_B$ is the magnetic polarization per unit volume. It is often convenient to expand the electrical polarization in a power series:

$$\vec{p} = \vec{p}_0 + \varepsilon_0 X_e \vec{E} + \varepsilon_0 X_2 \vec{E}^2 + \cdots \tag{5.5}$$

where $\vec{p}_0$ is the permanent polarization, X_e is the linear electric susceptibility, and X_2 is the quadratic coefficient. X_2 is significant for nonlinear optics and very large values of the electric field. For most of the exposure conditions described in this volume it is convenient to express the induced polarization in terms of the dielectric constant ε

$$\varepsilon = \varepsilon_0 (1 + X_e) \tag{5.6}$$

Note that in anisotropic materials, both ε and X_e may be tensors and complex numbers. The imaginary part of ε is associated with the loss or dissipation of energy by the bound charges. The solutions to Maxwell's equations for $\vec{E}$ and $\vec{B}$ are given for a variety of boundary conditions and under the assumption that values for $\vec{J}$, $\vec{p}$, and $\vec{M}_B$ are known (given in Chapter 10 in this volume by James C. Lin and Paolo Bernardi). These fields, in turn, determine the forces on the components of the biological material.

5.3 Physics of the Interactions of Electric Fields with Biological Materials

Biological systems consist of complex physical subsystems. In an attempt to understand them, we will start at the most elementary level. Perhaps the simplest level—which is already surprisingly complicated—is the effect of electric fields on biological fluids. These fluids contain a large number of components, including ions, polar molecules such as water, proteins, lipids, hormones, and colloidal particles. Current flow in these fluids is given by the sum of the drift and diffusion currents for each component. At low current densities the system is linear; however, at moderate to high current densities nonlinearities are observed [2]. In addition, the fields can change the orientation of molecules with dipole moments, induce dipoles by distorting electron orbits, and change the relative positions of some of the atoms within the molecule. This, in turn, leads to changes in the dielectric constant. The next level of complexity involves the interaction of the fields with membranes that behave like porous solids for fields applied perpendicularly to their surface and like viscous liquids for fields in the plane of the membrane [3,4]. Membranes are inhomogenous so that different portions of them may be affected differently by the perturbing fields. Additionally, membranes are involved in active chemical reactions that change their porosity to various ions selectively. Both electrical potentials and chemical signals may change the membranes' conductivity by orders of magnitude and transmit signals across membranes. The next level of complexity occurs in the interactions between

the biological fluids and the membranes in the presence of electric fields. Electric fields affect the selective transport of ions or molecules through the membrane. They change the buildup of charged ion layers at the surface and change the way new molecules are incorporated into the membrane or are bound to its surface. The result of changes in the transport of molecules or ions across cell membranes is changes in the performance of the cells and, in turn, of the organs of which they are a part. They can also lead to changes in the rate of exchange of electrons between molecules in the membrane and ions or molecules in the fluid [5]. For example, a biasing electric voltage across a pacemaker cell in the heart will change its firing rate and thus the pumping rate of the heart.

The fundamental law describing the forces on charged particles is given by

$$\vec{F} = q(\vec{E} + \vec{v} \times \vec{B}) \tag{5.7}$$

where $\vec{F}$ is the force, q is the charge on the particle, and $\vec{v}$ is the velocity of the particle. $\vec{E}$ and $\vec{B}$ are coupled by Maxwell's equations so that a time-varying magnetic field generates an $\vec{E}$ field and vice versa. This force may lead to ion currents and changes in the orientation of dipoles in molecules, and it may also lead to transitions between energy levels, to shifts in their spacing and induced dipole moments, $\vec{P}$. Additionally, if nonlinearities or time-varying impedances are present, alternating current (AC) fields can be rectified to produce direct current (DC), frequencies at the second and higher harmonics, and sum and difference frequencies with biological or molecular oscillations. Direct magnetic field effects may occur through the term $\vec{v} \times \vec{B}$. For example, for a Na^+ moving at a thermal velocity of 4×10^2 m/sec in the earth's magnetic field of about 5×10^{-5} T, this term has a magnitude of 2×10^{-2} V/m, and the force is at right angles to the field and the velocity.

In addition to the forces on charged particles, electric fields can induce forces on polarizable atoms, molecules, ions, and molecules with dipole moments. To first order these forces are described by

$$\vec{F}_{\mathrm{d}} = (\vec{P}_0 \cdot \vec{\nabla})\vec{E} \tag{5.8}$$

$$\vec{F}_{\mathrm{L}} = \boldsymbol{\alpha} V(\vec{E} \cdot \vec{\nabla})\vec{E} \tag{5.9}$$

where $\vec{F}_{\mathrm{d}}$ is the force on a molecule with a permanent dipole moment $\vec{P}_0$, and $\vec{\nabla}\vec{E}$ is the gradient of the electric field. $\vec{F}_{\mathrm{L}}$ is the force on a molecule with an induced dipole moment $\vec{P}_{\mathrm{i}} = \boldsymbol{\alpha} V\vec{E}$, where α is the tensor polarizability and V is the volume [6]. Note that biological materials are highly inhomogenous and that there are large electric field gradients at the boundaries between the fluids and membranes. Additionally, for induced dipole moments, when the sign of the dipole reverses with an alternating field the force along the gradient of the field can be in a constant direction.

The current flow $\vec{J}_{\mathrm{i}}$ of a given molecule or ion, in molecules or ions per second per meter square, has both drift and diffusion components that may be given by

$$\vec{J}_{\mathrm{i}} = N_{\mathrm{i}}\mu\vec{F} + qD\vec{\nabla}N_{\mathrm{i}} \tag{5.10}$$

where N_{i} is the ion concentration, μ is the mobility in seconds per kilogram, D is the diffusion constant in meter square per second, and $\vec{\nabla}N_{\mathrm{i}}$ is the gradient of the concentration. For charged particles, the force has two components [7]:

$$\vec{F} = q\vec{E} + (\vec{M} \cdot \vec{\nabla}\vec{E}) \tag{5.11}$$

where $\vec{M}$ is the sum of the permanent and induced dipole moments.

The drift portion of the ion currents takes the form

$$\vec{J} = \sum q_i N_i \mu_i \vec{E} + \sum N_i \mu_i (\vec{M} \cdot \vec{\nabla}) \vec{E} \tag{5.12}$$

The conductivity $\sigma = \sum q_i N_i \mu_i$, and N_i is the concentration of each ion, μ_i is the mobility, and $\vec{M}_i$ is the dipole moment. Table 5.1 shows some typical values of mobility.

The conductivity of biological fluids such as blood, which contains cells, is in the vicinity of $\sigma = 0.6\,\mathrm{S/m}$, while for physiological saline it is approximately $1.4\,\mathrm{S/m}$. For more detailed material on the conductivities and dielectric constants of biological materials, see Chapter 3 in this volume by C. Gabriel. If the fluid channels between cells are relatively thick and the fluids are relatively good conductors, the channels tend to short circuit the voltages that might otherwise appear across membranes that typically have conductivities at least a thousand times smaller.

The total dielectric constant for a material includes the sum of the induced polarizabilities of the components and interaction terms between them. It is sometimes useful to think of the dielectric constant as a way of describing the fraction of the electric field that is shorted out by the bound charges. This can be shown by considering an ideal parallel plate capacitor where the outside plates are separated by a distance l. The capacity for these plates is given by

$$C_0 = \frac{\varepsilon_0 A}{l} \tag{5.13}$$

If an ideal thin metal plate of thickness w is inserted halfway between these plates, then the resulting capacity is given by

$$C = \frac{C_0}{(1 - w/l)} = \frac{\varepsilon A}{l} \tag{5.14}$$

The corresponding dielectric constant is given by

$$\varepsilon = \frac{\varepsilon_0}{(1 - w/l)} \tag{5.15}$$

In this example it is apparent that as the fraction of the field that is shorted out by the metal plate of thickness w increases, so does the effective dielectric constant. The electrons or ions forming an induced dipole moment can be thought of as doing the same thing. If there is a significant time lag for the movement of the charge, the effective value of w is reduced. The very large values of the dielectric constants of some tissues at low-frequencies can be thought of as the resulting motion of ions that are trapped inside highly

TABLE 5.1

Typical Values of Biological Ionic Mobilities

Particles	Mobilities	Ions	Mobilities
Proteins	$\mu = 10^{-10}$ to $10^{-8}\ \mathrm{m^2/V\,sec}$	Ca^{2+}	$\mu = 6.2 \times 10^{-8}\ \mathrm{m^2/V\,sec}$
Na^+	$\mu = 5.2 \times 10^{-8}\ \mathrm{m^2/V\,sec}$	Mg^+	$\mu = 5.4 \times 10^{-8}\ \mathrm{m^2/V\,sec}$
K^+	$\mu = 7.6 \times 10^{-8}\ \mathrm{m^2/V\,sec}$	Cr^+	$\mu = 1.9 \times 10^{-8}\ \mathrm{m^2/V\,sec}$

resistive membranes. At higher frequencies, the ions can no longer move fast enough to fully charge the surfaces of the membranes, and the effective dielectric constant for the tissue decreases. If energy is absorbed in inducing the dipole moments, then the dielectric constant becomes a complex number.

The forces applied by an electric field superimpose a drift velocity on the much larger random thermal velocity in the opposite directions for positively and negatively charged particles. These forces can lead to a redistribution of ions or molecules as a result of the differential mobilities and to an increase in the concentration of ions at interfaces. The average drift velocity $\vec{v}$ for a charged particle is given by

$$\vec{v} = \mu_i \vec{E} \tag{5.16}$$

The separation of molecules as a result of the different velocities in a DC electric field is known as electrophoresis and is frequently used to identify large molecules or charged colloidal particles [8]. The separation of particles in an AC field gradient is known as dielectrophoresis [5].

For a spherical particle in a homogenous insulating fluid the mobility μ_i is given by

$$\mu_i = q/6\pi\eta a \tag{5.17}$$

provided that the particle is significantly larger than the background particles of the fluid, where η is the viscosity of the fluid and a is the radius of the particle. In a conducting medium, counterions, or ions with a charge opposite to that of the particle, and molecules with dipole moments are attracted to it. They change the effective radius of the particle and then partially shield its charge. Additionally, small counterions may flow in the direction opposite to the particle motion, exerting a viscous drag. The theory for motion of a rigid sphere through a conducting liquid is complicated if all these effects are taken into account. Often some of the parameters, including the charge on the sphere, are not measurable. However, a relatively simple expression for the electrophoretic mobility is often used:

$$\mu_i = \frac{\varepsilon_i \zeta}{4\pi\eta} \tag{5.18}$$

where ε_i and η are the dielectric permittivity and the viscosity of the fluid (in kg/m sec), respectively, and ζ is the electrical potential drop from the particle surface across the bound fluid to the interface where the liquid begins to flow under the shear stress. Stated another way the ''zeta potential,'' ζ, is the potential at the surface boundary between the stationary fluid and the liquid that is moving with the particle. It should be noted that ζ is less than the total potential ψ across the charge double layer surrounding the charged particle. Also, note that water molecules bind to the ions, increase the effective diameter, and reduce the effective charge. This, in turn, makes the mobility less than that which might be expected at first from the atomic size and Stokes' law.

In a uniform AC field a charged particle oscillates about its mean position, and the electrical energy added to the solution is largely converted to heat. If there is a gradient in the field, as is to be expected in biological materials that are highly inhomogenous, then the gradient of the field can lead to a net charge displacement if the fields are large enough to lead to nonlinearities in the mobility or induced dipole moments. For large $\vec{E}$ the velocity saturates and mobility varies as

$$\mu_i = \frac{\mu_0'}{\left|\vec{E}\right|} \tag{5.19}$$

and Equation 5.16 yields

$$|\vec{v}| = \mu_0'$$

Most biological systems are highly inhomogenous, and the induced currents will vary rapidly in space. For the case of an induced dipole moment and an ideal dielectric sphere with a permittivity ε_2 and a conductivity $\sigma_2 = 0$ in an ideal dielectric fluid with a dielectric permittivity ε_1 and a conductivity $\sigma_1 = 0$ and a nonuniform electric field prior to inserting the sphere, the force

$$\vec{F}_{\mathbf{L}} = \boldsymbol{\alpha} V(\vec{E} \cdot \vec{\nabla})\vec{E} = 4\pi a^2 \varepsilon_1 \left\{ \frac{\varepsilon_2 - \varepsilon_1}{\varepsilon_2 + 2\varepsilon_1} \right\} \{(\vec{E}_1 \cdot \vec{\nabla})\vec{E}_1\} \tag{5.20}$$

where $\vec{E}_1$ is the field in the fluid prior to insertion of the sphere. Written another way

$$\vec{F}_{\mathrm{L}} = (3/2)V\varepsilon_1 \left\{ \frac{\varepsilon_2 - \varepsilon_1}{\varepsilon_2 + 2\varepsilon_1} \right\} \vec{\nabla} \left| \vec{E}_1 \right|^2 \tag{5.21}$$

If we assume that the viscous drag on a spherical particle is given by Stokes' law, then

$$\vec{F}_{\mathrm{d}} = 6\pi a \eta \vec{v} \tag{5.22}$$

and the mobility μ_{i} is given by

$$\mu_{\mathrm{i}} = (2a^2/3\eta)\varepsilon_1 \left\{ \frac{\varepsilon_2 - \varepsilon_1}{\varepsilon_2 + 2\varepsilon_1} \right\} \vec{\nabla}\vec{E}_1 \tag{5.23}$$

Dielectrophoresis may also be used for identifying molecules, and a more general treatment of the forces needs to take into account the conductivity or a complex dielectric constant for both the fluid and the particle [9].

For particles with dipole moments to change their distribution under the influence of an electric field gradient the force $\vec{F}$ must be large enough to overcome other forces. One of these forces that frequently must be overcome is due to osmotic pressure or diffusion. The osmotic pressure can be thought of as the force per unit area arising from diffusion or the random motion of the particles and is given by

$$\Pi = N_{\mathrm{i}} kT \tag{5.24}$$

where k is Boltzmann's constant and T is the absolute temperature [10]. The average differential force on a particle is proportional to the gradient of the osmotic pressure and is given by

$$\vec{F}_{\mathrm{os}} = -\frac{1}{N_{\mathrm{i}}} \vec{\nabla}\Pi = \frac{kT\vec{\nabla}N_{\mathrm{i}}}{N_{\mathrm{i}} - k\vec{\nabla}T} \tag{5.25}$$

If we consider the case of a spherical volume with a radial concentration gradient at constant temperature, the force is given by

$$\vec{F}_{\mathrm{os}} = -kT \frac{\Delta N_{\mathrm{i}}}{N_{\mathrm{i}}} \cdot \frac{r_0}{\Delta r} \tag{5.26}$$

where r_0 is the unit vector, ΔN_i is the incremental change in concentration, and Δr is the incremental change in distance. The maximum change is given by

$$\frac{\Delta N_i}{N_i} = 1 \tag{5.27}$$

when the presence or absence of a particle occurs at a distance $\Delta r = 2a$, where a is the particle radius. In this case, we get the maximum force

$$\left|\vec{F}_{os(max)}\right| = -\frac{kT}{2a} \tag{5.28}$$

To get an idea of the size of these forces, consider a particle of fat with $a = 1\,\mu m$ in water. The maximum osmotic pressure at $T = 300\,K$ is $|\vec{F}_{os(max)}| = 2 \times 10^{-13}\,N$. The dielectric constant for water is approximately $\varepsilon_1 = 80\varepsilon_0$ and for a fat particle, $\varepsilon_2 = 2\varepsilon_0$, where $\varepsilon_0 = 8.854 \times 10^{-12}\,F/m$. To get a dielectric force greater than the maximum osmotic force, we need a value of $\vec{\nabla} \mid \vec{E}_1 \mid^2 > 10^{12}\,V^2/m^3$. This is given approximately by a voltage of 100 V across a 5 mm gap when the $\vec{E}$ field goes from zero to a peak value of $5 \times 10^4\,V/m$ over the same gap. For a particle with a single charge in a uniform field, we would need a field of $E = 1.3 \times 10^4\,V/m$ to get an equal force.

The electric current densities generated by a concentration gradient are given by

$$\vec{J}_d = -qD\vec{\nabla}N_i \tag{5.29}$$

where D is the diffusion constant and is given by

$$D = \upsilon kT \tag{5.30}$$

where $\boldsymbol{\upsilon}$ is the hydrodynamic mobility with the dimensions of velocity/force and D has the dimensions of meter square per second. For rigid spherical particles of radius a, where $a \gg a_{H_2O}$, the Einstein–Stokes equation gives

$$D = \frac{kT}{6\pi\eta a} \tag{5.31}$$

This is only a first-order approximation because D varies slightly with concentration, departure of the molecule from a spherical shape, and other factors. η is the viscosity (in kg/m sec).

It is sometimes of interest to estimate the ratio of the drift to the diffusion current in order to estimate the level of the applied fields or the applied field gradients that lead to biological changes. This ratio is approximately given by [6]

$$\frac{\vec{J}_{i,diffusion}}{\vec{J}_{i,drift}} = \left(\frac{kT}{F_i}\right)\cdot\left(\frac{\Delta N_i}{N_i}\right) \tag{5.32}$$

where $\vec{F}_i$ is the force on the particle due to both the charge on the particle and the gradient of the field on the dipole moment. If we now assume that the maximum change in N_i goes from N_i in the solution to 0 at the membrane surface over a distance of the diameter of the

molecule of N_i and that this is the same distance over which the field goes from the field in the fluid to the field in the membrane, then

$$\frac{\vec{J}_{i,\text{diffusion}}}{\vec{J}_{i,\text{drift}}} = \frac{kT}{W_i} \tag{5.33}$$

where W_i is the energy acquired by the particle moving through the field and its gradient. At room temperature the thermal energy $kT \cong 0.026\,\text{eV}$. A voltage drop from an externally applied source across the membrane liquid boundary on the order of $2 \times 10^{-3}\,\text{V}$ would be required in order to make the drift current significant with respect to the total diffusion current under these assumptions. One way in which smaller drift currents and smaller voltages could be significant is if the ions with low velocities perpendicular to the membrane are the most important in binding to the membrane. Slow molecules stay close to the membrane for longer times, and these molecules are most affected by the applied forces [6].

For different boundary conditions the results will be quite different. If, for example, the boundary was nearly perfectly reflective, then the concentration gradient would be nearly 0, and so would the net diffusion current. Additionally, the gradient in the concentration may occur over a larger distance than the gradient of the electric field. At steady state the concentration at the membrane can be expected to increase until the diffusion current and the drift current balance each other so that the net current is equal to the rate at which the molecules are bound to the membrane or pass through it.

There are four forces that may become important when considering the interaction between two particles in a fluid. These are the osmotic diffusion force, the electrostatic force, the van der Waals force, and the hydration force [9]. These forces may all become important in considering the interaction between particles or bilipid membranes in an aqueous fluid. Electrostatic or coulomb forces between particles of like charge are repulsive. Because the charged particles attract free ions of the opposite sign—which produces a double layer—they are effectively shielded or are screened by the charged ions of the opposite sign when immersed in a conducting fluid. This force decays exponentially or

$$\vec{F}_c = \vec{F}_0 \exp - \frac{r}{\lambda_d} \tag{5.34}$$

where λ_d is known as the Debye screening length [11]

$$\lambda_d = \left[\frac{2q^2 n}{\varepsilon kT}\right]^{1/2} \tag{5.35}$$

where n is the density of the ion species doing the shielding, q is the charge and ε is the dielectric constant of the solution, k is Boltzmann's constant, and T is the absolute temperature. For physiological saline solution of approximately 0.14 M, the Debye length is approximately 0.83 nm [12]. Thus, the electrostatic forces are important only at very short ranges.

For like particles, the forces are repulsive at short distances (0.1 to 0.2 nm) and attractive at longer ranges. These forces may be thought of as being generated by transient electromagnetic fields because of fluctuations that occur as a result of thermal agitation or natural uncertainties in the position and momentum of the electrons and atomic nuclei.

If one thinks of the local transient fluctuations in terms of the underlying contributions from oscillations at all possible frequencies, it can be shown that the strength of the contributions due to the local fluctuations at a given frequency is proportional to the absorption of light at that frequency by the material. For an individual atom these forces fall off very rapidly as $1/r^7$ [7]. However, when they are integrated over the surface of a membrane, which is thick compared to an atomic layer, they are correlated over many atoms, as the wavelengths are large compared to an atomic diameter.

A calculation of these fields has been performed starting with quantum field theory [13]. The size of the forces and the rate at which they decay depend on the distance between the membranes and the difference of the bulk polarizability of the membrane and the aqueous gap in a complex way. All frequencies of the charge fluctuations contribute to the attraction, and each gives rise to a different relationship between energy and the distance of separation. For many simple cases and for a classical explanation of these forces and potential distributions, see Ref. [14].

One case of interest is for two membranes with a distance d_w across the aqueous gap between them. The thickness of the membranes is assumed to be large compared to the spacing. The force between these two membranes is approximately given by

$$\vec{F}_w = \frac{H}{6d_w^3} \tag{5.36}$$

where H is the Hamaker coefficient [9]. In a typical situation, the distances over which the van der Waals force is estimated to be important extend out to separations of 10 to 20 nm, which is substantially longer than a Debye length or the rate of falloff for the electrostatic or coulomb forces. The hydration forces are repulsive forces that rise extremely rapidly as the membrane bilayers approach a separation distance of approximately an atomic spacing. Experimentally, these forces can be expressed in the form [9]

$$\vec{F}_H = \vec{F}_{H_0} \exp -d_w/\Lambda \tag{5.37}$$

where Λ is a scaling constant. In the case of egg phosphomonoesterase bilayers, $\vec{F}_{H_0} \approx 7 \times 10^{-13}$ N/m^2 and $\Lambda = 0.256$ nm. This force may be important up to about 2 nm and is assumed to come about as a consequence of the work required to remove water from the hydrophilic surface of the membrane.

Long-range attractive forces have been observed between hydrophobic surfaces [15]. These forces are proportional to the contact area and may be the orders of magnitude larger than the van der Waals forces. They may also have decay lengths up to 25 nm. The magnitude and range of these forces depends on the temperature and the length of the surfactant's chain, and they appear only when the chains are in a fixed ordered state. These forces appear to be generated when the fields emanating from one surface induce a larger polarization in the other surface layer than in the intervening medium. Some relatively complex expressions for these attractive forces have been worked out [14].

These forces are important in self-organizing processes such as protein folding, ligand binding to hydrophobic receptor sites, and transformation of membrane structures. All these forces act over relatively short ranges in typical biological fluids. The ion densities are so large that charge neutrality is maintained everywhere except very close to charged surfaces.

The effect of an electric field, or an electric field gradient in a fluid, is to superimpose a small drift velocity on a relatively large random thermal velocity. For example, if

we apply an electric field of 10^3 V/m to a Na^+ ion, we would expect a drift velocity of about 5×10^{-5} m/sec as compared to a thermal velocity of about 4×10^2 m/sec. For a protein, we would expect a drift velocity approximately one tenth of the speed of the Na^+ ion, although at higher fields. This means that if we are to transport proteins or other small charged particles over appreciable distances of a few millimeters, we can expect it to take minutes or longer. In the case of bacteria, we have measured drift velocities of 10^{-6} m/sec at 100 Hz in fields of about 10^4 V/m and gradients of 5×10^6 V/m^2 or about 0.2% of the velocity of the Na ions in the same field [5,16].

This drift velocity may also change chemical reaction rates if the rate is limited by the availability of one of the charged components. Consider the case of a chemical reaction that takes place in a homogenous fluid if the chemical reaction has the form

$$(A) + (B) \underset{k_2}{\overset{k_1}{\leftrightarrows}} (C) \tag{5.38}$$

where (A) and (B) are the concentrations of the two input chemical reactants and k_1 is the reaction rate for A + B to C and k_2 is the rate for the back reaction of C to A and B. If we simplify the system and let k_2 be small, then the initial reaction rate may take the form [17,18]

$$k_1 = k(A)^n(B)^m \tag{5.39}$$

where n and m refer to the order of the reaction. In order to find the values of n and m, one can make the concentration of one of the reactants small so that it takes the form

$$k_1 = k(A_0)^n(B)^m \tag{5.40}$$

where we have made the concentration (A_0) large enough so that it is approximately constant, and the changes in the reaction rate can be measured by varying (B). The value of k is given by

$$k = zpe^{-\Psi/RT} \tag{5.41}$$

where z is the collision frequency and p is the steric factor, which is <1 and reflects the fact that not all collisions occur with the right orientation of the molecules to react. ψ is the activation energy, R is the gas constant, and T is the absolute temperature. For many cases the collision frequency is proportional to the current density, and thus there are terms that are proportional to both the drift and the diffusion currents. For example, consider the case of an enzyme reaction on a charged substrate such as a biological membrane. The total current density for a given ion in the fluid incident on the membrane is given by Equation 5.10.

If the chemical reaction rate is limited by the number of ions arriving at the membrane surface with enough energy to overcome the barrier required to initiate the reaction, then a DC drift current may either add to or subtract from the diffusion current. If the field direction is such that it prevents the ion from reaching the surface, then the chemical reaction is blocked. If the direction is reversed, the rate can grow exponentially. These changes in chemical reaction rates with the direction of the electric field are likely to be responsible for changes in the growth and reabsorption of neuritis [19]. They are also likely to be involved in the mobility of cells such as leukocytes and fibroblasts [20,21].

An AC drift current will add to the diffusion current. For the AC fields, the drift current can be thought of as increasing the volume covered by a particle executing a random walk as a result of Brownian motion. Thus, in an asymmetrical environment an electric field oscillating in the x direction may increase the number of particles that will strike the $y-z$ plane in a fixed period of time and can increase the chemical reaction rate for a catalytic reaction at the $y-z$ plane. Seto and Hsieh show that AC fields as low as 5 V/m can increase enzyme reaction rates by a factor of 5 [22]. For a 60 Hz field, the peak-to-peak displacement for Ca^{2+} resulting from this field is estimated to be about 1.6 nm or about twice the thickness of the Debye layer. AC magnetic fields have also been shown to change the growth rate of corn roots at fields levels of 5×10^{-3} T. It is likely that these fields are inducing significant currents [23].

An additional mechanism by which AC or DC electric or magnetic fields can effect chemical reactions is by shifting the energy level and the distribution of particles in them. DC electric fields can shift the energy level by an amount that is given by the change in the dipole moment, $\Delta\vec{M}$, and in the polarizability, $\Delta\alpha$, associated with the transition. A DC field can either stretch or compress a dipole depending on its orientation with respect to the field, thus increasing or decreasing the energy levels for atoms or molecules with different orientations. It also can modify its rate of rotation, speeding it up when the dipole is pointed in the direction of the field and slowing it down when it is pointed away from the field [24]. In a vacuum the modifications of the rotational states have been worked out from the quantum mechanics for relatively simple molecules and can lead to a relatively complex set of allowed energy states that are a function of the applied field [23]. In a solid or a membrane the energy levels between the states corresponding to the different orientations shift, by different amounts, for each state as a function of the applied field. This is known as the Stark effect [25]. The frequency corresponding to this energy shift with a fixed orientation is given by

$$h\Delta f = -\Delta\vec{M} \cdot \vec{E} - \frac{1}{2}\vec{E} \cdot \Delta\alpha \cdot \vec{E} \tag{5.42}$$

where Δf is the frequency splitting between levels, $\Delta\vec{M}$ is the change in the dipole moment, $\Delta\alpha$ is the change in polarizability, and h is Plank's constant. These terms give the linear and quadratic Stark effects for a transition in a uniaxially oriented system. These energy levels will be inhomogenously broadened by the random orientation of the dipoles with respect to the applied field and by the thermal energy. Since the quantum of energy, hf, at microwave and lower frequencies is very much smaller than a quantum of thermal energy, low-lying energy levels are approximately equally populated. However, higher-energy states may be preferentially excited by chemical reactions or optical photons so that different excited states may contain different populations. These states may be further defined by the magnetic field and separated by a Zeeman splitting. Thus, radio- and low-frequency fields corresponding to energy separation between these states may excite transitions between levels that are separated by the Stark splitting and change the population distribution in these excited states. The transition rate between an excited molecule and its final product depends on the overlap between the energy levels of the two states. Thus, the application of an electric field can shift the energy levels so as to either increase or decrease this overlap and the transition rate. This has been discussed at length in Ref. [23] for the case of Zeeman splitting of the energy levels by a DC magnetic field and free radicals [26]. See also Chapter 6 in this volume by S. Engstrom.

5.4 Biological Amplification

Biological systems are not in a state of thermal equilibrium. In a typical cell, energy is supplied by hydrolysis of an ATP molecule, which leads to the pumping of three sodium ions out of a cell and two potassium ions into the cell. The net result is creation of potential difference between the inside and outside of a cell in the range of 50 to 100 mV so that the interior of the cell is at a negative potential with respect to the external environment [27]. This potential difference can be used to amplify a variety of external signals just as a typical electronic amplifier can use a small AC signal to convert DC energy into a larger AC signal. For example, the input from many dentric junctions can be summed in a pyramidal cell to trigger an action potential that is larger than any of the input signals [28]. The input from a single synaptic junction might change the cell resting potential by 0.5 to 1 mV, and 10 to 20 inputs might be required to fire an action potential of 50 to 100 mV [27]. Additionally, subthreshold inputs can lead to the release of neural transmitters that, in turn, can release from 2 to 10,000 Ca^{2+} ions from internal stores. These neural transmitters may remain bound to the postsynaptic membrane for up to 4 sec and reduce the threshold for the firing of successive pulses [29]. Feedback from the postsynaptic membrane to the presynaptic membrane can further reduce the firing potential for the synaptic junction.

Another mechanism of amplification that may be of interest is the extraction of energy from a high-frequency signal. If a low-frequency electric field is added to a higher-frequency field and is incident on a nonlinear reactance, then the low-frequency signal may be amplified parametrically. This mechanism for amplification is valuable in the optical region for the generation of tunable signal sources and for low-noise microwave amplifiers [1,30]. In a biological system the low-frequency signal might be generated by an ongoing process such as the heart and amplified by mixing with an external signal from a power line field.

An additional mechanism for amplifications is stochastic resonance. Stochastic resonance differs from the foregoing mechanisms of amplification in that the energy is extracted from the noise. Consider, for example, a small, externally applied sinusoidal electric field incident on an ion in a potential well. If the energy acquired from the external signal is not large enough to exceed the potential barrier, the ion stays trapped in the potential well. However, if noise is added to the system, then when the sum of the applied electric field and the noise are large enough to provide enough energy to exceed the height of the potential barrier, the ion may escape the potential well. This happens most frequently at the peaks of the applied electric field so that the signal is amplified at the applied frequency. Gains on the order of 20 to 30 dB and increases in the signal-to-noise ratio of 18 dB have been observed for stochastic resonance amplifiers [31]. For an extensive review of this subject and some application neuronal systems, see Gammaitoni [32]. For a bistable system, such as a pacemaker cell that is driven by both noise and a periodic signal, it has been shown that the signal-to-noise ratio can be enhanced by the addition of noise to a weak periodic signal and that power can be extracted from the noise. A strong periodic signal can be generated at signal-to-noise ratios <1 [31,33]. This phenomenon occurs when two energy states are separated by a barrier, and the probability of a transition increases exponentially with increasing noise power. For periodic signals that are insufficient to cause a transition over the barrier but periodically increase the energy of the particle, the transition rate at the signal frequency first increases with increased noise power up to some maximum. When the noise power is increased above this level, the output signal becomes more random (see also Chapter 9 in this volume by Weaver and Bier).

5.5 Effects of Electric Fields on Cell Membranes

Electric fields play a very important role in the normal biological functioning of membranes. Membranes are complex structures containing lipids, voltage-activated ion channels, and proteins. It would be surprising if externally applied fields did not affect the membrane behavior. First, an electric field exerts a mechanical force on a membrane by means of the force exerted on charges in the Debye layer on either side of it and on charged proteins that may protrude from the lipid bilayer. Note that although as a first approximation the membrane is often modeled as a smooth planar or spherical surface, it is highly inhomogenous, and the charges are sparsely disturbed. Thus, the field on a protein may be widely different from the average field. See Figure 5.1a. and b for a partial indication of a membrane and cell complexity. The effects from fields in the plane of the membrane, where large molecules such as proteins are free to move as in a viscous fluid, are significantly different from the effects of fields in the transverse direction, where the membrane components are bound in a layer typically 5 to 15 nm thick.

The field distribution incident on a particular part of a cell membrane is a function of its geometry, frequency, and the cells around it. As can be seen from the models in Figure 5.1d, a wide variety of environments may exist. The currents that flow through and along the membranes are dependent on the geometry and frequency. A variety of equivalent circuits have been used to model both the impedance of the membrane and the extracellular fluids. The simplest of these are a resistor and capacitor in parallel. At very low-frequencies a collection of cells can be modeled with resistors as indicated in Figure 5.1c.

The interiors of cells are normally negatively biased in relation to the surrounding fluid by 50 to 150 mV, which leads to average transverse electric fields up to tens of millions of volts per meter [34]. The effective membrane resistance (R_m) per unit area takes on values of 0.14 to 15 Ω/m^2 in the transverse direction. This corresponds to resistivities in the range of $\rho_m = 10^7$ to 10^9 Ω m. The relative dielectric constant for the membrane is typically in the range of 2 to 4. Both the surrounding fluid and the interior of a cell have resistivities ρ_f of about 2 Ω m and a relative dielectric constant of 50 to 80. This means that the cell membrane tends to shield the interior of a cell very effectively from externally applied fields at frequencies below a few kilohertz and becomes almost a short circuit in the multimegahertz region of the spectrum. In most cells the interior of the cell contains complex structures that are functions of time as the cell grows and divides. See Figure 5.1b.

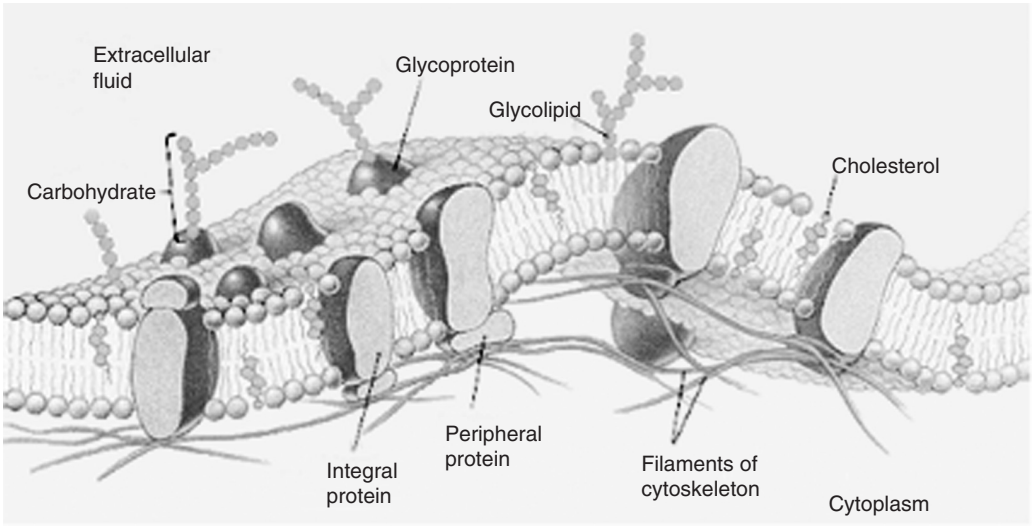
Consider the case of an oversimplified hypothetical rectangular cell as shown in Figure 5.1c. At low-frequencies, an external field $\vec{E}$ causes a current density $\vec{J}_f = \vec{E}/\rho_f$ to flow in the external medium, where ρ_f is the resistivity of the fluid. The corresponding voltage drop is $V = \vec{E}L = \vec{J}_f\rho_f L$, which we can consider to be applied to the cell. This voltage is distributed across the cell length as

$$V = [\rho_m 2t + \rho_f(L - 2t)]|J_m| \tag{5.43}$$

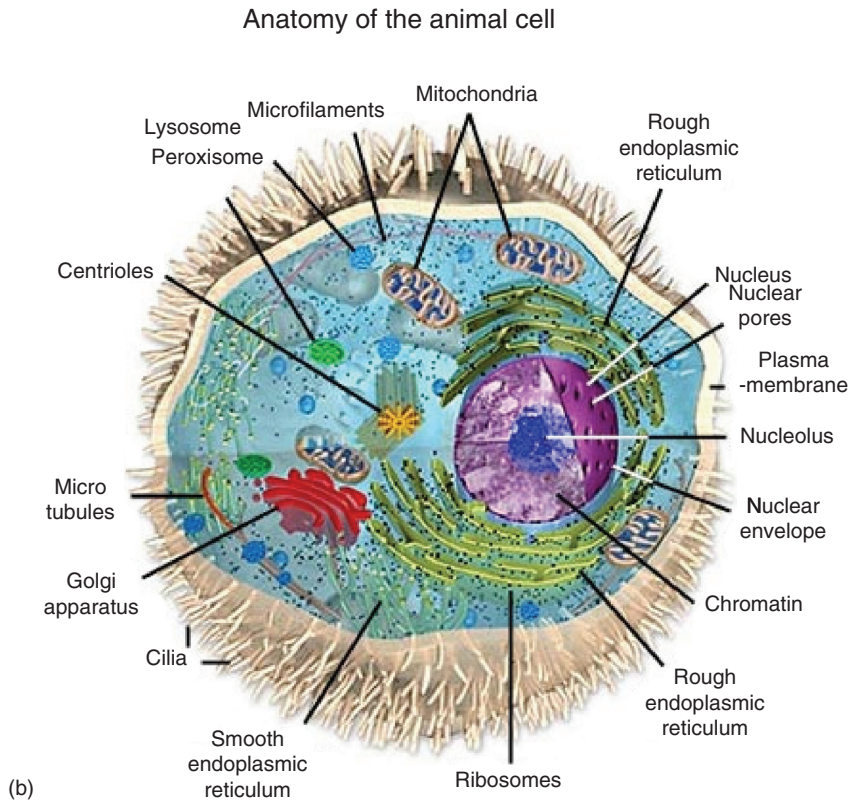
where $\vec{J}_m$ is the current density through the cell and ρ_m is the resistivity of the membranes. Typical cell membrane thicknesses are 6 to 10 nm, and typical dimensions are 10 to 150 μm. Setting $L = 100$ μm and

$$\rho_m 2t = 10\,\Omega m^2 \tag{5.44}$$

$$V = (10\,\Omega m^2 + 2 \times 10^{-6}\,\Omega m^2)|J_m| \tag{5.45}$$



(a)



(b)

FIGURE 5.1 (See color insert following page 380.)
(a) Model of a cell membrane. (From Chiras, D., *Human Biology*, © 5th edition, 2006, Jones and Baretlett Publishers, Boston. With permission.) (b) Anatomy of the animal cell. (From *Molecular Expression*, http://microscopy.fsu.edu, accessed Sep. 30, 2005; drawing © M.W. Davidson and Florida State University. With permission.)
(*continued*)

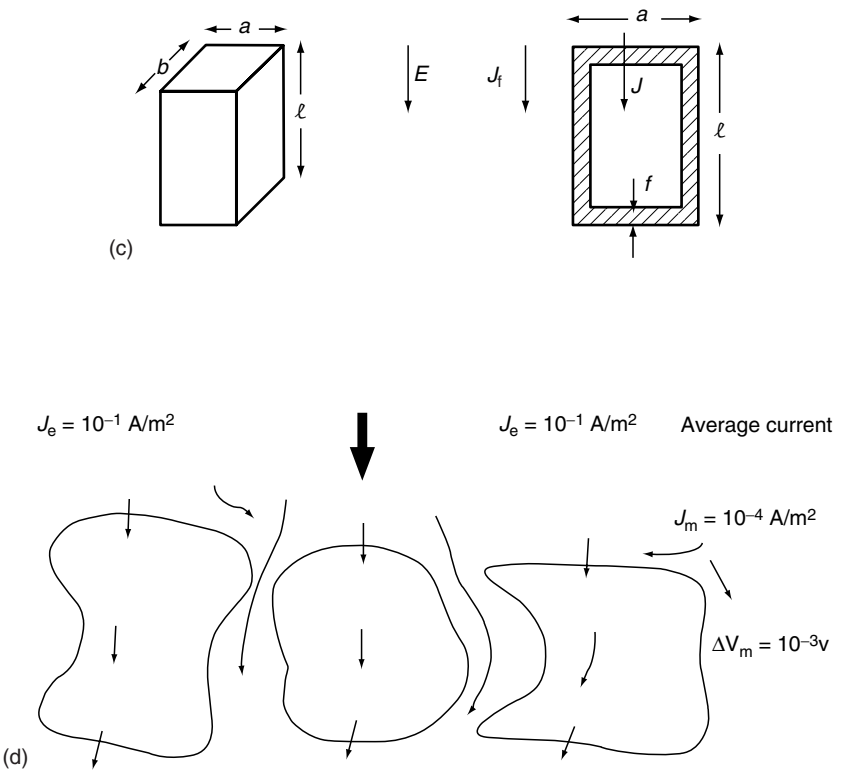


FIGURE 5.1 (continued) (See color insert following page 380.)
(c) Current distribution in a hypothetical rectangular cell. (d) Partition of 60-Hz currents through and around cells for an average current density $J = 10^2$ A/m^2. J_c is the current density between cells, and J_m is the current density through the membrane. (From Wachtel, H., private communication. With permission.)

This shows that essentially all of the transverse voltage drop occurs across the membrane at low-frequencies and the interior of the cell is almost completely shielded from external fields. A more complete theory for long cells that accounts for the internal resistance of the cell is given by Cooper et al. [35]. See also Chapter 11 by Pila [114]. Note that muscles, nerves, and a number of other cells may be much longer than 100 μm and may have dimensions in centimeters. Additionally, blood vessels form long, low-resistance paths that may concentrate currents due to externally applied fields. The anisotropic characteristics of cells are reflected in an anisotropy of the dielectric and conductive properties of tissue, which may give variations of as much as 10 to 1 in conductivity, depending on the direction of measurement relative to cell orientation [36]. A number of fish, including sharks, have been shown to use very long cells and to sum signals in both series and parallel to increase the voltage drop across a sensitive membrane in order to sense fields as low as 10^{-6} V/m [37–39]. The long cell may be thought of as an antenna that concentrates the field across a very thin, voltage-sensitive detector membrane. This membrane appears to have a built-in amplifier that allows detection of signals that are only a little above the natural electrical noise.

Membranes are not just simple linear resistors, but they usually are nonlinear and, in the case of nerve cells, are time varying as well. For a passive membrane in which the membrane potential is primarily determined by the concentration gradient of a single ion such as K^+, the Nernst equation predicts a diode-rectifying characteristic of the form [31]

$$I = I_0\left[\exp\left(\frac{V_m}{\eta V_T}\right) - 1\right] \tag{5.46}$$

where V_T is given by

$$V_T = \frac{kT}{q} = 0.026\,\text{V} \tag{5.47}$$

at $T = 300\,\text{K}$. q is the charge on the electron, V_m is the voltage across the membrane, I_o is the current for ideal back-biased current in amperes, and η is a dimensionless constant. Thus, for currents flowing through a membrane in one direction, the current is nearly constant, whereas for flow in the other direction the currect increases exponentially with voltage. In addition to passive currents, cells also use the energy from metabolic processes for the active transport of ions against the fields established by the concentration gradients. These processes are usually modeled as current sources and described as pumps [31]. A thermodynamic approach to pumping shows that ions can be pumped if they form a compound with a material that can flow through the membrane and that is created on one side of the membrane and destroyed on the other [40]. A large variety of models have been generated to characterize the effects of externally applied fields on the transport of ions through membranes [41–43]. However, the details of the pumping process are not well understood. In addition to ion transport, electrical fields can change the binding of ions or molecules to the membrane surface.

In the case of pacemaker cells, there are also feedback processes that lead to an oscillating membrane potential and a membrane resistance that is a function of time. The current flow for these cells is described empirically by the Hodgkin–Huxley equation [31]. An alternate approach that treats the nerve pulse like a plasma instability has been proposed by Triffet and Green and Vaccaro and Green [44,45]. Na^+ and K^+ currents are the dominant carriers for the propagation of nerve impulses along a cell. It is generally believed that the Na^+ and K^+ currents that flow through the membrane in opposite directions are carried through separate channels. Ca^{2+} ion currents are involved in the activation of at least a portion of the K^+ currents and are voltage gated. By activating the K^+ currents, the Ca^{2+} ions shorten the length of time the cell is depolarized and thus speed up the firing cycle [46]. A statistical approach to the formation of protein channels in the membrane by Baumann and Easton predicts many of the observed characteristics [47–49].

During the firing of a nerve cell, the Na^+ current pulse precedes the K^+ current pulse, which returns the cell to its resting potential [31]. The overall concentration balances are maintained by active ion pumps. Cl^- Mg^{2+}, and possibly OH^- and H^+ ions may also be involved in the current flow across a cell membrane.

The firing of a nerve cell typically involves voltage spikes of $10^{-1}\,\text{V}$ and peak current densities of $1.5\,\text{A/m}^2$. Changes in the firing rate can be induced by the injection of charge through a microelectrode of $<10^{-9}\,\text{A}$ for a few milliseconds. However, in cases where electrodes are used to stimulate muscles or to control epilepsy, the current is injected through a series of cell membrane fluid boundaries at a distance from the controlling nerve fiber. Thus, typical injected currents to produce behavioral changes in cells are in milliamperes, and current densities are $10\,\text{A/m}^2$ or higher.

For fields parallel to the plane of the membrane, it is possible to obtain electrophoresis or a rearrangement of charged particles. This has been shown by Poo in a striking fashion in cultured embryonic *Xenopus* myotomal muscle cells [50,51]. Receptors on the surface of the cell were labeled with a fluorescent dye and allowed to uniformly distribute themselves. Exposures to electric fields of 10^2 to $10^3\,\text{V/m}$ were sufficient to concentrate the

fluorescent-labeled receptors on the side of the anode in about 10 min. After shutting off the field, diffusion returned the dye to its uniform distribution in about 2 h. This corresponds to an in-plane diffusion constant of about $3 \times 10^{-12}\,m^2/sec$. The force on the receptor molecules or particles in the membrane includes not only $q\vec{E}$ but also any viscous drag that may be generated by the flow of ions of the opposite sign moving along the surface in the opposite direction. The direction of motion for a given charged particle seems to depend on whether it has a larger or smaller zeta (ζ) potential than the potential across the charged double layer at the interface between the cell surface and the fluid (see Equation 5.16).

Additional work has shown that the distribution of acetylcholine (ACh) receptors is changed by external fields [48,49]. These receptors are concentrated on the cathode-facing surface of the cell in fields of $10^3\,V/m$ over a period of 30 min by literally rearranging channels already existing in the cell membrane. The concentration or clustering persists for at least 5 h after the field has been turned off, indicating that the clustering is relatively stable. Single-channel patch measurements show both a higher density of ACh channels in the clusters near the cathode and a longer mean duration of the pulses through the transmembrane channels. The length of the current pulse near the anode does not differ from the controls, indicating that the field itself does not have a direct effect on the channel kinetics. The lateral diffusion coefficient, D, of ACh receptors in the plasma membrane of cultured *Xenopus* embryonic muscle cells is estimated to be $2.6 \times 10^{-6}\,m^2/sec$ at 22°C [48,49]. Lateral concentration gradients in lipid monolayers have been shown to be induced by externally applied electric field gradients. For binary mixtures of dihydrocholesterol and dimyristoylphosphatidylcholine, the application of an electric field gradient at pressures below the critical pressure produces a liquid–liquid phase separation in a monolayer that is otherwise homogenous [52]. This separation occurs at field levels on the order of $10^7\,V/m$ and gradients of 10^9 to $10^{11}\,V/m^2$.

5.6 Nonlinear Effects of AC Fields on Cells

5.6.1 Introduction

The application of an AC electric field to nonlinear systems, which can be described by either a nonlinear resistance or capacitance, leads to at least partial rectification of the input signal and the generation of harmonics. If two or more signal frequencies are applied, it also leads to frequency mixing of the form

$$f_o = \pm mf_1 \pm nf_2 \tag{5.48}$$

where f_o is the output frequency, f_1 and f_2 are input frequencies, and m and n are integers. The rectified component of the AC current can, in turn, lead to ion accumulation at interfaces, which results in changes in ion concentration [53,54]. These changes in ion concentration, in turn, can affect biological function. Another important additional effect is the dependence of the dielectric constant on frequency. This leads to changes in the electric field distributions in tissue with frequency. Thus, both the electrophoretic and the dielectrophoretic forces become both size and frequency dependent. A third—possibly important—additional effect is the excitation of frequency-sensitive biological systems in a resonant manner. By driving systems near their resonant frequency, we may change the effective amplitude of the stimulating signal and change the frequency of the nerve cells firing.

In this section we will review the rectification process at the cell membrane in some detail. Additionally, we will show that cell nonlinearities lead to frequency-dependent effects such as injection phase locking of pacemaker cells. We will also briefly examine some problems associated with the exposure of cells to very low, extremely low-frequency (ELF) fields and the application of large ELF fields to biological systems.

5.6.2 Rectification by Cell Membranes

The rectification of currents flowing across membranes has been studied by many authors, beginning with Katz in 1949. Much of this work is referenced by Hayashi and Fishman in their paper on the inward rectifier K^+ channel kinetics [53].

For many passive cell membranes, an approximate relation for the transmembrane current can be derived from the Nernst equation as given in Equation 5.41 [31]. If we apply an AC signal across the membrane of the form $V_M = V_0 + V_1 \cos \omega t$, the resulting current can be approximated for small values of V_M (i.e., $qV_M < \eta kT$) by a Taylor series yielding

$$I = \frac{I_0}{\eta V_T}\left(V_0 + \frac{V_1^2}{4\eta V_T} + V_1 \cos \omega t + \frac{1}{4\eta V_T} V_0 V_1 \cos \omega t + \frac{V_1^2}{4\eta V_T} \cos 2\omega t + \cdots\right) \tag{5.49}$$

It is to be noted that the second term in the expression is the first approximation to the fraction of the applied AC voltage V_1 that yields a DC current component ΔI,

$$\Delta I = \frac{I_0}{4}\left(\frac{V_1}{\eta V_T}\right)^2 \tag{5.50}$$

or an offset voltage V_{DC} given by

$$V_{DC} \approx \frac{I_0}{4}\left(\frac{V_1}{\eta V_T}\right)^2 R_m \tag{5.51}$$

where R_m is the membrane impedance. This predicted voltage offset for an applied AC current has been measured by Montaigne and Pickard [55]. In their experiments, an AC signal was applied to a large plant cell by a strip line, and the measured voltage shift was obtained through microelectrodes located outside the applied AC fields. For an applied AC field of about 0.2 V, they measured a DC offset of 1 to 2 $\times$ 10^{-4} V. For frequencies above 2.5 kHz, the effects of the membrane capacitance must be taken into account, and the effective driving voltage is reduced to

$$(V_1)_{eff} = [\sqrt{2}\, a\sigma_e\, \vec{E}_{1rms}][(\sigma_e + aG)^2 + (a\omega C)^2]^{-1/2} \tag{5.52}$$

where a is the cell radius, σ_e, is the conductivity of the medium $\vec{E}_{1rms}$, is the electric field strength in the medium surrounding the cell, G is the membrane conductance per unit area, ω is the frequency, and C is the membrane capacitance per unit area [56]. This leads to the usual roll-off in the measured DC offset with increasing frequency. Note that the DC effect gets still smaller at higher frequencies (above 1 MHz) because of transit time limitations for ion flow across the membrane [57].

The relaxation times for a typical K^+ channel in an *Aplysia* membrane has been measured to be from 2 to 8 ms [51]. Rectification has also been demonstrated in thin lipid membranes [58]. In these systems, both the conductivity of the membrane and the ion concentration differences across it can be controlled. The Nernst equation was shown

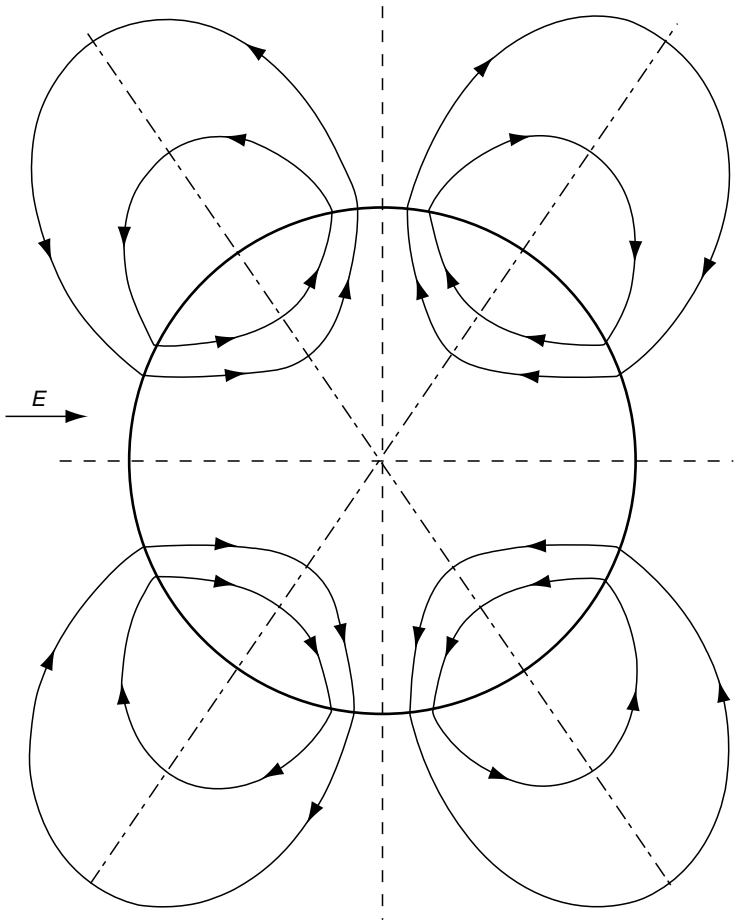


FIGURE 5.2
Induced DC current distribution in a spherical cell. (From Bisceglia and Pinto, I., personal communication, 1984. With permission.)

to apply to the I vs. V curve over a range of voltages from -60 to $+40$ mV. Depending on the ion concentration and membrane doping, the values of η ranged from 1 to 0.25.

A different treatment of the nonlinear response of passive cell membranes to an applied AC field has been carried out by Franceschetti and Pinto and by Casaleggio et al. [59,60]. Both these groups have expanded the Nernst equation in a Volterra series that takes into account memory of the preceding state of the cell. They have also treated the cell in spherical rather than planar geometry. The inclusion of a spherical cell requires that the total current into and out of the cell be equal to zero, and thus loops are formed circulating through the cell membrane (see Figure 5.2). All the theoretical treatments predict a DC component that varies as the square of the input signal V and tends to hyperpolarize the cell or make the interior of the cell more negative.

Cain has considered the effects of an AC field on nonlinearities of the nerve cell by numerical analysis of the Hodgkin–Huxley equation [61].* He applied a voltage

*Bisceglia and Pinto have applied a Volterra series expansion to the Hodgkin–Huxley equations. This approach gives an alternate method to Cain's of computing the current shifts resulting from applied AC signals [62].

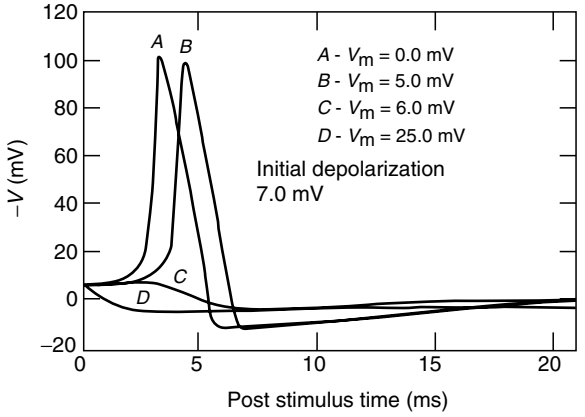


FIGURE 5.3
Computed membrane action potentials in response to an initial membrane depolarization of 7 mV for different values of V_m. Curves are solutions to the Hodgkin–Huxley equations. (From Cain, C.A., *Bioelectromagnetics*, 2, 23, 1981. With permission.)

$$V_m = V_0 + V_1 \cos \omega t[u(t) - u(t - \tau)] \tag{5.53}$$

across the membrane, where $u(t)$ and $u(t - \tau)$ are unit step functions that define an AC pulse of length τ. For the case where the AC frequency is large compared to the reciprocal of the pulse length, if a 7 mV depolarizing pulse is also applied to the membrane, the action potential is obtained as shown in Figure 5.3. Cain has assumed coefficients appropriate to the giant squid axon. Increasing V_1 first delays, and then suppresses, the action potential. If no depolarizing pulse is applied, the predicted changes in g_{Na} and g_K and the deviation V from the resting potential are as shown in Figure 5.4 for a 10 msec AC pulse with $V_1 = 25$ mV. Note that the applied AC frequency is assumed high enough not to be resolved in these figures. From these results, it is clear that AC signals can induce substantial changes in the operating characteristics of nerve cells at moderate to high levels of applied voltage. Although the appropriate coefficients were not measured in order to make a direct comparison between theory and experiments, Wachtel's results on *Aplysia* at frequencies above the lock-in range would appear to support Cain's theoretical predictions [63].

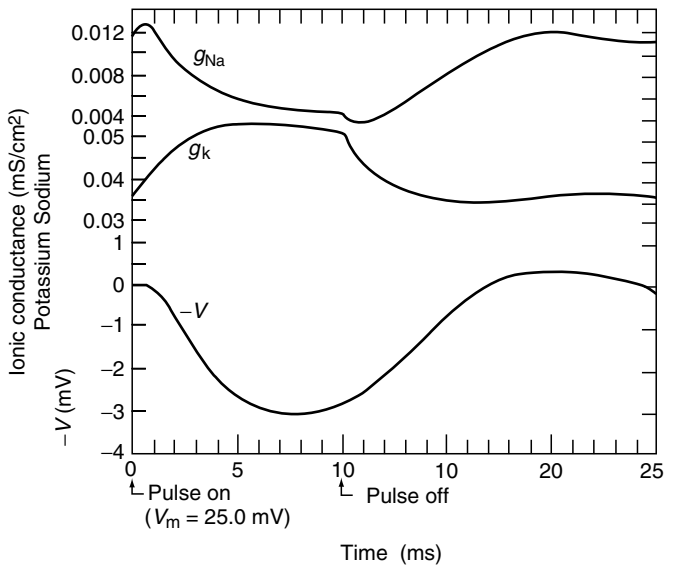


FIGURE 5.4
Response of model axon to a pulsed oscillating component of membrane electric field (10-ms pulse, V_m = 25 mV). The membrane potential and the sodium and potassium conductances are shown. These curves are solutions of the Hodgkin–Huxley equations. (Note: 1 mS/cm^2 = 10 S/m^2.) (From Cain, C.A., *Bioelectromagnetics*, 2, 23, 1981. With permission.)

Wachtel has made a series of measurements that demonstrate the nonlinear characteristics of pacemaker cells from *Aplysia* [61]. First, he measured the current input through a microelectrode that changed the firing rate of the cell. The current threshold for a minimum detectable change was approximately 6×10^{-10} A at frequencies between 0.8 and 1 Hz (see Figure 5.5). The natural firing rate for this cell is about 0.8 Hz, and an increasing current is required to synchronize the cell to the injected signal as the frequency deviates from the natural firing rate. A theory for injection locking of electronic oscillators predicts that the signal required for locking an oscillator to an external signal increases linearly as the difference between the two frequencies $\Delta\omega$ increases [64]. The signal required for lock-in according to this theory is given by

$$I_t \approx |A\Delta\omega|\ I \tag{5.54}$$

where I_t is the injected signal current and I is the peak unperturbed oscillator current. $A = \partial\phi/\partial\omega$ is the rate of change of phase with respect to frequency in the unperturbed oscillator. $\Delta\omega_0$ is equal to the difference between the frequency of the free-running oscillator and the injected signal. This expression is applicable as long as

$$\Delta\omega_0 \leq \frac{2\pi}{\tau} \tag{5.55}$$

where τ is the time constant for adjusting the gain of the circuit. The time constant τ for the *Aplysia* cells varied between 0.1 and 0.5 sec, and this corresponds to a maximum measured lock-in frequency of about 10 Hz. The results in Figure 5.5 show the threshold for one-to-one locking up to about 2 Hz. In the range from 2 to 10 Hz, Wachtel observed a lower threshold for subharmonic locking than one-to-one locking. At frequencies above 80 Hz, he observed a constant shift in the firing rate of the neuron in response to the injected transmembrane AC signal. The natural firing rate would be restored by also injecting a transmembrane DC signal equal in amplitude to about 1% of the peak-to-peak value of the AC current. This DC current was in the depolarizing direction, making the exterior of the cell more negative with respect to the cell cytoplasm to increase the firing rate (i.e., to restore it to its natural value). Apparently, the applied transmembrane AC current was partially rectified so as to hyperpolarize the membrane (making the interior of the cell more negative with respect to the external fluid). The details of how the applied field modifies the ion flow are only partially understood, but one characteristic is an increase in the conductivity for K^+, which increases its flow out of the cell. Wachtel also

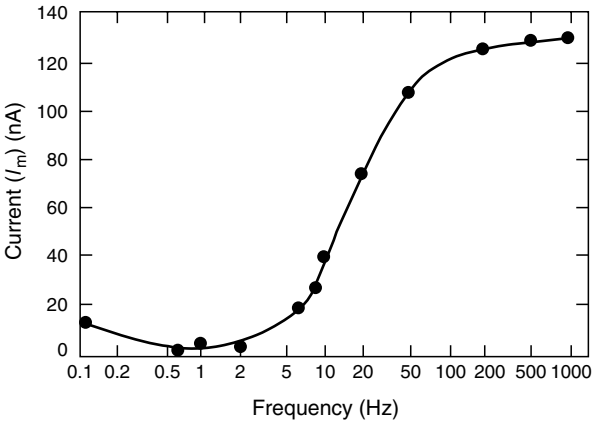


FIGURE 5.5
Intracellular (transmembrane) currents I_m (in nA) needed at different frequencies to produce firing-pattern changes (in a pacemaker neuron). Note that the detectable changes take on different forms at different frequencies. (From Wachtel, H., *Proceedings of the 18th Annual Hansford Life Science Symposium*, Technical Information Center, U.S. Department of Energy, Richland, WA, 132, 1978. With permission.)

injected low-frequency currents into the seawater surrounding the cell preparation through external electrodes [61]. In this case, the minimum current densities flowing in the vicinity of the cell preparation for injection locking were estimated to be about $10^{-2}\,\mathrm{A/m^2}$, and there was about a 30 to 1 variation between the maximum and minimum sensitivities for changes in angle between the applied field and the cells. At frequencies above 100 Hz, a minimum of about $0.35\,\mathrm{A/m^2}$ was necessary to obtain a detectable change in firing rate.

These studies have been extended by Barnes et al., and injection locking at harmonic and subharmonics has been shown to occur. It is suggested that phase locking may provide a mechanism for narrow banding or time averaging so that a weak coherent signal may be distinguished from noise by a cell. In an electronic circuit model we showed we could phase lock an oscillator at signal-to-noise ratios <1 [65]. Extensive modeling of phase locking for a squid axon using two versions of the Hodgkin–Huxley equations has been carried out by Fohlmeister et al. [66]. They show that phase locking can occur for a wide variety of frequencies with AM-modulated signals at injected current densities greater than $0.1\,\mathrm{A/m^2}$ [67]. For natural oscillation frequencies less than the externally applied signal, the system may be treated as a parametric process. For parametric amplification, a phase stability such that

$$\frac{\mathrm{d}\Phi}{\mathrm{d}t} < \Delta\omega - KV_\mathrm{s} \tag{5.56}$$

is required for injection locking of the frequency of oscillation to an external signal, where $\mathrm{d}\Phi/\mathrm{d}t$ is the rate of change of the phase, $\Delta\omega$ is the frequency offset, K is the linear control characteristic in units of $(2\pi\,\mathrm{Hz/V})$ and is closely related to the loop gain, and V_s is the injected signal [68]. Stated in words, this equation requires that the amplified signal, KV_s be large enough to correct for the random frequency fluctuations $\mathrm{d}\Phi/\mathrm{d}t$ generated by the noise for the system to become phase locked to a signal that is displaced by $\Delta\omega$ (see Figure 5.6 for some examples of injection locking of pacemaker cells to an external signal) [65]. An increase in the sensitivity to electromagnetic fields has also been shown in isolated frog hearts for signals that approach the natural resonant frequency or firing rate [69]. In these experiments, the firing rate of the heart was shown to increase as much as 30% when a signal in the vicinity of 10 to 20 V/m was applied through Ringer's solution to the isolated frog hearts at a frequency between 0.5 and 1 Hz. The natural firing rate of these excised hearts started out at approximately 1 Hz and dropped to about 0.5 Hz

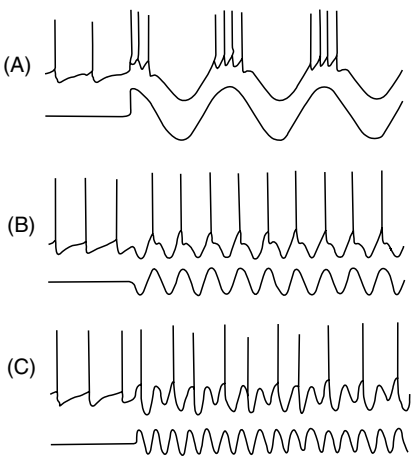


FIGURE 5.6
Examples of several modes of synchrony between an imposed ELF field and neuronal patterns. In each case the ELF current is shown below the transmembrane potential recording. (A) For ELF frequencies well below FR_0, several nerve impulses (spikes) are locked to each ELF half cycle. (B) ELF frequencies slightly above FR_0 are effective in phase locking the rise of neuronal spikes on a one-to-one basis. (C) For ELF frequencies several times greater than FR_0, phase locking can take the form of spikes occurring on alternate cycles (two-for-one synchrony). (From Barnes, F.S., *Bioelectromagn. Suppl.*, 1, 67–85, 1992. With permission.)

over a period of 2 h, where they remained stable for at least 5 h. To get a 30% increase in firing rate at 60 Hz, it was necessary to apply field strengths of 60 to 80 V/m. Thus, we have additional evidence that electric fields with repetition rates near the natural biological signaling frequencies are more likely to induce changes than those of higher frequencies and that signal strengths required for a given shift increase approximately linearly up to some cutoff, as shown in Figure 5.5.

For weak fields, it has been shown that cells can respond differently to signals that are both space and time coherent than they do for signals that look like the background noise. Litovitz et al. have shown that the application of 10 μT magnetic fields at either 55 or 65 Hz doubles the specific activity of ornithine decarboxylase (ODC) in L929 cells if the signals are coherent for periods of 10 sec or longer during the course of a 4 h exposure [70]. The applied signal and the corresponding ODC response as a function of the coherence time are shown in Figure 5.7. The ODC response of the cell can be fitted to an exponential curve of the form

$$(\text{ODC}) = 1 + 1.26\left[1 - \exp\left(\frac{\tau_{\text{coh}}}{\tau_{\text{cell}}}\right)\right] \tag{5.57}$$

where τ_{coh} is the length of the time between shifts in frequency and the introduction of a random phase shift and τ_{cell} is the effective time constant of the cell [70]. τ_{cell} has a value of about 8 sec for these cells. If a spatially coherent noise signal with a power spectral density ranging from 30 to 90 Hz is superimposed on the coherent signal, the increased ODC response decreases with a decreasing signal-to-noise ratio and is less than 10% at a signal-to-noise ratio of 1 [71]. This work has been extended to show that temporally incoherent magnetic fields inhibit 60 Hz-induced changes in the ODC activity of developing chick embryos [72].

For the exposure geometry used in these experiments, the magnetic field induced a corresponding electric field of 4 μV/m. This signal is well below the calculated thermal noise field of 0.02 V/m for a 20 μm cell diameter. The combined results of the experiments cited above indicate that both space and time coherence may be used by cells to separate useful signals from larger natural background noise signals. For example, to get a significant biological response, some threshold number of channels or receptor molecules may need to be activated within a given period of time; this, in turn, requires nearly

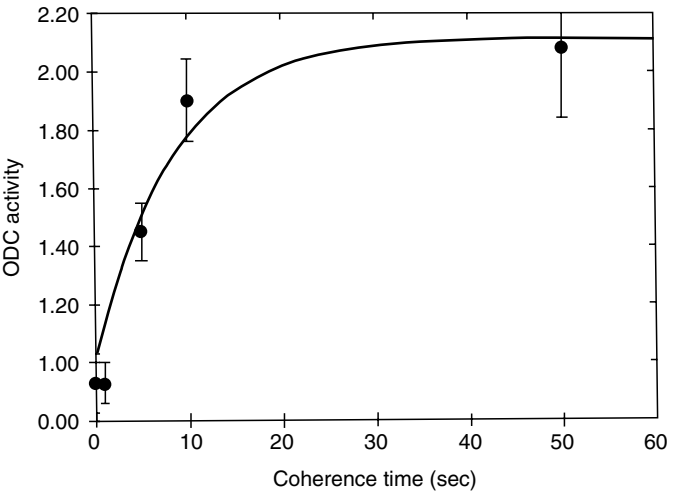


FIGURE 5.7
Plot of the enhancement of ODC activity (exposed/control) as a function of the coherence time, τ_{coh}, of the applied field. The solid line is the best fit to the mathematical function given by Equation 5.44, where τ_{cell} is found to be 8.2 sec. The experimental points shown represent a minimum of six different exposures. (© Academic Press; From Litovitz, T.A., Krause, D., and Mullins, J.M., *Biochem. Biophys. Res. Commun.*, 178, 3, 862, 1991. With permission.)

simultaneous activation over a significant fraction of the cell surface. Similar results have been obtained for developing chick embryos, where weak coherent signals lead to an increased incidence of abnormalities [73]. In this work, Litovitz and his colleagues show an increase in the incidence of abnormalities of approximately a factor of 3 for White Leghorn chicken embryos incubated in periodic magnetic fields with peak field strength of 1 μT (100 Hz repetition rate, 500 μs pulse duration, 2 μs rise, and decay times) when compared with the controls. This increased rate of the incidence of abnormalities was nearly eliminated with the addition of band-filtered noise with a spectrum running from 30 to 100 Hz and a root mean square value of 1 μT. Thus, Litovitz makes a strong case for a requirement of both space and time coherence for biological systems to detect signals below the natural noise environment.

A number of experiments indicate that at least two mechanisms are involved in the effects of low-level time-varying magnetic fields on membrane transport. The first of these is through Faraday's law or the induced electric field, which, in turn, induces electric currents. In these experiments, one would expect to get the same effects by introducing electric fields with electrodes at levels that induce the same current densities. The second group of experiments indicates that the background DC magnetic field is also important and that the combined effects of AC and DC magnetic fields are observed.

The initial experiments by Walleczek and Liburdy showed an enhanced uptake of Ca^{2+} in Con. A-activated rat thymocytes with exposures of 1 h to 60 Hz magnetic fields of 22 mT and induced current densities of 0.16 A/m^2 [74]. In this paper the exposure system consisted of concentric rings on cell culture plates, which, in turn, were placed in a water-cooled solenoid that produced a uniform magnetic field. This was followed by a group of experiments by Liburdy on Ca^{2+} transport across mitogen-activated lymphocyte membranes [75]. In these experiments, both the DC and the AC magnetic fields were controlled so that the DC geomagnetic field and the ambient 60 Hz fields were perpendicular to the exposed and control plates. The results show an increase in the Ca^{2+} influx during the plateau phase of the calcium signaling for Con. A-activated lymphocytes, which was a function of the induced electric field and which could be reproduced by applying the electric fields across the cells with a salt bridge at levels between 0.1 and 0.17 V/m. This corresponds to induced current levels of 0.168 to 0.28 A/m^2 in the fluid surrounding the cells, which had a conductivity, $\sigma = 1.68$ S/m, that is approximately a hundred times larger than the current densities observed around growing cells. Thus, the approximately 20% to 25% increase in the initial Ca^{2+} uptake is the result of a relatively large external current. In other experiments it was also shown that the response is dependent on the age of the animals from which cells are taken [76].

Most other reported experiments have not been done in a way to sort out the differences between possible direct effects of the magnetic fields and the induced electric fields. Yost and Liburdy [77] have also conducted experiments in the same system that show a direct dependence of the calcium uptake on the DC magnetic field.

The experiments by McLeod et al. [78] show both a frequency dependence and a dependence on the electric field strength across the cell membrane. They exposed neonatal bovine fibroblast cells to electric fields in culture through a media bridge. The fibroblasts populated a collagen matrix that enabled the cells to be grown with a dominant orientation and exposed to a well-defined current. An estimate of newly synthesized protein was made by measuring the incorporation of (^{3}H) proline into macromolecules after a 12 h exposure to current densities ranging from 10^{-3} to 10 A/m^2 and frequencies from 0.1 Hz to 1 kHz. The results in Figure 5.8 show an approximately 30% reduction in the ^{3}H counts with current densities as low as 10^{-2} A/m^2. This reduction is interpreted as a reduction in the incorporation of newly synthesized protein into the extracellular matrix rather than as a change in the cell number. The frequency specificity for this threshold is

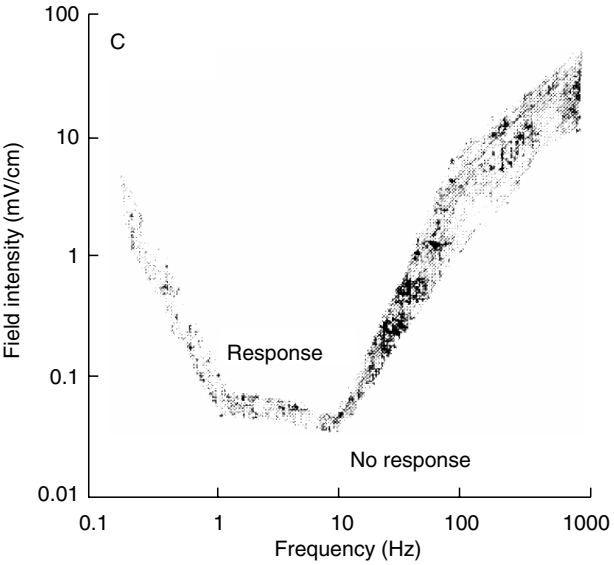


FIGURE 5.8
Minimum field intensity for a detectable response. Summary of results for all tested frequencies and current densities. Current densities were converted to peak field intensities by using the measured media resistivity of 65 Ω cm. The lower boundary of the gray region represents the highest field intensity at which no significant change in extracellular protein accumulation was detected; the upper boundary represents the lowest intensity evoking a statistically significant change ($n = 6$). (From McLeod, K.J., Lee, R.C., and Ehrlich, H.P., *Science*, 136, 1465–1469, 1987.)

shown in Figure 5.8; the peak sensitivity was recorded at $5 \times 10^{-3}\,A/m^2$ and 10 Hz. The corresponding peak electric field intensity was 4.5 mV/m. The fractional change in the (^{3}H) proline was nearly independent of the current density for increases in current density up to two orders of magnitude above $10^{-2}\,A/m^2$. The cell membranes have a resistance many times higher than the resistance of the matrix as a whole. The cells are also asymmetric, with a ratio of major to minor axes of about 7 to 10. Thus, the current through the cell membranes would be expected to be at a maximum when the long axes of the cells are parallel to the applied field. For randomly oriented cells, current densities of $3\,mA/m^2$ produced no significant effect on the rate of proline incorporation. However, when the cells were oriented parallel to the electric field that was estimated at 2 mV/m and 10 Hz, a little more than a 30% reduction was observed. The estimated transmembrane potential was 0.5 μV. With the cell oriented perpendicular to the field, no significant change in proline incorporation was measured at $5\,mA/m^2$.

In addition to the nonlinear conductances associated with Na^+ and K^+ currents, membranes also exhibit nonlinear (i.e., potential dependent) and frequency-dependent capacitances and inductances. It is sometimes useful to think of these effects in terms of a phasor diagram as shown in Figure 5.9, where the electric field vector $\vec{E}$ is rotating at a velocity ω, and ϕ is the phase angle between $\vec{E}$ and the current density $\vec{J}$. If there is, for example, a fixed time delay between the field activation of a current gate and the current flow, then, depending on the frequency, $\vec{J}$ may be in any of the four quadrants and appear capacitive or inductive or even present a negative resistance to an external driving source.

Nonlinear inductive effects seem to be associated with the time delay for the onset of the K^+ currents under excitation in a typical excitable membrane, and they have been studied in the giant squid axon [79]. The nonlinear capacitive effects are difficult to measure at frequencies below a few kilohertz. Extra care needs to be exercised to minimize the series resistance and the end effects of the wire being used to measure the capacitance or inductance. Additionally, corrections must be made in the calculations of the membrane capacitance to take into account the appropriate variations in the frequency response that these terms introduce. However, when this is done, it can be shown that the membrane capacitance has both frequency- and voltage-dependent terms. The capacitance of giant squid axons is shown in Figure 5.10 and Figure 5.11 as a function of frequency and membrane voltage.

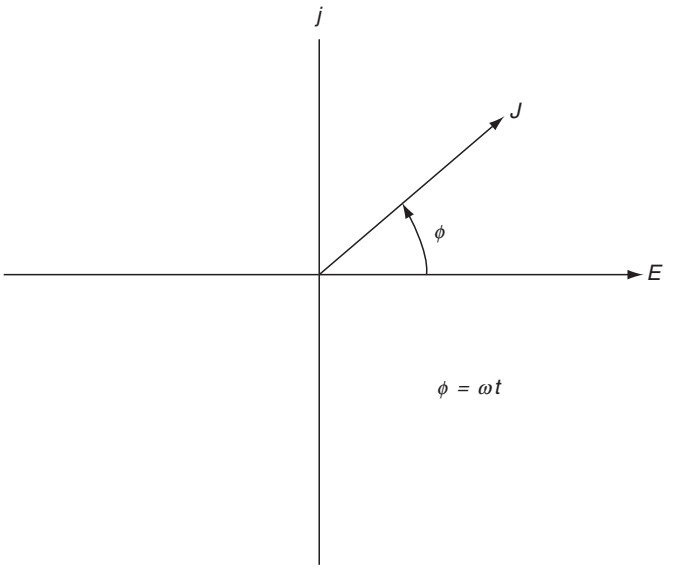


FIGURE 5.9
Steady-state vector characterization of electric fields $\vec{E}$ vs. current density $\vec{J}$ in polar form. ϕ is the phase angle between the sinusoidal electric field $\vec{E}$ and the resulting current density $\vec{J}$.

Variation of the capacitance of these membranes with frequency and amplitude differs from that of a simple bilipid membrane that has nearly constant capacitance. The variation appears to be associated with changes in the conformation of the proteins associated with the Na^+ conductance channels. Nonlinearity in conductance and capacitance can be induced into a bilipid membrane by the addition of Alamethicin. The nonlinear inductance or capacitance may also generate both sum and difference frequencies if two signals are applied. For the case of the single signal, a DC term is added to the current density that is proportional to membrane potential and the square of the applied AC signal [80]. The effects due to nonlinear membrane capacitance thus far observed are small. They

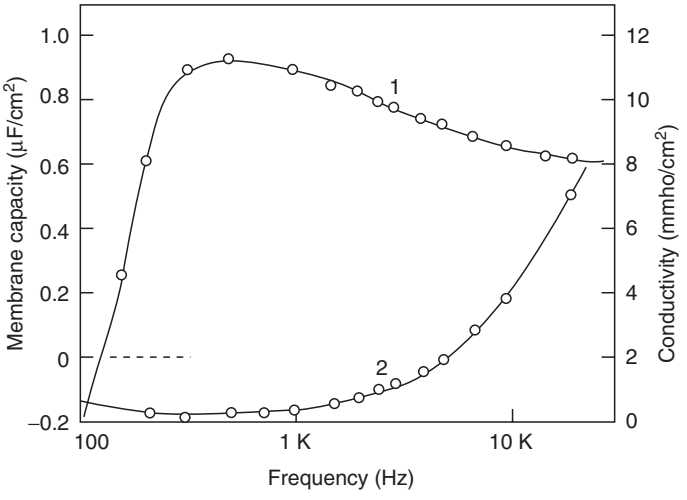


FIGURE 5.10
Membrane capacitance (Curve 1) and conductivity (Curve 2) of squid giant axon at various frequencies. Note the anomalous behavior at low-frequencies. (Note: 1 μF/cm^2.) (From Takashima, S., in *Biological Effects of Nonionizing Radiation*, ACS Symposium Series, No. 157, Illinger, K.H., Ed., 133–145, 1981.)

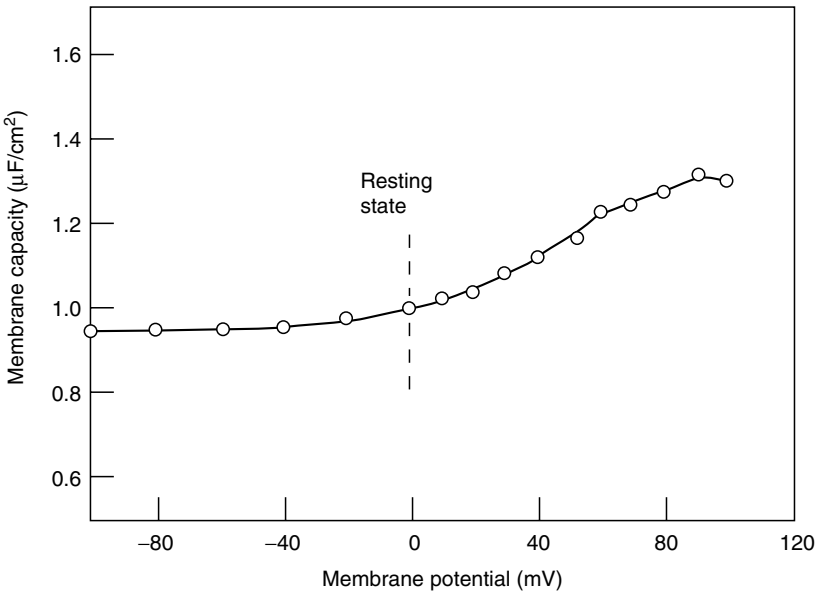


FIGURE 5.11
Membrane capacitance of squid giant axon at various membrane potentials. Membrane potential was shifted by injecting currents. The abscissa shows the actual potential across the membrane in millivolts. (From Takashima, S., in *Biological Effects of Nonionizing Radiation*, ACS Symposium Series, No. 157, Illinger, K.H., Ed., 133–145, 1981.)

appear likely to be more important in providing an understanding of the possible gating mechanism in membranes than as a mechanism for introducing rectification.

Another form of nonlinearity in the electrical response of cells comes about in what is often described as adaptive processes. For example, we found that repetitive exposures of pacemaker cells (taken from the ganglion of an *Aplysia)* to microwave pulses resulted in a decreasing reduction in the firing rate by successive pulses. This kind of change has also been shown to occur in neurons that have been conditioned with repetitive stimulation. Studies of conditioning have shown decreases in potassium ion conductance through membranes, thus raising the internal potential and enhancing the excitability [81,82]. The decrease in resistance between adjacent cells can occur in two ways. First, the resistance of gap junctions may be reduced by repetitive electrical stimulation, which increases the electrical coupling between the cells by up to 62%. Second, repetitive electrical stimulation can modify the chemical excitatory postsynaptic potential by amounts ranging from 31% to 140% [83]. This change is associated with the movement of protein kinase C from the interior of the cell into the membrane. An accompanying change in Ca^{2+} concentrations and the movement of a second messenger, diacylglycerol, into the membrane reduce the potassium ion flow. This enhanced excitability reduces the voltage or the charge required to initiate an action potential. If charge is transferred efficiently between cells, either actively or passively, cell length is effectively multiplied in the linear model by the number of cells in the chain; this, in turn, reduces the external electric field required to generate a given voltage across a terminating membrane (see Chapter 11 in *BMA* by A. Pilla).

An interesting speculation that is raised by these adaptive processes is whether or not a neural network can be trained to identify a repetitive signal such as 60 Hz in the presence of larger electric fields generated by the surrounding biological material. To test this hypothesis, we programmed a computer to simulate a neural network as shown in Figure 5.12 [65]. Using a backpropagation algorithm to adjust the connecting weights between neurons, a sigmoidal summing junction to model the neurons, and a pseudorandom noise generator,

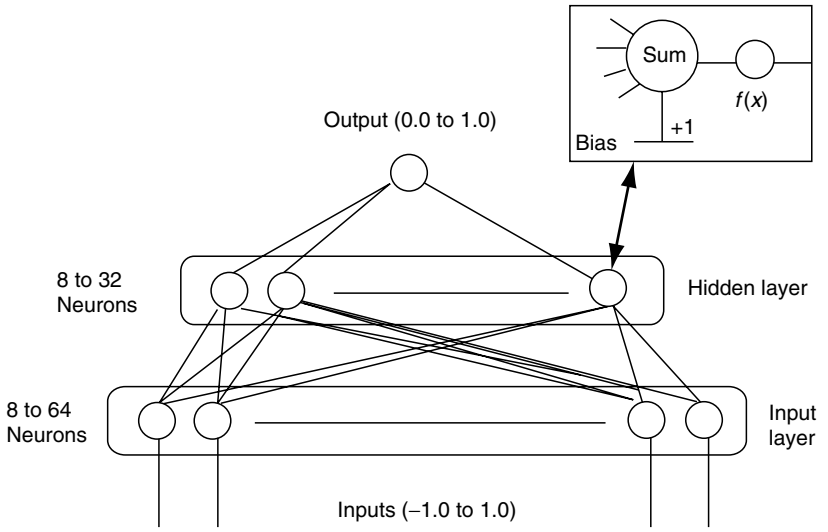


FIGURE 5.12
Backpropagation neural network. (From Barnes, F.S., *Bioelectromagn. Suppl.*, 1, 67–85, 1992. With permission.)

we measured the number of runs required to train the network to recognize a 60 Hz signal with 97% accuracy as a function of the input signal-to-noise ratio. The results in Figure 5.13 show that the training time increased from about 200 runs to about 1400 runs as the signal-to-noise ratio decreased from 1 to 0.001. The way the noise is presented to this network during the training makes a difference. For example, if you want the network to separate 59 Hz from 60 Hz, it helps to tell the network that 59 Hz is noise. This computer network model is clearly too simple to describe a biological nervous

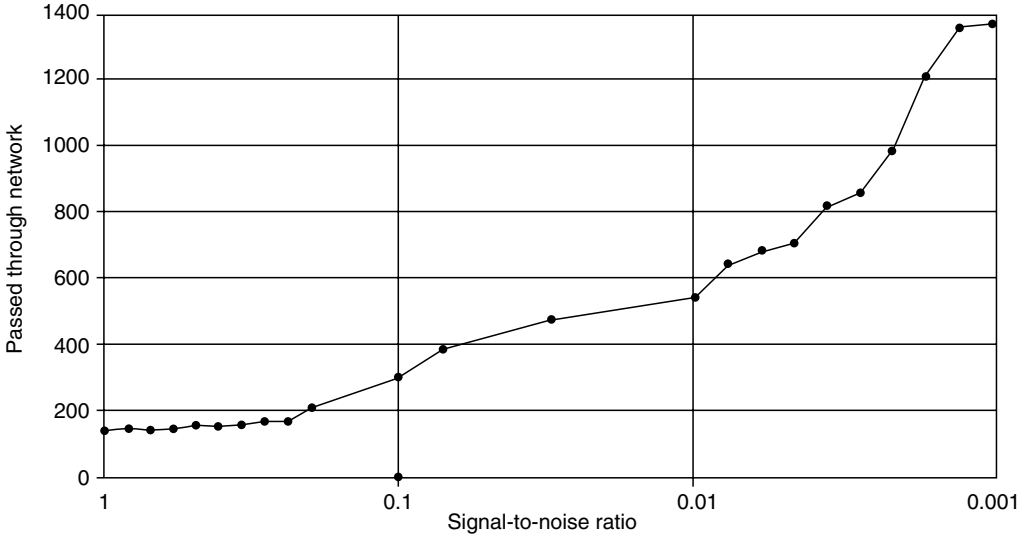


FIGURE 5.13
The learning response of a neural network with 64 input neurons, 8 neurons in the hidden layer, and 1 output neuron to a 60 Hz input signal and a pseudorandom noise signal with a decreasing signal-to-noise ratio. (From Barnes, F.S., *Bioelectromagn. Suppl.*, 1, 67–85, 1992. With permission.)

system, but it may provide a clue to one way in which a collection of cells may be able to respond to weak, externally applied electric fields, but a single cell would not.

5.7 Thermal Effects

One important effect of current flow due to electric fields is heating. The power input to a given volume of material can be expressed by $P' = I^2R$, where I is the total current and R is the resistance of the sample. For many calculations, a more useful expression is given by the power per unit volume or $P = \sigma E^2$, where σ is the conductivity, E is the electric field intensity. (For a more complete treatment of heating, see Chapter 10 and Chapter 12 of *BMA*.) The temperature rise resulting from this heat input is determined by the thermal capacity of the volume and the mechanisms for carrying the heat energy away. Typically, these thermal loss mechanisms include a combination of conduction and convection processes. For short current pulses, the heat dissipation is usually dominated by thermal conduction, and the basic equation for the rate of change of temperature is given by

$$\frac{\partial T}{\partial t} = \frac{P}{\rho' C_p} - \frac{T - T_0}{\tau_c} \tag{5.58}$$

where T is the temperature, T_0 is the initial temperature, t is time, and P is the power supplied per unit volume. ρ' is the density of the material (in kg/m^3), C_p is the specific heat under constant pressure, and τ_c is the thermal relaxation time.

If we consider a homogenous sphere of radius a immersed in an infinite fluid, the thermal conductive relaxation time is approximately given by

$$\tau_c = \frac{a^2}{4\overline{K}} \tag{5.59}$$

where $\overline{K}$ is the thermal diffusivity and is measured in meter square per second [84]. The thermal diffusivity is given by

$$\overline{K} = \frac{K'}{\rho' C_p} \tag{5.60}$$

where K' is the thermal conductivity (in cal/m sec °C), ρ' is the material density (in kg/m^3), and C_p is the thermal capacity (in cal/°C kg). If an applied current pulse is short compared to τ_c, the maximum temperature change is given by

$$\Delta T_{max} = \left(\frac{3}{2\pi e}\right)^{3/2} \frac{\overline{H}}{\rho' C_p a^3} \tag{5.61}$$

where $\overline{H}$ is the total input energy in calories and e is the base of natural logarithms [84]. For current inputs that are long compared to the thermal relaxation time τ_c, the peak temperature is determined by a balance between the input power and the dissipation process controlled by conduction and convection. It is interesting to note that if we assume the thermal properties of water as a first approximation to various kinds of tissue, then τ_c for a sphere with a equal to 1 μm is a little less than 2 μs. Since a sphere has the

smallest surface to volume ratio, Equation 5.60 gives an upper bound on τ_c, and Equation 5.61 gives an upper bound on the peak temperature excursion for small structures and pulses that are short compared to τ_c. Simply stated, it takes high power densities and large differential absorption coefficients to get significant differential temperature rises in small biological structures.

For situations where the volume involved is a cubic millimeter or larger, the thermal time constant is controlled by the amount of blood flowing through the volume. In these cases, temperatures may be more easily measured than calculated since a complicated thermal and electrical boundary value problem would have to be solved to calculate the temperature rise. This is particularly true since the viscosity η and other thermal and electrical parameters such as ρ, C_p, $\overline{K}$, etc. are functions of temperature. For example, C_p for an artificial bilipid membrane is shown in Figure 5.14 [85]. Another example of the importance of change in temperature is the conductivity of saline,

$$\sigma \approx C_1[10^{[(1/T)+\alpha](1/b)}] \times 10^{-4}\,\mathrm{S/m} \tag{5.62}$$

where C_1 is the concentration of NaCl in milligram equivalents per liter, T is the absolute temperature, $\alpha \simeq 6.23 \times 10^{-3}$ degrees^{-1}, and $b \simeq 1.4 \times 10^{-3}$ degrees^{-1} [86]. In the range around 37.5°C, this means that a 5°C change in temperature corresponds to a little less than 9% change in conductivity [86].

Changes in temperature are important, not only because they change transport properties such as viscosity, mobility, and the diffusion coefficient D, but also because they change chemical reaction rates. Typical biochemical reactions can be described by an equation of the form

$$\frac{dS}{dt} = -K'S \tag{5.63}$$

where S is the fraction of the material that has undergone the chemical reaction, t is the time, and K' is the reaction rate [87]. K' is often given by

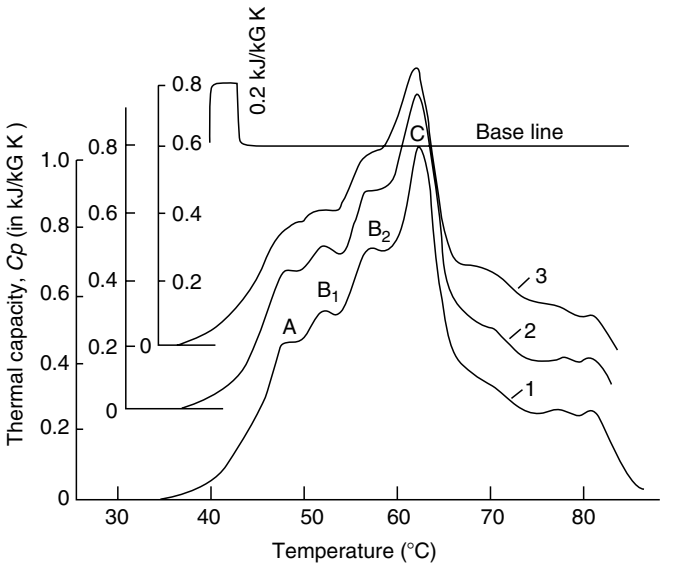


FIGURE 5.14
Differential changes in the heat capacity, C_p, of erythrocyte membranes as a function of temperature in 5 mmol/L sodium phosphate with pH 7.4 and a concentration of 5 mg protein per milliliter. The changes at A, B, B_2, and C correspond to changes in the structure of the membrane with temperature and are irreversible. Curve 1: intact membranes. Curve 2: irradiated at 330 mHz for 5 min (SAR 9 W/kg). Curve 3: irradiated at 300 mHz for 30 min (SAR W/kg). (From Shuyrou, V.L., Zhodan, G.G., and Akorv, I.G., Academy of Science, Institute of Biophysics, Pushchino, Moscow Region, Russia, personal communication, 1984. With permission.)

$$K' = \frac{kT}{h} \exp\left(\frac{+\Delta H' - T\Delta S'}{R'T}\right) \tag{5.64}$$

where k is the Boltzmann constant, T is the absolute temperature, H' is the free energy, S' is the entropy, h is Plank's constant, and R' is the gas constant. The significant feature is that the reaction rate K' varies exponentially with temperature, and $\Delta H'$ and $T\Delta S'$ are large numbers. Thus, very small changes in temperature can lead to big changes in chemical reaction rates.

In addition to chemical reaction rate changes, there may be changes in the binding of the proteins to cell membranes that lead to a shedding of proteins with a small increase in temperature. An exponential temperature dependence of the binding to membrane receptors is to be expected just as it is for chemical reactions [88].

A rule of thumb that the author uses to estimate whether or not significant biological changes are likely is to see if ΔT is $>10^{\circ}$C for 10^{-6} sec, 5°C for 1 sec, or 2°C for hours. If the ΔTs are larger, then they can be expected to lead to important changes in the biological system. Typical mammalian temperature regulatory systems will hold the internal body temperature constant to within $+/-0.5^{\circ}$C.

In addition to the magnitude of the temperature change, it can be shown that the rate of temperature rise, dT/dt, is important and can induce current to flow across membranes. Changes in the firing rate of pacemaker cells from the ganglion of *Aplysia* have been induced by total temperature changes of as little as $1/10^{\circ}$C when the rates of change are about 1°C/sec [89]. This change of the firing rate corresponds to the injection of approximately 1 nA into the cell. By taking the time derivative of the Nernst equation, which describes the passive equilibrium potential across a membrane for a single ion, it can be shown that a current proportional to the temperature derivative is to be expected, or

$$I = -qV_1'C_1\left(\frac{\phi}{\phi_T}\right)\left(\frac{\dot{\phi}}{\phi} - \frac{\dot{T}}{T}\right) \tag{5.65}$$

where q is the charge of the ion, V_1' is the volume of the cell, C_1 is the concentration of ions inside the cell, ϕ is the resting potential, ϕ is given by $\phi_T = \frac{kT}{q}$, $\dot{\phi}$ is the derivative of the membrane potential with respect to time, T is the temperature, and $\dot{T}$ is the temperature derivative with respect to time [90].

Bol'shakov and Alekseyev [91] have observed similar changes in the firing rate of pacemaker cells taken from the large parietal ganglion of the central nervous system of *Limnea stagnalis*. In their experiments they observed a slow increase in temperature (1°C/min or slower) to increase the firing rate of the pacemaker cell and a rapid increase in temperature (0.1°C/sec or faster) to decrease or stop the firing. They ascribe these changes to changes in the Na^+ pump as the rapid temperature effect was completely blocked by adding ouabain to the solution. In addition to the changes in the Na^+ currents, Ca^+ currents have been shown to be sensitive to rapid changes in temperature [92]. The rate of rise has also been shown to be significant in exciting a brain slice from a mouse with pulses of 10^{-3} sec and peak temperature rises of less than 0.5°C [93].

Temperature rises also lead to thermal expansion, and rapid temperature rises lead to the generation of acoustic waves [94]. These acoustic waves, in turn, can affect stretch receptors in nerve cells and other tissue and thus generate a biological response that may be at a considerable distance from the electrical heating [95].

To get an idea of the magnitudes of both heating (as described in Equation 5.58) and the effect of the rate of rise (as given by Equation 5.65), consider the case of liver tissue with $\sigma = 0.14$ S/m and a field strength in the tissue of 2×10^3 V/m. The rate of

temperature rise is approximately 13°C/sec assuming no conduction or convection heat losses and the thermal capacity of water. For this high field, a significant temperature rise occurs in about 1/2 sec. However, the rate of rise has been shown to be significant in exciting a brain slice from a mouse with pulses of 10^{-3} sec [96].

5.8 Natural Fields and Man-Made Fields

It is of interest to compare man-made with naturally occurring fields. First, we would like to know the approximate magnitudes of the fields that occur in nature outside man or the biological system of interest. Second, we would like to have values for the internal or physiological fields.

The natural electric fields at the surface of the earth have both DC and AC components [97]. One may think of the earth as a spherical capacitor where the surface is negatively charged with respect to an electrical conducting ionosphere that is about 50 km above the surface. This capacitor is being continuously charged by about 100 lightning strokes per second from thunderstorms worldwide. Since the atmosphere is a finite conductor, it also discharges with an *RC* time constant of about 18 sec. The result is an average electric field of about 130 V/m. This field is not uniform with height and typically falls off to 30 V/m at 1 km above the surface. The local values vary widely with temperature and humidity. In the Sahara during dust storms caused by winds in the dry season, a field of 1500 V/m has been measured with the polarity reversed from the normal. In thunderstorms, fields of up to 3000 V/m have been measured without lightning, and the polarity has been known to reverse in minutes. Storms as far as 50 km away have been shown to affect local fields. See Chapter 1 in this volume by Mild and Greenebaum for more details.

The atmosphere is a relatively poor conductor and as such will suspend a significant number of charged ions, dust particles, etc. This helps to contribute to local field variations of 20% to 50% over the course of the day and is a normal characteristic of our environment. The level of natural AC fields in the atmosphere falls very rapidly from a DC value of about 130 V/m [97]. The average value of the vertical component of the electric field above 1 Hz has a typical value of 10^{-4} V/m $\text{Hz}^{1/2}$. However, this value fluctuates widely with the time of day, the season of the year, and location. Additionally, the Schumann resonances impose multiple-cavity resonances on this spectrum with a periodicity of about 10 Hz. These resonances may be explained in terms of standing waves in a cavity formed by the earth and the atmosphere. These very low levels of the natural fields are one of the reasons why electronic communications in the ELF band are useful for ships at sea and submarines. However, because of the very low level of the natural atmospheric fields at frequencies above a few hertz, there is very little reason for biological organisms to develop natural protection against perturbations at these frequencies. It also means that biological systems could communicate internally at these frequencies using very low signal power levels and still maintain a good signal-to-noise ratio.

The signals generated within the body are the result of nerve firing and other cell activity. A typical nerve cell fires with an action potential of 50 to 100 mV and transmits a current pulse about 0.4 ms long [98]. The rise time for this current spike is approximately 0.1 ms, and the fall time is about 0.5 ms. Each pulse is followed by a refractory period that is typically on the order of 1 to 3 ms. The longitudinal fields along the exterior of a nerve cell membrane are estimated to have a maximum value of about 5×10^{-2} V/m during an action potential when the cell is surrounded by a relatively high conductivity fluid of 5 S/

m [98]. If we look at these signals closely, it will be noted that the interspike interval along any given nerve cell fluctuates in time. Additionally, variations in the beat-to-beat intervals for the ECG are random or chaotic, and the period can vary up to 30%. This is frequently seen, particularly at slow heart rates.

In looking at the natural fields in the body, we have two concerns. The first is how large an external signal takes to perturb the ongoing natural signal that is being used to communicate or control some biological process [99]. The second is how much of the signal field typically leaks away from active nerve fibers or bundles to form a background noise environment for surrounding tissue and processes. Regarding the first of these questions, it is interesting to look on the microscopic level at the electrical noise, i.e., the fluctuations that occur fundamentally as a result of the electrical process itself.

The first of several sources of noise that are always present is blackbody radiation, or Johnson noise, which is given by

$$P_{\mathrm{n}} = kTB \tag{5.66}$$

where P_{n} is the noise power, k is the Boltzmann constant, T is the absolute temperature, and B is the bandwidth [100–102]. The voltage equivalent of this noise power, which can be delivered to a matched load, or the mean squared voltage fluctuation $\overline{V}_{\mathrm{n}}{}^2$ across a resistance R, is given by [101,102]

$$\overline{V}_{\mathrm{n}}^2 = 4kTBR \tag{5.67}$$

or by the mean squared current fluctuations

$$\bar{i}_{\mathrm{n}}^2 = \frac{4kTB}{R} \tag{5.68}$$

Johnson noise applies to systems at thermodynamic equilibrium. Living systems are not at thermodynamic equilibrium. Thus, the foregoing expressions must be applied with caution to only those portions of biological systems where thermodynamic equilibrium is a good approximation. In the case of lasers, the spontaneous emission noise associated with the nonequilibrium population inversion of the energy levels can be obtained from Planck's radiation law by defining a negative temperature that assumes a Boltzmann distribution of atoms with N_2 atoms in the excited energy level E_2, which is greater than the N_1 atoms in the energy level E_1, such that

$$\frac{N_1}{N_2} = \exp\left[\frac{E_2 - E_1}{kT}\right] \tag{5.69}$$

In this case, the spontaneous emission noise $P_{\mathrm{n}} = h\upsilon B$, where h is Planck's constant and υ is the frequency of the radiation corresponding to a transition from E_2 to E_1 [100]. In those situations where the nonequilibrium characteristic may be described by an amplifier that can be modeled by a negative resistor or by energy storage in an inverted population distribution, the concept of a negative temperature may be a useful approach. Note that an equivalent temperature, T, is a convenient way to describe the energy distribution of a large number of particles. A much more complete description of nonequilibrium noise is given in Chapter 7 in this volume.

The second source of noise that is also present is the shot noise, which is given by

$$\bar{i}_{\mathrm{n}}^2 = 2q\bar{I}_{\mathrm{DC}}B \tag{5.70}$$

where $\bar{i}_n^2$ is the mean-squared current fluctuation. This noise comes about because of the discreteness of the electronic charge q and the assumption that the motion of each charge is independent. With negative feedback, this noise may be reduced, as has been shown for space charge-limited diodes. Shot noise results in an AC fluctuation, $\bar{i}_n^2$, which is proportional to the average value of the current, $\bar{I}_{DC}$. A third source of noise is $(1/f)$ noise. This noise may be generated by many processes, some of which are described in Chapter 7 in this volume. $1/f$ noise can be synthesized from Gaussian noise by filtering it with a circuit that requires about one low pass state variable per decade for the period of time over which the model is used to generate noise with a power density spectrum $S(f) = (C/f^{\alpha})$, where C is a constant and α is a constant between 1 and 2 [103]. We can expect to find this kind of noise for processes that evolve with time and, or have memory. $1/f$ noise describes the power spectral density of the fluctuations at low-frequencies in such diverse phenomena as transistors, quartz crystal oscillators, the closing Dow Jones Averages for the stock market, and the weather. It is also generated by the flow of ion currents through an orifice and thus is a fundamental part of the transport of current through channels in membranes [102]. Measurements of the noise voltage across a 10 μm hole in a 6 μm Mylar film showed that for a wide range of ionic concentrations the voltage noise spectral density $S(f)$ is given by

$$\frac{S_\phi(f)}{\phi^2} = \frac{a}{bnr^3 f} \tag{5.71}$$

where b is a numerical geometric factor, n is the density of ions in the solution, r is the radius of the hole, a is a constant, and ϕ is the applied voltage. The data showed that $2.5 < a < 40$ with a mean value of 10 for a wide range of solutions including HCl, KCl, and AgNO, with concentrations from 0.05 to 5 mol.

For natural membranes, this noise has been shown to take the form of

$$S_E(f) = \frac{C_E}{f^{\alpha}} \tag{5.72}$$

where $0.7 < \alpha < 1.2$ with a mean close to $\alpha = 1$. For the frog node of Ranvier, the noise is a function of the membrane voltage as shown in Figure 5.15 [104]. The dominant source of this noise appears to be the K^+ current, and it has a minimum when the membrane is biased, so that this K^+ current is biased to zero.

To get an estimate of the size of these noise sources, let us consider a pacemaker cell from the abdominal ganglion of *Aplysia*. This cell fires 20-ms pulses at about 1 Hz/sec. It has a resting voltage of about 50 mV and a resistance R measured with a microelectrode between the inside of the cell and the surrounding solution of approximately 10^6 Ω. If we assume a system bandwidth of 100 Hz and $T = 300$ K, the Johnson noise voltage would be $\overline{V}_n \approx 3 \times 10^{-6}$ V. This gives a resting potential-to-noise ($\overline{V}_n$) ratio of about 4×10^4. The peak current flow in these cells is estimated to be about 10^{-7} A, and thus the estimated shot noise current is $\bar{i}_n \approx 2 \times 10^{-12}$ A, and the ratio of the peak current to the noise current is about 2×10^4. We do not have the available value $S(f)$ for the *Aplysia*, $\bar{v}_\phi = \sqrt{S(f)B}$, where B is the bandwidth. If it is assumed that the maximum value of the noise is the same as that of the frog node of Ranvier, then for a bandwidth of 1 Hz we get $\bar{v}_\phi = 1.4 \times 10^{-5}$ V at a center frequency of 1 Hz from the curve for −50 mV in Figure 5.15. This is about a factor of 10^3 greater than the Johnson noise. It is likely that $(1/f)$ noise is the largest source of noise at the cell membranes for frequencies below 160 Hz [105,106].

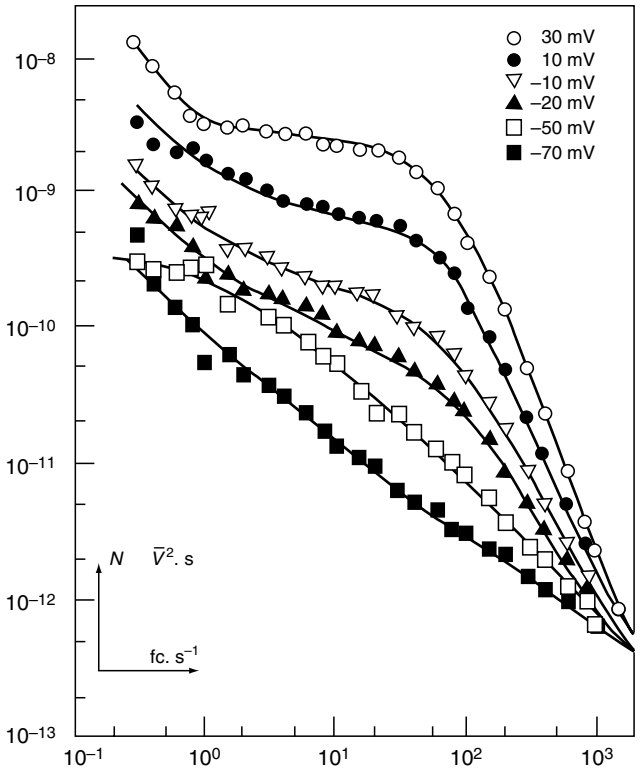


FIGURE 5.15
Voltage noise spectra of a frog node of Ranvier at different levels of membrane potential. (From Sichenga, E. and Verveen, A.A., in *Proceedings of the 1st European Biophysics Congress*, Vol. 5, Verlag Wiener Medizinischen Akademic, Vienna, Austria, 219, 1971. With permission.)

These fundamental sources of noise, which are generated by random fluctuations in the position of ions and their transport through channels, are spatially incoherent [73]. For many processes the important quantity in deciding whether or not an electrical signal is biologically important is the signal-to-noise ratio S/N where S is the power in the signal and N is the noise power. Typically, it is assumed that a signal-to-noise ratio of 1 is required for an externally applied signal to be detectable. In the foregoing discussion for both thermal and shot noise the movement of each charge was assumed to be statistically independent of each other. If for an externally applied signal the openings of the channels in a cell are excited in parallel and coherently and the noise is generated by incoherent random firing, then the signal-to-noise ratio increases with the square root of the number of channels. Similarly, the signal-to-noise ratio for a bundle of nerves would be expected to increase with the square root of the number of nerves for a signal applied externally to the whole bundle. Thus, a collection of cells can be expected to detect smaller signals than a single cell.

In addition to the electrical noise generated by currents and voltages that are part of the single-cell operation, electrical signals propagate through the body as a result of the incomplete confinement of electrical signals propagating in nerve cells. In a sense, these signals may be thought of as noise if they are not pertinent to the activity in that portion of the body through which they are propagating. If, on the other hand, they are used by tissue within the organism at some distance from the source, they must be thought of as signals. In the brain, the fraction of these signals that reach the scalp is called the electroencephalogram (EEG). The EEG is obtained by placing two or more conducting electrodes on the scalp and measuring the voltage between them. For electrodes placed 5 cm apart, the peak-to-peak voltages range up to 30 μV [107]. The author views this voltage as the integral of the vector sum of the leakage fields from the firing of the nerve

cells in the brain between the two electrodes. Since there are a very large number of cells firing, most of the 50 mV signals from an isolated nerve are canceled by summing over many like cells firing at different times and by the attenuation caused by propagation through the tissue. Estimates of surface potential gradients along a nerve fiber range from 3×10^{-4} to 5×10^{-2} V/m, and the corresponding current densities external to the nerve cells range from 5×10^{-2} to 4 A/m^2 [107,108]. The EEG voltage has a strong periodic component (particularly during sleep) near 10 Hz, which is known as the alpha (α) wave. A peak amplitude of this component may be as large as 50 μV when measured at the surface of the scalp. It is interesting to note that the EEG signal contains significant information on the brain's activity, and a few individuals have been trained to control these signals so as to control a computer in way that allows them write messages.

At the surface of the chest, a signal may be recorded between two electrodes known as the ECG or EKG (electrocardiogram). This signal results from the highly coordinated firing of the cells in the heart and has a definite wave shape that is closely related to the operation of the heart. The peaks of the so-called R wave in this signal may range up to 2.5 mV and are typically 0.5 to 1.5 mV, depending on the placement of the electrodes, the amount of body fat, etc. The pulse repetition rate is usually in the range of 1 to 2 Hz, and the ''QRS spike'' of the typical cardiogram is 40 ms long. Again, the signal measured at the surface of the skin is the result of leakage from electrically active cells located at a distance. The estimated current density near the firing heart cell ranges up to 1 A/m^2 [109]. In this case the shape of the signal reaching the skin is so closely related to the activity of the heart that it provides detailed information on heart function.

One result of electric discharges in the atmosphere, as well as natural ionizing radiation, is the creation of small positive and negative ions in the atmosphere. In clean country or mountain air, the typical ion density is about 10^{10}/m^3 with an average ion lifetime of a few minutes [110]. When a hot dry wind is blowing, positive ions created by the shearing forces can increase in concentration significantly. It has been shown that increases in the negative ion concentration reduce the amount of serotonin (5-HT) in mice and rabbits, possibly by accelerating the enzymatic oxidation process [111]. A similar result has been demonstrated in the oxidation of cytochrome *c*. Positive ions appear to block monoamine oxidase action, thus raising the concentration of free 5-HT [111]. Changes in 5-HT levels produce significant changes in the central nervous system, with high levels of positive ions raising the anxiety levels under stress. Other effects of increased positive ion concentration include a decrease in the survival rate of mice exposed to a measured dose of influenza virus, while an increase of negative ions reduced the mortality rate [111].

The significance of these results is that it is relatively easy to change the ion concentration in air using high-voltage DC systems where a leakage current of 1 μA from a burr or other sharp point would correspond to the generation of about 10^{12} ions per second.

Relatively few high-voltage DC transmission lines are in use today for distribution of power. Because the shocks resulting from a short contact across a high DC voltage are so painful and obviously dangerous, these systems are nearly always shielded. Thus, one is rarely exposed to DC electric fields $>10^3$ V/m. An additional feature of this exposure is that air is such a good insulator that the DC currents flowing through the body in a noncontacting situation are very small, as explained in the Introduction. For example, 1000 V across a 1-cm gap would yield a current density of approximately 10^{-7} A/m^2 flowing across the air gap. Thus, the principal hazards from DC fields occur when parts of the body make contact with a conductor.

5.9 Discussion and Summary

In this review some of the physical mechanisms by which DC and time-varying electric fields affect biological systems are presented. A few typical values of electric field strengths and current densities that are known to affect the biological system are compared with those of natural fields and other forces. Some values of electric fields and their gradients that are shown to modify the currents and shift energy levels are given. These in turn are shown to modify chemical reaction rates, which can lead to changes in the growth cells and other characteristics of biological systems. It is hoped that this information will help the readers to make their own estimates of when a given exposure to electric fields will be significant in modifying biological systems and provide a basis for understanding some of the biological results presented in other chapters of this handbook.

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6

Magnetic Field Effects on Free Radical Reactions in Biology

Stefan Engström

CONTENTS

6.1 Introduction

The physical chemistry of spin-correlated free radical pairs offers several mechanisms explaining how magnetic fields may influence biochemical processes. The mechanisms are classified on the basis of the dominating contribution to spin interconversion, and they cover a wide range of field strengths. Of particular interest is what is called the low-field mechanism, which has been extensively developed over the last decade and is now capable of explaining biological effects induced by magnetic fields well below 1 mT.

The principal mechanism behind the free radical mechanism was discovered in the physical problem of magnetic field dependence on positronium decay (Deutsch and Brown, 1952; Halpern, 1954). However, the development of the radical pair mechanism in chemistry has its roots in the work of Kaptein and Oosterhoff (1969), Closs (1969), and Brocklehurst (1969).

An ambitious survey of the literature up to its date of publication is the review of Steiner and Ulrich (1989), which lists some 775 references, 58 of which are themselves reviews on magnetokinetic phenomena. Another, now classic, reference on the subject is the book by Salikhov et al. (1984). McLauchlan and Steiner (1991) published a review including the possible mechanisms at lower fields. The review by Grissom (1995) explored the higher-field mechanisms with particular attention to the context of biological systems. A didactic paper geared toward the issues in biological systems is that of Brocklehurst and McLauchlan (1996). There are also some recent reviews on the free radical mechanism in general (Woodward, 2002) and with particular attention to biological systems (Brocklehurst, 2002).

6.2 Theoretical Background

A radical is an atom or a molecule with an unpaired electron. It tends to be highly reactive, a property that defines their best known roles in biology. A spin-correlated (or geminate) radical pair is typically created by hemolytic cleavage of a covalent bond, that is, each molecule retains one of the electrons that formed the chemical bond that was broken. The electron spins may remain correlated for a significant time (microseconds) after the pair's creation. As the radicals separate, the electron interaction term becomes small, and the electron states of the pair will fluctuate between antiparallel (singlet, or ''S'') and parallel (triplet, or ''T'') because of coherent spin evolution by hyperfine interactions between the electron spin and the nuclei. There is a chance of reencounter between the spin-correlated radicals. Reforming the bond is only permitted by quantum spin selection rules if the electron spins are oriented in the singlet state.

Magnetic fields can affect the electron state in the time before the reencounter; and if singlet and triplet pairs have different chemical fates, we have a basis for magnetic field effects on free radical chemistry (Figure 6.1). In exemplifying the process, we will assume that the radical pair is formed in the singlet state, the normal case for biologically relevant reactions (Eveson et al., 2000).

Many physical transduction mechanisms proposed to explain magnetic field effects in biology are very vulnerable to the randomizing effects of thermal noise at normal temperatures of living systems (Binhi and Savin, 2003). The free radical mechanism is uniquely resistant to this obstacle since it is a nuclear effect and is not strongly coupled to the thermal bath (Adair, 1999).

A quantum mechanical formulation of the free radical mechanism contains many possible contributions to the hamiltonian; Steiner and Ulrich (1989) provide a good categorization of the main components. The stochastic Liouville equation (SLE) is a tool

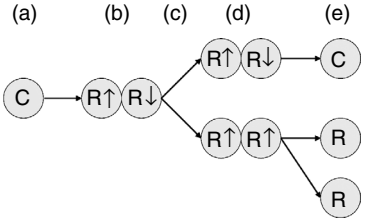

FIGURE 6.1
A molecule ''C'' (a) is split into two radicals (b). After diffusion and spin interconversion (c), the radicals may reencounter while still spin correlated (d). If the encounter occurs in the singlet state (e, top), the radicals may recombine. If the encounter occurs in the triplet state (e, bottom), recombination cannot occur, and the radicals will diffuse apart again and eventually lose their spin correlation. A magnetic field can influence this reaction by changing the rate of spin interconversion as long as the singlet and triplet products have different chemical fates.

for addressing the problem of simultaneous spin mixing and diffusion, but simplified models in which these two components are treated separately are often useful for the great reduction in problem complexity (Brocklehurst and McLauchlan, 1996). Recently, analytical results using a backward SLE have been presented (Pedersen and Christensen, 2004).

6.2.1 Hyperfine Interaction-Induced Singlet-to-Triplet Conversion

Hyperfine interactions between the spins of the electron and the nucleus cause the electron spins of the radicals to precess and induce singlet-to-triplet conversion. The triplet state has a net magnetic moment, and in the presence of an external magnetic field the energy levels of the triplet states that have a moment aligned with the magnetic field (T_+ and T_-) will be separated by Zeeman splitting. As the applied field strength is increased, the T_+ and T_- energy levels will be shifted away from the singlet state so much that they are decoupled from the spin interconversion process between singlet and triplet states, and only the remaining triplet state (T_0), which has a magnetic moment that is oriented perpendicular to the field, is capable of participating in the spin conversion process. In this way the magnetic field can reduce the number of triplet states that can be converted into singlet states and subsequently reform the original chemical bond. This is the ''normal'' magnetic field effect on free radical chemistry. It becomes relevant for external fields larger than the effective field driving the hyperfine interaction mixing, typically 1–10 mT.

A way in which singlet-to-triplet conversion can be facilitated is when an applied field causes the T_- energy level to cross the nonmagnetic singlet level, which occurs when the Zeeman differential matches the electron exchange interaction energy (cf. Figure 6.2). This effect has been observed for fields as low as 6.6 mT (Werner et al., 1993), but it can in principle be observed for much lower fields if the radical pairs are fixed with an appropriate separation.

6.2.2 High-Field Regime: Spin Rephrasing through the Δg Mechanism

The product of the magnetic field and the Landé g-factor determines the precession of the unpaired electron spin, independent of the hyperfine contribution. If the two radicals have slightly different g-factors, this provides an additional source of spin conversion. Differences are usually quite small, so this mechanism typically becomes significant only for quite large fields, $B > 0.1$–1 T.

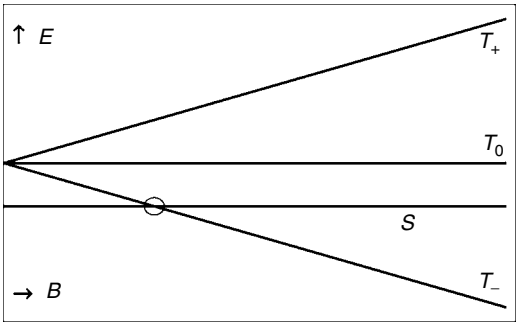

FIGURE 6.2
Energy level diagram for singlet and triplet states of a radical pair. At high fields, T_+ and T_- become completely disconnected from the singlet state, and only the T_0 state is left for singlet–triplet interconversion. At a specific B-field, the Zeeman split causes the T_- state to closely match the singlet state (circled), increasing the likelihood of transitions between the two states.

6.2.3 Low-Field Effect: $B < 1$ mT

At fields below the hyperfine interaction energy, it is still possible to see effects of external fields under certain circumstances. It was found by Brocklehurst (1976) that the selection rules of the hyperfine-induced spin mixing are more restrictive in zero field than when a field is applied (McLauchlan and Steiner, 1991). This becomes relevant, even for a very small field, as long as the coherence of the pair's state is maintained for long periods (100 ns to 1 μs). A helpful vector model to visualize this effect, along with some illustrative numerical examples, is given by Till et al. (1998).

The low-field effect (LFE) can theoretically produce a large (40%) drop in the singlet yield if the conditions are optimal (Timmel et al., 1998), but in practice only smaller effects attributed to this mechanism have been reported in the experimental literature.

Since long coherence times are required, it is necessary to understand spin relaxation effects and under what conditions they may be sufficiently long. Anisotropic hyperfine interactions provide noncoherent spin relaxation in solution, and it appears that the relaxation is slower in the low-field situation than has been generally thought (Fedin et al., 2001, 2003). It is becoming clear that understanding the local environment is crucial for evaluating LFEs (Eveson et al., 2000).

An important way to extend free radical magnetic field effects into the low-field region is to extend the lifetime of the spin-correlated pair. Integrating the magnetic field's influence over a longer time increases its ability to influence the spin evolution. Spin relaxation is not the primary problem here; rather, it is the reencounter probability that needs to be enhanced. There are several ways to achieve this:

1. Increased viscosity to restrict diffusion (Krissinel et al., 1999; Christensen and Pedersen, 2003; Kitahama et al., 2004)
2. Oppositely charged radicals that will oppose a tendency to diffuse apart (Adair, 1999)
3. Physically restricted mobility of the radicals through confining them to a surface or having the reaction taking place inside micelles, which are nanometer-scale compartments that form and reform on microsecond timescales and are able to confine the radical pairs and increase the reencounter probability (Eveson et al., 2000).

6.2.4 Free Radicals in Radio Frequency Fields

For higher-frequency fields ($f > 1$ MHz) the time modulation of the field starts to correspond to timescales present in the reaction dynamics, and a range of resonant interactions become available (Timmel and Hore, 1996). A detailed treatment of the coenzyme B_{12} system demonstrated resonant phenomena for relatively low-level radio frequency (RF) fields using a variety of mathematical techniques (Canfield et al., 1994, 1995).

6.3 General Characteristics of the Free Radical Mechanism

Free radical reactions are generally quite fast. There is evidence of picosecond reactions (Gilch et al., 1998; Musewald et al., 1999), but many known reactions occur over nanosecond timescales. If the free radical diffusion is constrained by micelles (Eveson et al.,

2000; Christensen and Pedersen, 2003) or by Coulomb attraction (Horiuchi et al., 2003), it may be possible to extend the radical pair lifetimes to hundreds of nanoseconds or even microseconds.

Since the free radical mechanism is practically instantaneous when compared to the timescale of time-varying magnetic fields in the extremely low-frequency regime (<300 Hz), one would expect that the observable output from a biological detection of the field should depend only on the time-averaged absolute field amplitude (Scaiano et al., 1995). However, if there is a downstream system that is able to decode the low-frequency signal, this statement is not necessarily true (Engstrom, 1997; Engstrom and Fitzsimmons, 1999).

6.3.1 Experimental Discrimination of Free Radical Models

The relative orientation of a static and a much smaller oscillating field will provide a discriminating test for a free radical-based model as long as the timescale of the applied field is long compared to the lifetime of the radical pair. In an isotropic system, such as a liquid suspension, described by this field situation, only the amplitude of the magnetic field is relevant. While the smaller parallel field adds linearly to the larger static field, the perpendicular component is effectively reduced by the calculation of vector length and will cause a much smaller variation in field amplitude (Engstrom, 1997).

For oriented systems in which the free radical chemistry steps have spatial preferences, it is possible to have angular dependence with respect to the angle of the applied field, $f(\theta)$. One can argue that some symmetry properties are very likely to be present in that kind of situation (Ritz et al., 2000). Polarity changes are not expected to be relevant, so $f(\theta + 180^\circ) = f(\theta)$. Furthermore, due to the isotropic distribution of nuclear spins in the initial state of the radical pair, one also expects that $f(180^\circ - \theta) = f(\theta)$.

If the free radical mechanism is active for low-frequency fields, one can also expect a response to RF fields in the same system, a property not expected by any other suggested physical transduction mechanisms for magnetic fields (Henbest et al., 2004). In a comparison between static fields in the range 0–2 mT, it was shown that a 300-μT, 5-MHz RF field applied perpendicularly or in parallel with the static field induced a response that was dependent on the magnitude of the static field (Henbest et al., 2004). This is qualitatively, if not quantitatively, similar to the observation that the magnetic sense of migratory birds can be disrupted by a 470-nT, 7-MHz field when the field is applied at an angle with the geomagnetic field (Ritz et al., 2004).

Magnetic isotope effects are another possible discriminating character of free radical effects, and it is possible to differentiate this signature from pure mass effects (Brocklehurst, 1997).

6.4 Free Radicals in Biology

6.4.1 Biological Transduction Mechanisms

Direct detection methods for free radicals have been developed in chemistry only relatively recently (Woodward, 2002). In biological systems, almost all experimental evidence for free radical involvement remains indirect. Generating hypotheses based on the signatures of free radical systems as outlined above are necessary to link free radical chemistry

to magnetic field effects, but there is circumstantial evidence that free radical chemistry underlies some effects reported in the bioelectromagnetics literature.

It has been suggested that complex dynamical systems may have special sensitivity to magnetic field influences (Grundler et al., 1992; Walleczek, 1995). This idea has been elaborated in a series of theoretical models of oscillatory systems (Eichwald and Walleczek, 1996a,b; Kaiser, 1996). These models show that enzyme dynamics involving free radical chemistry may be frequency specific, although only for timescales comparable to or slower than the chemical kinetics of the system (Eichwald and Walleczek, 1997). Field amplitude can influence enzyme dynamics in some instances and this can be used to exert some control over enzyme systems (Eichwald and Walleczek, 1998).

The peroxidase–oxidase system has interesting, well-documented dynamical properties (Scheeline et al., 1997). Detailed modeling of this system has shown how a magnetic field-induced perturbation can affect its dynamical behavior (Eichwald and Walleczek, 1998; Moller and Olsen, 1999). The point of interaction in this system is suspected to be electron-transfer enzyme intermediates (Moller and Olsen, 2000; Moller et al., 2000).

Downstream effects from changes in chemistry must be taken into account to evaluate biological significance (Brocklehurst and McLauchlan, 1996). This can both facilitate detection (Walleczek, 1995) as well as introduce interventions that could block the biological significance of a physical detection event.

It may be relevant that other enzyme systems have been studied in detail without the specific intention of addressing free radicals as a possible mechanism. Examples include electric and magnetic field effects in ATPase (Blank and Soo, 2001b). Direct interactions with DNA have been suggested; and electron transfer reactions are proposed interaction targets (Blank and Goodman, 2000; Blank and Soo, 2001a), although not by mechanisms addressed here. Myosin phosphorylation is another enzyme system that has shown sensitivity to time-varying (Markov et al., 1993) and static magnetic fields (Markov and Pilla, 1994), as well as gradient-specific effects (Engstrom et al., 2002).

6.4.2 Role of Freely Diffusing Radicals

Free radicals observed in biology are most commonly oxygen or nitrogen based with an unpaired electron, leading to the terms reactive oxygen species (ROS) and reactive nitrogen species (RNS). A dominant role for these radicals is to act in immunological defense. They are secreted by macrophages and neutrophils and during attempts to kill bacteria, viruses, and tumors (Nathan, 1992). The highly reactive nature of the radicals also means that damage to normal cells is possible, and various defense mechanisms against this have evolved as well (Yu, 1994). This immunological weapon with checks and balances already suggests that there is a signaling system built around free radicals, but it seems that the ROS and RNS also have roles in intracellular cell signaling (Lander, 1997) as well as intercellular communication (Thannickal and Fanburg, 2000).

Consider a biochemical reaction producing a spin-correlated free radical pair in the singlet state. Depending on the specific mechanism at work, the ratio of singlet-to-triplet product at reencounter will be modified. This will increase or decrease the fraction of pairs that tend to recombine because of a reencounter finding the spins in singlet versus the triplet states. For the LFE, the triplet state is favored, and we would see an excess of escape product. The situation is the opposite for the ''normal'' field effect, in which the T_- and T_+ states are decoupled from the interconversion process, increasing the proportion of singlet reencounters leading to a larger amount of cage product and leaving fewer freely diffusing radicals. The Δg mechanism brings the T_- and T_+ states back into play and therefore again boosts the triplet-reencounter escape products.

Given the wide involvement of free radicals in signaling and biological function, it is clear that there is the potential of both subtle and not-so-subtle effects on biological systems if we are able to alter the production of free radicals and thereby change the dynamics of already ongoing processes. The conventional wisdom regarding the deleterious effects of magnetic field effects on free radical recombination has been that more escape product means more radical-induced damage. This may be an oversimplification since the direct effects on cage or escape products are typically fairly small, certainly not larger than tens of percent, implying that drastic biological effects must involve downstream responses that amplify this relatively slight modulation. The answer may lie in the signaling properties of free radicals.

6.4.3 Animal Navigation Models Based on Free Radicals

The free radical mechanism was the first mechanism suggested as an explanation of avian use of magnetic fields for navigation (Schulten et al., 1978; Schulten, 1982). This model has since undergone several iterations of refinement (Ritz et al., 2000; Cintolesi et al., 2003). One interesting aspect of this work is a connection between photosensitivity and magnetoreception (Ritz et al., 2002). Dependence on light is a well-known feature of the avian magnetoreceptor (Deutschlander et al., 1999; Wiltschko et al., 2004a,b), but it has also appeared in other behavioral studies of animal magnetic field sensitivity (Prato et al., 1997, 1998).

The Ritz-Schulten model (Ritz et al., 2000) has an appealing geometrical application. Being integrated into the bird's retina, the suggested compass would appear as a modulation overlay on the bird's field of view. The mechanism operates through the so-called low field effect (LFE), based on a single nuclear spin, and operates near the limit of the theoretical sensitivity, despite omitting degrading effects such as the presence of multiple nuclear spins, dipolar effects, and various spin relaxation process that will start to become relevant for the long radical pair lifetimes (>100 ns) considered in the model.

Cryptochromes provide one possible source of free radicals in a spatially ordered system (Ritz et al., 2002). A recent theoretical model for avian magnetoreception develops that idea by investigating a flavin–tryptophan radical pair with a high degree of homology to the cryptochromes (Cintolesi et al., 2003). This multinucleus model is realistic in that it still manages to provide sensitivity to fields in the geomagnetic field range. Interestingly, it does not operate through the LFE described above (the multinucleus approach appears to remove most signs of that mechanism), but rather it depends on immobilized radicals and assumes that the free radical pair may have a lifetime up to 5 μs.

6.4.4 Coenzyme B_{12}-Dependent Reactions

Magnetic field effects in the coenzyme B_{12} are well explored experimentally with matching theoretical predictions (Harkins and Grissom, 1994; Grissom and Natarajan, 1997; Taoka et al., 1997). While most work on this model system has been concerned with intermediate and higher-field mechanisms, there are also detailed theoretical investigations suggesting that weak (<100 μT), relatively low-frequency (<100 kHz), might be able to affect this system (Canfield et al., 1994, 1995, 1996).

6.4.5 Other Experimental Observations

The addition of iron ions or exposure to a 7-mT static magnetic field (SMF) did not affect the survival of rat lymphocytes *in vitro* when performed in isolation, but combined

exposure led to a significant increase in cell death (Jajte et al., 2002). One possible explanation of this behavior is that the addition of iron ions enhanced levels of ROS and that the field exposure further promoted the creation of free radicals, leading to cell death by both apoptosis and necrosis. An experiment with a similar rationale used added $FeCl_2$ to stimulate ROS production, and a 930-MHz, 5-W/m^2 cell phone-generated field affected a biological marker for ROS production. It should be noted that the vacuum magnetic field associated with this exposure is quite low (approximately 0.14 μT) and the frequency is a relatively unexplored region for this mechanism.

Proliferation of chick fibroblasts was observed to be enhanced by a 100-Hz, 0.7-mT sinusoidal magnetic field (Katsir et al., 1998). In a follow-up study it was found that free radical scavengers (Katsir and Parola, 1998) suppressed this effect, suggesting that that free radicals may have a role in mediating the magnetic field effect on proliferation.

Genotoxic effects from intermediate static magnetic fields (250 mT) have been studied in *Escherichia coli* DNA, both *in vivo* and *in vitro* (Potenza et al., 2004). Free radical formation was stimulated, and the genetic damage was mapped as a function of exposure duration. *In vitro* experiments showed detectable genotoxic effects, but the *in vivo* assays did not, indicating that cellular protective responses may prevent damage in the intact system.

A reported effect on the oxidative burst in neutrophils by a 0.1-mT field was attributed to free radicals (Roy et al., 1995). In that study, the connection to free radicals lies in that the fluorescent probe used to study the neutrophil activity reacts specifically with free radical-derived oxidants that create the fluorescing compounds. Work in neutrophils in humans (Heine et al., 1999) using a much larger field (1.5 T) did not find any effects of magnetic fields on the respiratory burst of human neutrophils or on the production of radical species.

Phagocytosis was observed to be affected by 0.5–1.5-mT, 50-Hz sinusoidal magnetic fields (Simko et al., 2001). An attendant increase in superoxide production may be an indication that the field stimulated the system through a free radical process.

6.5 Conclusion

Free radical reactions are ubiquitous in biology, and recent developments of the low-field mechanisms (Timmel et al., 2001) and the consideration of detailed biochemical systems (Cintolesi et al., 2003) make this mechanism a contender for field effects down to geomagnetic field strengths. The physical transduction step is not vulnerable to thermal perturbations, a significant advantage over competing models.

This model does not produce large (factors >2) changes at the initial field detection step. Theoretical models and direct experimental observations in the low-field region typically operate around or below the 10% level, so we should expect the physical detection mechanism to need cooperation from downstream processes for biologically relevant detection of magnetic fields with free radicals as the starting point.

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7

Signals, Noise, and Thresholds

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CONTENTS

7.1 Signals, Detection, and Measurement

Measurement is a quantitative observation and well known to be of great importance to science. However, measurements involving biological systems are complicated by the complexity of cells and tissues, particularly if fields are expected to interact weakly and field-induced changes are found to be small. Some key parameters, for example, temperature coefficient of a measured quantity, may be inadequately characterized, and related quantities may be determined incompletely (e.g., measurement or modeling of the time-dependent temperature throughout the volume of the biological system being studied). Detection is a special case of measurement, that is, the measurement is so coarse that an observer can only distinguish between ''signal'' and ''no signal.''

Generally speaking, the smaller the change in an observed quantity (e.g., cell biomass) due to a stimulus (e.g., an applied electromagnetic field), the more difficult the experimental interpretation. There may be multiple candidate causes if small changes in biomass are found, for example, any of many growth-altering biochemical changes, unnoticed and uncharacterized temperature variations, or even changes in ambient light or mechanical vibration. In physical science a model can often be made of the experiment. This allows estimates of the influence of various quantities and parameters on the expected experimental outcome (change in observed quantity in response to a stimulus) and is valuable in the interpretation of experiments. Similar approaches to bioelectromagnetics should also be valuable.

Consider an illustrative measurement on a biological system: a population of microorganisms contained within a glass toroid. Application of an alternating magnetic field to a primary coil wrapped around one part of the toroid induces an alternating current. The induced current can be measured with a coil wound around part of the toroid. The induced current is related to the electrical conductivity of the aqueous electrolyte. The electrical conductivity of the extracellular medium changes when small, charged metabolites are excreted, and measurement of microbial metabolic activity can thus be accomplished electrically. First observed in 1899 by a nulling technique [1], electrical impedance detection of microorganisms has received significant attention as a measurement method [2,3]. A toroidal device has actually been explored as the basis for determining microbial activity [4], with metabolic acid production causing a change in extracellular ion concentration (activity) and therefore creating a change in the electrical conductivity of the extracellular medium. But complications may arise. If cytotoxic chemicals leach from the glass, there can be a time-dependent poisoning of microbial activity. Ambient temperature changes couple through the glass to create internal temperature variations that alter the conductivity. In short, because electrical conductivity change has more than one candidate cause, this measurement system lacks specificity. This also illustrates a basic challenge to measurement of effects of electromagnetic fields on biological systems, namely, demonstrating both a statistically significant change and convincing evidence that it is the field interaction with the biological system, not an associated competing influence, that is responsible for the observation.

7.2 Specificity

Specificity is a hallmark of biological interactions involving biochemicals. A cell contains a large number of coexisting molecules whose interactions are not spontaneous but are instead highly regulated. Enzymes can be highly specific in the reactions they catalyze. Antibodies and receptor–ligand binding are also often specific. However, interactions of electromagnetic fields with a biological system are rather general. Magnetic fields interact indirectly by inducing electric fields and directly through magnetically sensitive reactions [5] and through interactions with magnetic material. Such magnetic materials may be contaminant ferromagnetic particles in the human body [6] or they may be biologically synthesized magnetite granules [7,8]. Electric fields interact nonspecifically with charge and polarizable material. Thus, unlike ligand–receptor biochemical interactions, there are no molecular receptors that are highly specific for electromagnetic fields. Instead, magnetic and electric sensory systems interact broadly and can be regarded as nonspecific. Evolved sensory systems are rather special. To date, it appears that biological, electric and magnetic field reception is indeed accomplished by organized systems.

Lack of electromagnetic field specificity has important implications for interpreting experiments. If an experiment quantifies a change in an observed parameter, the cause of the change is not automatically known. Continuing the example of cell growth determination based on biomass measurement, if an increase in biomass (or cell number) is associated with a field exposure, then additional analysis is needed to determine whether this change is due directly to the field or is instead due to interfering influences such as temperature change or biochemical concentration changes.

The challenge of specificity is not limited to weakly interacting fields. Consider the case of strong, electroporating fields *in vivo*, for which the motivation is local tumor treatment

or gene therapy. Strong fields can generate tissue movement by stimulating muscles and possibly also by bulk tissue polarization forces. Tissue motion can itself create membrane openings, and these can lead to biochemical transport [9–11]. Thus, observation of molecular uptake associated with electrical pulsing does not by itself show that electroporation is responsible. Specificity is an issue.

7.3 Signal-to-Noise Ratio

We adopt a recent discussion of the signal-to-noise ratio (S/N) for experiments with biological systems exposed to weakly interacting electromagnetic fields [12]. The observed quantity is x. For bioelectromagnetics experiments, examples of x include a local or spatially averaged transmembrane voltage change, temperature rise at a particular site, radioactivity of an incorporated unstable isotope, specific enzyme activity, intracellular calcium ion concentration, cell biomass, etc. Typically, experiments obtain data that can be characterized by their means and standard deviations, often presented as a bar chart. One bar of each bar pair represents the control result, and the other bar represents the exposed result. Each bar height represents the mean value, and the error bar is usually the standard deviation. (In some cases the error bars instead represent the standard error, that is, the uncertainty in the mean, rather than the standard deviation, but generally a report states which is being used.) Bar charts present a concise summary of an investigator's knowledge of the underlying natural distributions. The measured mean and standard deviation of the control distribution can be defined to be $\bar{x}_{\text{con}}$ and σ_{con}, respectively. Similarly, $\bar{x}_{\text{exp}}$ and σ_{exp} are the observed mean and standard deviation of the exposed distribution.

When repeating the same experiment and doing the same measurement many times over, one generally finds a Gaussian distribution of outcomes. This is because in a complex system there are many variables and sources of inaccuracy that are not under the control of the experimentalist. For the cumulative effect of all these imprecisions the central limit theorem becomes applicable. This theorem says that with many independent stochasticities involved, the outcome will be a Gaussian distribution [13]. As an example of this theorem in practice, do 100 coin tosses and record the number N of ''heads.'' Repeat this experiment many times. The result will converge to a Gaussian distribution of N that is centered around 50.

The threshold for a field exposure effect occurs under conditions of detection, that is, the minimum change of x that is discernable using generally accepted statistical criteria. This is equivalent to determining whether or not the control statistical distribution and the exposed distribution are distinguishable (significantly different by accepted criteria). This requires sufficiently precise knowledge of the statistical distribution parameters. Increasing the number of determinations of the natural distribution generates more precise knowledge of its parameters. For example, if an investigator carries out a number, m_{con}, of determinations of x_{con} and another number, m_{exp}, of determinations of x_{exp}, then the empirically determined values can be reported as

$$x_{\text{con}} = \bar{x}_{\text{con}} \pm \frac{\sigma_{\text{con}}}{\sqrt{m_{\text{con}}}} \quad \text{and} \quad x_{\text{exp}} = \bar{x}_{\text{exp}} \pm \frac{\sigma_{\text{exp}}}{\sqrt{m_{\text{exp}}}} \tag{7.1}$$

The ratio $\sigma/\sqrt{m}$ actually represents the aforementioned standard error. Increasing the number of determinations reduces the standard error and the ensuing uncertainty in the mean. However, it does not decrease the standard deviation, σ_{exp}, of the underlying distribution, which is assumed unperturbed by the measurement process.

As the means $\bar{x}_{con}$ and $\bar{x}_{exp}$ become better known through more determinations, the potential distinguishability of the two distributions increases. The p-value of the experiment is often reported as a measure of this distinguishability. The p-value is the probability that the two means would be found to be as different as observed (or even more different) purely because of random variability. For example, $p = 0.01$ indicates that there is only a 1% chance that the difference between the control mean and the exposed mean would be due to the (assumed) random variability of the measured quantity, namely, the standard deviation [14]. After an investigator completes an experiment and finds a reasonably small p-value (.01 and .05 are widely used values), it is a common practice for the investigator to report that an effect due to the field exposure has occurred. However this assumes specificity, namely, that the field exposure rather than an associated competing influence is responsible. Indeed, a small p-value supports an effect of some sort but not necessarily one due to the field during the exposure. Additional analysis that considers other competing influences such as temperature variations, vibrations, and chemical concentration variations [15,16] is required for that conclusion.

Bioelectromagnetics experiments with weakly interacting fields typically involve determination of changes with respect to background values of, for instance, transmembrane voltage, fluorescence intensity, enzyme activity, or cell number. Observed changes in ''exposed'' relative to ''control'' are generally small. At the other extreme, strongly interacting fields create large changes with respect to background, for example, molecular uptake by electroporation (see Chapter 9 on electroporation in Ref. [127]). For the ''weakly interacting'' situation the uncertainties (error bars) are about the same for exposed and control. However, there is another figure of merit, distinct from the p-value, namely, an empirically determined signal-to-noise ratio $(S/N)_{obs}$, which is associated with the observation and which is presumed due to the underlying statistical distributions for the control and exposed cases. Classical detection theory shows that the associated distributions are expected to be Gaussians [17].

In continuation of a recent discussion [12], we consider the observed signal (S_{obs}) to be the difference between the control and the exposed means, and the observed noise (N_{obs}) as the standard deviation of the control distribution [17]. This yields

$$S_{obs} = \bar{x}_{exp} - \bar{x}_{con} \quad \text{and} \quad N_{obs} = \sigma_{con} \tag{7.2}$$

so that the empirically determined signal-to-noise ratio is the magnitude of

$$(S/N)_{obs} = \frac{\bar{x}_{exp} - \bar{x}_{con}}{\sigma_{con}} \tag{7.3}$$

Like the p-value $(S/N)_{obs}$ is a measure of the distinguishability of the two distributions. However, unlike the p-value, the signal-to-noise ratio is an inherent characteristic of the biological system, its environment, and a particular field exposure and does not depend on the number of determinations. In this view, S_{obs} is the observed change and is assumed to be a measure of the strength of the perturbation to the biological system by the field exposure. N_{obs} is a measure of the natural variability in the system for the conditions of the experiment. In the absence of an exposure, N_{obs} provides the appropriate scale to gauge the strength of S_{obs}.

$(S/N)_{obs}$ is based only on experimental determinations of x. However, in many cases the field exposure is believed to *indirectly* alter x. According to this general hypothesis, the field exposure affects one or more molecular-level biochemical processes through physical interactions. In this sense, the exposure is creating a ''primary'' molecular change, which is then amplified through a biochemical cascade that creates a downstream change. It is this downstream change that is eventually measured. The signal-to-noise ratio cannot be increased by the amplification process. Later in this chapter, we will describe how amplification generally adds noise to a signal.

7.4 Detection Criteria

The criterion $(S/N) \leq 0.1$ is a very conservative basis for ruling out a particular class of biophysical mechanism for a given field exposure. Similarly, the criterion $(S/N) \geq 10$ is a conservative basis for ruling in a candidate biophysical mechanism for a given exposure, retaining that biophysical mechanism hypothesis for further evaluation. This approach provides a quantitative basis for rejecting or accepting hypothetical biophysical mechanisms as candidate explanations for an experimental measurement. The traditional choice $(S/N) \approx 1$ is a useful but somewhat arbitrary dividing line, which indicates conditions for which an effect might appear. $(S/N) \leq 0.1$ and $(S/N) \geq 10$ provide criteria for stronger conclusions, allowing rejection or provisional retention of a biophysical mechanism hypothesis.

We should recognize that thresholds are defined by generally accepted statistical criteria. The widely used p-values of .01 and .05 are examples of such generally accepted statistical values. In the case of signal-to-noise ratios, a commonly accepted value is $(S/N) \approx 1$, where the approximately equal symbol denotes the imprecision. Specifically, if (S/N) (empirical or theoretical) exceeds 1, then the threshold is viewed as being exceeded. Similary, if (S/N) is less than 1, the response is interpreted as subthreshold. Clearly, it makes little sense to take a strong position if (S/N) is close to 1. But, as noted above, if the signal-to-noise ratio is significantly greater or less than 1, then some confidence can be attached to the result. In short, a threshold is imprecise but nevertheless a useful guide.

7.5 Equilibrium Noise

In this section we will examine how Brownian noise, the simple random motion of molecules due to thermal agitation, interferes with the coupling of an electromagnetic field to a biochemical system. Some organisms have evolved an ability to sense and effectively ''measure'' electric and magnetic fields. We will see that the thermal noise that a signal has to compete against sets fundamental limits on detectability. We will also see how evolution has come up with structures to optimize the signal-to-noise ratio in sensory perception.

Fish generally carry a small dipolar field relative to the water that they swim in. Sharks, skates, and rays have developed special organs to detect such fields [18,19] and they use this ability to pinpoint the position of their prey when they get close and the water is too turbulent to rely on smell. To be effective, the shark should be able to sense its prey

instantaneously. So, for the signal not to be mistaken for Brownian noise and for Brownian noise not to be mistaken as a signal, a signal should carry an energy that is significantly larger than *kT*. *kT* constitutes the average energy in the thermal noise band [20]. This baseline criterion already works to explain some of the physiology of the electric sensing organs. The electric fields are picked up by the ampullae of Lorenzini. These ampullae terminate at pores in the skin around the fish's head. They are enclosed in a highly resistive material and are filled with a very conductive gel. The eventual setup is equivalent to an electrical wire with no voltage drop inside. These ampullae are, furthermore, well insulated against electrical noise that originates from the fish's own physiology. Two pores that are about 10 cm apart on the surface of the fish's head can, on the inside ends, be separated only by a few nanometers. A field of 500 nV/m can be detected. Two pores that are 10 cm apart on the surface could thus transfer 50 nV into a transmembrane potential.

By having a lot of ion channels that are sensitive to such small voltage variations, the thermal noise can be effectively averaged out. With N ion channels instead of just one, N times as much signal strength is picked up. The thermal noise at each channel is independent of that at any other channel. The noise is zero-average and the noise variances are added up for N channels. So the average noise amplitude will be only $\sqrt{N}$ times as large if N channels are involved instead of one. After detection, the fish has to amplify this signal to the millivolt range that the nervous system operates with. Amplifier noise constitutes a problem that builders of electric circuits have dealt with for decades. Amplifier noise is nonequilibrium noise, and we will discuss it in the next section. Over the past decade, researchers have built up a good and detailed understanding of the physiology [21] and physics [22,23] of the fishes' amplification system.

Many animal species have the ability to detect the geomagnetic field. Two mechanisms have been proposed for magnetosensitivity. The first mechanism involves chemical transitions that are sensitive to external magnetic fields. Upon excitation by light, many polyatomic molecules will start transiting between the singlet ground state, the singlet excited states, and the excited triplet state. The energy difference between a singlet ($\uparrow\downarrow$) state and a triplet ($\uparrow\uparrow$) state is affected by an external magnetic field. This energy difference is generally small for fields of the magnitude of the Earth's magnetic field. But the magnetism that living cells generate is even smaller. A magnetically sensitive reaction of this type is therefore not subject to significant thermal noise. However, a detection limit can be established by considering a model in which reacting product molecules can bind to receptors. There is an innate stochasticity in chemical reactions; rates represent an average behavior, and there is a Gaussian distribution around this average. This is called fundamental chemical noise, and we will come back to it later in this chapter. In this model, the average number of occupied receptors varies with the magnetic field, and the detection limits are set by this fundamental chemical noise [24]. The fact that many bird species actually need light for their magnetic compass to work is a strong indication that singlet–triplet transitions are involved in the navigation. Recently, additional evidence was found when it turned out that robins get disoriented when they are subjected to an RF magnetic field that oscillates at the singlet–triplet resonance frequency [5] (for more details, see Chapter 6 on free radical models).

The second mechanism that has been proposed to explain magnetosensitivity involves the small (<100 nm in diameter) granules of magnetite (Fe_3O_4). This material, also known as lodestone, is biochemically formed and has about 30% of the magnetic strength of pure Fe. In the 1970 s, it was discovered that certain microbes use single-domain magnetite granules, also called magnetosomes, as a kind of rudder to help them stay under water right at the interface between the water and the mud at the bottom. There is a force trying to align the magnetic granule(s) with the Earth's magnetic field,

and the microbe thus ''finds out'' what its own orientation is relative to the inclination of the Earth's magnetic field [25,26]. For a single-domain magnetite granule of about 100 nm in diameter, the product μB of the magnetic moment μ and the Earth's magnetic field B amounts to about $5kT$. This $5kT$ alignment is sufficient to exceed the kT thermal agitation in the granule's rotation. In higher animals it appears that the granules are commonly embedded in biopolymers and lined up to form a rigid linear rod. Such an alignment effectively increases the magnetic moment and thereby the sensitivity to small variations in the magnetic field [27]. Indications are that there can be up to a million magnetite-containing cells in the brain of almost any animal. Even humans, who exhibit no apparent magnetosensitivity, have magnetite in their brain tissue [7,8].

The intensity of the Earth's magnetic field varies from 25 to 65 μT, and the direction varies from parallel to perpendicular to the Earth's surface. The magnetic sensitivity of, for instance, homing pigeons has been shown to be such that field variations smaller than 10 nT can be detected. With such a sensitivity the pigeon can use the change of the magnetic field vector to furnish itself a kind of global positioning system (GPS) [29]. Recent data indicate that some birds incorporate both magnetite and singlet–triplet chemistry in their magnetosense [5].

It is tempting to hypothesize that extremely low-frequency (ELF) radiation or microwave radiation could have a physiological effect through the interactions with magnetosomes. Cells produce their own electricity and concurrent electric noise. But there is no significant endogenous magnetic field noise. So the magnetic part of ELF radiation or microwave radiation would not have to compete against such endogenous biological noise. The average 24-h personal 60-Hz magnetic field due to house wiring, distribution lines, electric motors, etc., for individuals in the U.S. population is about 10^{-7} T [30], that is, orders of magnitude smaller than the earth's stationary magnetic field. Starting from this premise, the magnetosome in the cytoplasm was modeled as a damped harmonic oscillator with an external 60-Hz modulation [31]. The restoring force is the force pushing to align the magnetosome's moment with the earth's magnetic field, and the damping is due to the viscosity of the cytoplasm. The associated equation is easily solved. Using reasonable values for the involved parameters, it is was found that even with exposure to a 60-Hz field with an amplitude of 5 μT, the alternating field transfers an amount of energy to the magnetosome that is orders of magnitude smaller than kT. In other words, the thermal agitations in the rotation far overwhelm any ''signal'' from an ambient 60-Hz field. But subsequently, the legitimacy of a simple linear approximation was questioned [32]. It was pointed out that there are intricacies that make the viscosity of the cytoplasm, which determines the damping coefficient in the model, hard to specify. Most importantly, the possibility of many individual magnetosomes in a cell acting in concert should be considered. With N magnetosomes in a cell instead of just one, the signal-to-noise ratio is $\sqrt{N}$ times larger. The explanation for this apparent amplification is the same as with the aforementioned N ion channels in the shark's electroreception. An alternative model that includes such cooperativity leads to a signal-to-noise ratio that is well over unity with a 2-μT amplitude 60-Hz magnetic field [32]. However, almost nothing is currently known about how forces on magnetosomes are transduced into physiological signals. More solid estimates of detection thresholds can probably be derived only after such biophysical mechanisms are revealed.

Electric fields are also of interest. Close to a power line, a human can be exposed to an electric field of about 10 kV/m. Two steps have to be taken to get to an assessment of the transmembrane voltage that such an exposure leads to. First of all, living tissue is much more conducting than air. So, charge in the tissue will move and follow the external field until it is compensated. Depending on the amount of movable dipoles, different materials

have different dielectric permittivities. The ratio between the internal field and the field in the air is [33,34]:

$$\frac{E_i}{E_0} \approx \varepsilon_0 \omega \rho_t \tag{7.4}$$

Here $\varepsilon_0 = 8.8 \times 10^{-12}\ \mathrm{C^2/(N\,m^2)}$ represents the dielectric permittivity of a vacuum, ω is the angular frequency ($2\pi f$), and ρ_t is the resistivity of the tissue. So for a frequency of about 100 Hz and with a typical tissue resistivity of about 1–2 Ω m, the attenuation factor for the field entering the body is found to be in a range of 10^{-8}–10^{-7}. Hence, most of the external field goes around the person in the way water in a river flows around a big rock. Once inside the tissue, an amplification at the cell membranes occurs again through the mechanism explained in the previous paragraph. For a spherical cell with a diameter of about $d = 10\,\mu\mathrm{m}$ in a field E, the voltage across the diameter will be $\Delta V = Ed$, and the eventual field in the membrane will be of the order of $E_{\mathrm{mem}} \approx E(d/h)$, where h is the thickness of the membrane. With $h \approx 5\,\mathrm{nm}$ we find an amplification factor of about a 1000. We thus find a net conversion factor of 10^{-5}–10^{-4} and an electric field of about 0.1–1.0 V/m across a membrane as a result of the 10-kV/m power line exposure. This leads to an ELF-induced potential difference of at most 10^{-8} V across the membrane. It should, however, be noted that muscle cells or nerve cells are cylindrically shaped and may have lengths in the millimeter or even centimeter range. When the imposed field is along the axis of the cylinder, there may be a conversion factor at the caps of the cylinder that is two to three orders of magnitude higher.

When a living cell is suddenly exposed to an external electric field, ions will start flowing in the conducting interior to compensate for this field. In a typical mammalian cell, it is generally within microseconds that ions have accumulated near the membrane to achieve a zero intracellular electric field. This means that stationary electric fields and ELF (<300 Hz) AC fields distribute over cell membranes. Power lines and high-voltage distribution stations have been the subject of a lot of public anxiety. The power grid operates at 60 Hz in the United States and at 50 Hz in most other countries, that is, well within the ELF regime.

The 10^{-8} V that we derived may appear small relative to, for instance, the transmembrane potential of about 0.1 V that is present in about every living cell. However, when we talk about detectability, this 10^{-8} V should first be compared to the transmembrane voltages due to Brownian motion. The thermal noise voltage across standard resistors was already detected in the 1920s [35]. A formula was subsequently derived by Nyquist [36]:

$$\langle dV^2 \rangle = 4kTRdf \tag{7.5}$$

This equation gives the average square voltage in a frequency window of width df. The noise is white, that is, it has the same intensity at all frequencies. Technically, this would lead to an absurdity. It would imply that the noise carries an infinite amount of energy. However, as Nyquist already pointed out, $\langle dV^2 \rangle$ starts vanishing when we get to high frequencies f where $hf \approx kT$. Here, h represents Planck's constant, $h = 6.6 \times 10^{-34}\,\mathrm{J\,sec}$. At these high frequencies, quantum physics takes over and makes $\langle dV^2 \rangle$ go to zero. Such high frequencies are not in our realm of interest.

What Nyquist had in mind for a resistor in his derivation was a Brownian gas of frequently colliding charge carriers. With a 5-nm cell membrane that consists of a lipid bilayer with embedded proteins, the charge carriers are small ions (Na^+, K^+, Cl^-, etc.).

The ions do not form a ''gas'' inside the membrane, and it is not *a priori* obvious that Nyquist's formalism would apply. The equilibrium noise current through a membrane that separates two ionic solutions is due to two-sided shot noise. Shot noise was first described by Schottky [37] in the context of vacuum amplifier tubes. It is due to the elementary charge being finite and the charge carriers making random ''jumps.'' It can be shown that two-sided shot noise ultimately leads back again to Nyquist's Equation 7.5 [38,39]. Ultimately, Equation 7.5 is a manifestation of something much more general than Nyquist may have had in mind. What underlies Equation 7.5 is Einstein's fluctuation–dissipation theorem. This theorem says that the same random collisions that cause diffusion, thermal noise, or shot noise also cause dissipation, friction, or resistance. The theorem, moreover, makes this connection quantitative:

$$\beta = \frac{kT}{D} \tag{7.6}$$

For the motion of a macromolecule in a liquid, D is the diffusion coefficient and β is the coefficient of friction, that is, the ratio $\beta = F/\upsilon$, where F represents the pulling force and υ represents the resulting average speed. But in the context of the current through a membrane, β represents the electrical resistance ($R = V/I$). For D we find $D = e^2 P_S c$ in the membrane electrical case. Here, P_S is the membrane permeability to the monovalent ion S that is responsible for the current, c represents the concentration of this ion on both sides of the membrane, and e is the elementary charge.

Electrically, a cell membrane can be modeled as in Figure 7.1a. A lipid bilayer membrane has a capacitance of about 1 $\mu F/cm^2$. The capacitance of an actual cell membrane is generally not much different. The resistance of a pure lipid bilayer depends on the ionic concentrations of the solutions on either side of the membrane. With these concentrations at biological levels the resistance of a lipid bilayer membrane can be as high as $10^9\ \Omega\,cm^2$. Because of the presence of ion channels, ion transporters, and ion pumps [40,41], an actual cell membrane has a resistance that is orders of magnitude smaller (typically about $10^3\ \Omega\ cm^2$). The resistance of a patch of membrane is inversely proportional to the area of that patch. So, in order to characterize a membrane, the approach is to measure the resistance through an actual patch and then multiply it with the surface area of that patch. That is why we give the resistance of a membrane in terms of $\Omega\ cm^2$.

The setup in Figure 7.1a is equivalent to the one in Figure 7.1b, that is, an ordinary RC circuit. When calculating the characteristic time, RC, of the circuit, the surface area cancels

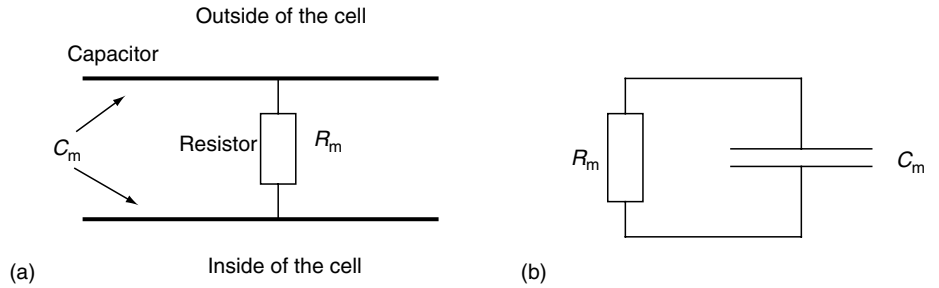

FIGURE 7.1
The electrical structure of the membrane is shown on the left. R_m and C_m are the resistance and capacitance between the inside and outside of the cell, respectively. The resistor also provides a thermal electromotive force. The equivalent circuit is shown on the right.

out. For a pure lipid bilayer the *RC* time constant can be of the order of minutes. But for a cell membrane it is of the order of milliseconds.

In our context, the resistor in Figure 7.1 is not just a resistor, but, following Nyquist (cf. Equation 7.5), also a white noise generator. At each frequency the resistor generates a harmonic oscillation. All these harmonic oscillations have the same amplitude. To evaluate the voltage across the capacitor, we thus have to analyze a simple *RC* circuit with an AC source. It has been argued that the high frequencies, that is, $f > (RC)^{-1}$, that are generated in the resistor do not have enough time to build up across the capacitor [42]. However, for low-frequencies, that is, $f < (RC)^{-1}$, changes are sufficiently slow for the capacitor to keep up and follow the voltage in the resistor. In this view the transmembrane voltage is the voltage across the capacitor, and the equilibrium noise is thus expected to occur mostly at low-frequencies. As mentioned before, the *RC* time of a cell membrane is of the order of milliseconds, and ELF fields thus operate in the $f < (RC)^{-1}$ regime where the noise is largest. A straightforward quantitative analysis shows that the low-frequency equilibrium noise far overwhelms any reasonable ambient power frequency field [42]. There would be no way to ever instantaneously detect such a field.

It was later put forward that everything that is happening in the cell membrane should, in the model of Figure 7.1, be imagined to happen inside the resistor [43]. Membrane proteins go through their catalytic cycle against a background of intramembrane noise. Inside the membrane means, in the context of Figure 7.1, inside the resistor. In this picture, the thermal noise voltage (cf. Equation 7.5) derives from a net electric field that results from inhomogeneities in the distribution of the charge carriers. Now at low-frequencies, the capacitor will be able to follow the imposed oscillation and effectively produce a field to counter the field generated inside the resistor (Figure 7.1a). This model thus leads to a vanishing net potential inside the membrane at low-frequency. At high frequency, the voltage changes in the resistor are too fast for the capacitor to keep up with. The capacitor will remain uncharged, and the thermal AC voltage will not be compensated for.

However, Figure 7.1 is no longer the appropriate model when we try to derive the intramembrane electric fields. For a cell of about 20 μm in diameter, the surface area amounts to about a billion square nanometers. The membrane is only about 5 nm thick, so the resistor resembles a very thin sheet. The lateral conductivity, that is, the conductivity from one place on the sheet to another, is very low. So at different spots on the sheet, different unrelated noise fields are generated. The more sensible model would therefore be one where the resistor in Figure 7.1 is cut up into millions of independent parallel resistors. Each of these resistors creates its own field. The capacitor plate corresponds to the conducting liquid on either side of the membrane, and it can be conceived of as having perfect lateral conductivity. So each resistor generates its own particular field, but they all experience the same field from the capacitor. With this model the noise gets very large. Not only there are more, say *N*, resistors producing noise. Each of these resistors has a resistance *NR* (*N* parallel resistors of resistance *NR* lead to a net resistance of *R*) and, according to Equation 7.5, thus produces more noise. Because the *N* parallel resistors that make up the resistance *R* are independent, they oscillate out of phase at each frequency *f*. As a result the parallel resistors end up pushing a lot of current in and out of each other. Most of the generated noise current thus remains intramembrane and never reaches the capacitor. The mathematics associated with this parallel setup is challenging, but an exact solution can be derived [39,44]. The capacitor, and therefore the *RC* time, plays no role in the intramembrane noise. The intramembrane noise is white and has an intensity that is many orders of magnitude larger than the noise that reaches the capacitor. What matters for biological function is actually the intramembrane noise. This, after all, is the noise that a membrane-embedded protein would ''feel.'' The protein's catalytic cycle takes place

against the background of such noise. The parallel setup model leads to a noise intensity that is much larger than that of the earlier models.

At first sight, all this extensive treatment of intramembrane noise may seem to have little to do with the two-sided shot noise that a membrane is subject to. However, when rigorously modeling the membrane as a thin sheet in an ionic solution, something similar to the overwhelming intramembrane noise is found. The ions that constitute the net charge on the membrane in Figure 7.1a move across the membrane–solution interface with an average speed of about 100 m/sec. This is just their thermal motion, and it is easily derived from $(1/2)mv^2 \approx kT$. This effectively causes laterally traveling electric pulses in the membrane. The noise intensity of these traveling electric pulses appears to be many orders of magnitude higher than the noise that is due to the shot noise-like membrane passages by the ions [39].

Current models of membrane noise thus lead to transmembrane voltage noise estimates that far exceed the strength of any reasonable magnitude ELF field-induced ''signal.'' What the previous paragraphs lead up to is the conclusion that an ELF signal cannot be detected instantaneously.

However, under certain conditions and given enough time, even the smallest signal can get out of the noise band. The following example is meant to illustrate this. Consider the system depicted in Figure 7.2. Let the the resistance R represent a membrane patch. For simplicity, imagine that on either side of the resistor there is an infinite reservoir (i.e., a capacitor with infinite capacitance), so no net voltage can develop across the resistor. The average square charge $\langle q^2(t)\rangle$ that accumulates on either side of the membrane can be easily derived from Equation 7.5 and amounts to

$$\langle q^2(t)\rangle = \frac{2kT}{R}t \tag{7.7}$$

Again, there is an obvious analogy between Equation 7.7 and the well-known diffusion formula $\langle x^2(t)\rangle = 2Dt$, which describes the average square displacement of a particle with a diffusion coefficient D during a time interval of length t. The above formula clearly shows how, in an electrical context, kT/R plays the role of the diffusion coefficient D.

From Equation 7.7 we infer that for the accumulated charge as a function of time we have $|q_{\mathrm{Br}}(t)| \approx \sqrt{\langle q^2(t)\rangle} \propto \sqrt{t}$. The thermal noise-driven accumulation of any charged or uncharged molecule on either side of the membrane carries this $\sqrt{t}$ proportionality. The coupling of ELF electromagnetic fields to biochemical activity occurs mostly through

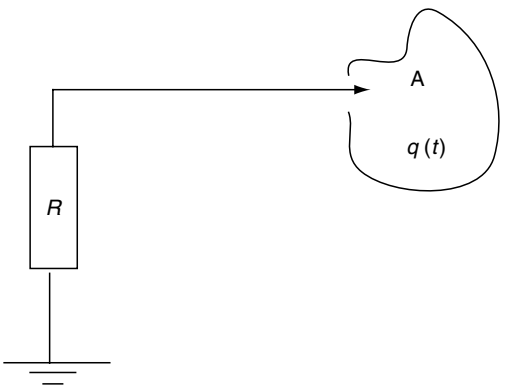

FIGURE 7.2
A resistor is connected to the ground and to an infinite reservoir A. The net voltage between the reservoirs remains zero. The situation is like the one in Figure 7.1 with the capacitor having infinite capacitance. Because of Brownian motion of electrons in the conduction band, there is a zero-average fluctuating current through the resistor. The net charge accumulating in the reservoir A is the result of these fluctuations in the same way that diffusive displacement is the result of random Brownian kicks. We have $\langle q^2(t)\rangle = 2(kT/R)t$ for the average square charge accumulation in time t.

membrane proteins. Membrane proteins whose conformational changes involve significant changes of the dipole moment are particularly sensitive. ELF fields can affect the catalytic rates of such proteins. So, for instance, electrogenic ion pumps [41], and also transporters or pumps that just carry a dipole, may have a slightly altered throughput in the presence of an ELF field. If there is no restoring force for a transported or pumped molecule, the accumulation will continue. The cumulative effect of the altered throughput will be a linear function of time. The excess charge that accumulates because of an ELF field thus follows $q_{\mathrm{ELF}} \propto t$.

Consequently, we see that on a small timescale the Brownian noise ($\propto \sqrt{t}$) will be stronger than the signal ($\propto t$). But there will always come a time $t = t_*$ when $|q_{\mathrm{B}r}(t_*)| = |q_{\mathrm{ELF}}(t_*)|$, and we then achieve S/N = 1. It depends on the values of the proportionality constants when t_* occurs. If molecular change is the measurement criterion, then it is only on timescales of the order of t_* that the effect becomes measurable. Estimates for t_* with realistic ELF exposure have been made [45] and have led to a timescale larger than the age of the universe.

7.6 Nonequilibrium Noise

In the previous section, we considered equilibrium noise. A living cell, however, constitutes a system that is far from equilibrium. Between the intracellular and extracellular solutions there is an electric potential difference of about 100 mV. For ions like Na^+, K^+, Cl^-, and Ca^{2+} there is a more than tenfold difference between intra- and extracellular concentration. The 100-mV transmembrane voltage over a width of about 5 nm implies a very strong field of tens of megavolts per meter.

The electrochemical potential across the cell membrane is an energy source for many processes [41]. The Na, Ca exchanger, for instance, is a membrane protein that picks up a sodium ion on the outside and then goes through a cycle in the course of which it drops the sodium ion off on the inside. The protein couples the energetically downhill movement of sodium to the uphill transport of calcium. In the course of the cycle a calcium ion is picked up on the inside and pumped, against the electrochemical potential, to the outside. The membrane potential is maintained by ATP-driven ion pumps. The most common of these is Na, K-ATPase. This is a membrane protein that, in the course of its catalytic cycle, hydrolyzes one ATP and uses the released energy to transport three sodium ions out of the cell and bring two potassium ions in.

Each working protein is like a small engine. A living cell contains millions of these engines: they are continuously converting energy from one form to another, and in the process, they are also generating heat, that is, dissipating energy. A living cell constitutes a far from equilibrium system, and the continuous transduction and dissipation of energy generates noise, which adds to the thermal, Brownian noise that was discussed in the previous section.

It would not be against the first law of thermodynamics (i.e., conservation of energy) if ion pumps were to extract heat from the environment and use it to power the maintenance of the transmembrane potential. This would, however, be in gross violation of the second law of thermodynamics. There are many equivalent formulations of the second law. The most common formulation is the proposition that every isolated system strives to increase and maximize its entropy. The teleological form of this formulation is somewhat bewildering. After all, most laws in science are formulated as conservation laws, for

example, conservation of energy, or as causal laws, for instance, Newton's $F = ma$. However, after properly defining entropy, entropy maximization is often the easiest form of the second law to work with when dealing with macroscopic systems.

When going to the molecular realm, the second law can pose some challenging paradoxes. Consider, for instance, an ion channel in a cell membrane. Many ion channels rectify, that is, they pass current more easily in one direction than in the other. So the I–V characteristic is not a straight line through the origin, but it also has a curvature. Any frequency from the white spectrum of equilibrium noise should, in principle, be rectified. It thus might look like a rectifying ion channel could use zero-average equilibrium Nyquist noise to charge a battery. It would not work, of course. As pointed out above, it would be in violation of the second law. Thinking in the context of rectifying p–n junctions, solid-state physicists ran into this paradox long before ion channels were discovered. In 1950, L. Brillouin wrote a paper ''Can the Rectifier Become a Thermodynamic Demon?'' [46]. In this paper, he presents a short derivation to show that in a circuit with all components at the same temperature, no diode can rectify. He is aware that his case represents a special case of the so-called principle of detailed balance: ''No system in thermal equilibrium in an environment at constant temperature spontaneously and of itself arrives in such a condition that any of the processes taking place in the system by which energy may be extracted, run in a preferred direction, without a compensating reverse process.'' The principle is a consequence of the second law [47,48] and, for our rectifier, basically states that there must, on average, be as much current in one direction as there is in the opposite direction.

In the *Feynman Lectures on Physics* [49] a ratchet and pawl system, originally thought up by Smoluchowski [50], is considered and eloquently discussed. The device operates as a mechanical rectifier (Figure 7.3) and essentially establishes the mechanical equivalent of Brillouin's paradox. The paradox is solved with the realization that the pawl must also be

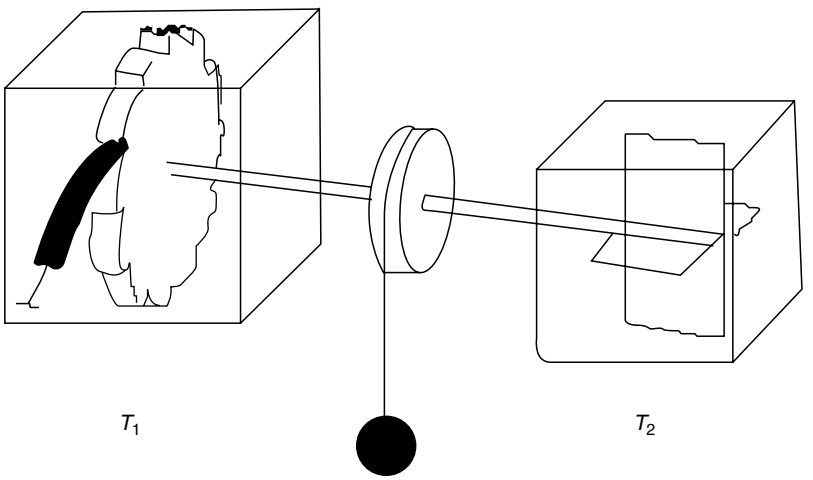

FIGURE 7.3
The mechanical thermal ratchet as it was originally conceived by Smoluchowski [50] and later discussed by Feynman et al. [49]. The device is small, and the paddle wheel in the right reservoir is moved by collisions of the molecules from the surrounding medium against the paddles. Because of the asymmetry of the teeth, the ratchet and pawl in the left reservoir allow motion in one direction and block it in the opposite direction. With the resulting net rotation it should be possible, in principle, to lift a weight. However, it would be in violation of the second law of thermodynamics to extract work from thermal fluctuations in the equilibrium situation, that is, $T_1 = T_2$. The solution of the paradox lies in the realization that the ratchet and pawl are also subject to thermal fluctuations if the system is small.

subject to thermal noise. The pawl involves a spring, and the spring will, at thermal equilibrium, exhibit a Boltzmann distribution over the accessible energy range. Even here the second law is involved, though on a deeper level. Given the macroscopic variables (e.g., temperature, concentration, pressure, etc.) there are still many possible molecular arrangements, that is, microstates, that correspond to that macrostate. For a fixed amount of energy the Boltzmann distribution is the energy distribution that has the most permutations [20]. It is therefore the most likely distribution. On the level of statistical mechanics, the second law can be formulated as the rule that given a macrostate, every microstate that corresponds to that macrostate has equal probability.

Second law issues can be subtle. The connection between statistics, entropy, information, and physical work still poses paradoxes that are hard to fathom. Books and articles still appear in which researchers are attempting to come to a fuller understanding and a better intuition [51,52]. At the scale of ion channels the simple invocation of detailed balance reveals little. An appropriate description is like the one Feynman gave for his mechanical ratchet and pawl: it involves Boltzmann distributions and Brownian motion. So it would simply be wrong to take any frequency from the white spectrum of equilibrium noise and model a rectifying ion channel as subject to this oscillation. The ion channel itself and its Brownian fluctuations have to be included in the description. At equilibrium, no part of a system can be ''subject'' to any other part. This is what detailed balance can be interpreted to mean.

However, when energy is dissipated, it is possible for one part of the system to impose its fluctuations on another part. When a rectifying ion channel is subject to nonequilibrium fluctuations, it will actually rectify the fluctuations and drive a net current. Consider, for instance, an electrogenic ion pump like Na,K-ATPase. As was mentioned before, this pump utilizes the energy of ATP hydrolysis to pump three sodium ions out and pump two potassium ions in. All this transport is against the electrochemical potential and requires about $15kT$ units of energy per stroke under physiological conditions. The power source is the hydrolysis of ATP, which under physiological conditions, releases about $20kT$ units of energy per cycle. It is the remaining $5kT$ that drives the process forward and that is ultimately released as heat. Na,K-ATPase is binding and releasing ions and thus generates fluctuating electric fields in its direct vicinity. For a nearby ion channel these fields can be conceived of as imposed because the $5kT$ that drives the Na,K-ATPase cycle is enough to overwhelm the small amount of energy ($<1kT$ [53]) necessary for the opening or closing of a channel. There is no feedback from the channel to the pump. The channel will rectify the fluctuations as a result, and a zero-average field can thus lead to net charge transport. In essence, the nonequilibrium fluctuations generated by the pump and imposed on the channel are part of the conversion of chemical energy, that is, the energy in ATP, to an electrochemical potential across the membrane.

So energy-dissipating, nonequilibrium oscillations and fluctuations are able to do work. ELF radiation from outside the organism can impose a varying field on an ion channel in much the same way that the nearby ion pump from the previous paragraph can impose a field on an ion channel. ELF radiation brings energy into the organism. Part of this energy will be dissipated to become heat, and part of it may be converted into chemical or electrical work. There is obviously no feedback from an ion channel back to the ELF source.

The selectivity of ion channels for the different kinds of ions is still hard to understand and model. But the rectification property is much easier to intuit (Figure 7.4). The channel is shaped like an asymmetric double cone, and charges in the lining of the channel are

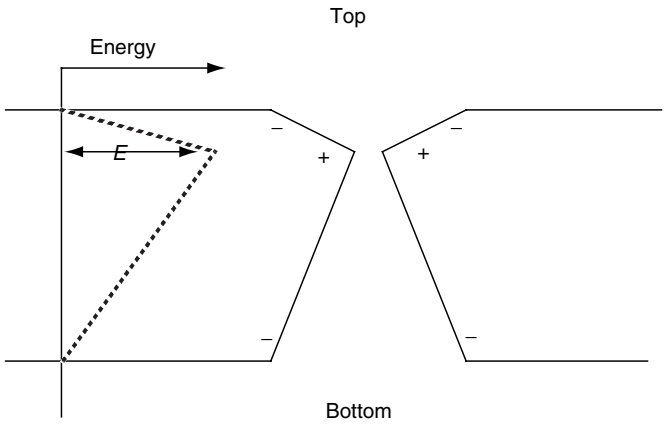

FIGURE 7.4
A simple continuum model of an ion channel imagined to be shaped like an asymmetric double cone. The energy profile on the left depicts the activation barrier that a positive ion going through the channel has to pass. The barrier has an obvious anisotropy.

indicated in the figure. A sodium or potassium ion that is going from the top to the bottom of the channel faces a rapid increase of the potential and then a slow decrease. A sodium or potassium ion that goes through in the opposite direction faces a slow increase and a fast subsequent decrease. A positive ion thus has a larger force to overcome when going from top to bottom than when going from bottom to top. Because of this, an imposed zero-average oscillation will lead to a net current [54]. As a matter of fact, any anisotropic potential shape along the length of the channel will rectify a zero-average harmonic field to lead to a net current [55]. Ion channels are proteins consisting of many amino acids, and anisotropy along the inside lining will be the rule rather than the exception.

The plethora of ratchet research in the late 1990s has made it clear that almost any zero-average oscillation or fluctuation imposed on a ratchet-like structure as in Figure 7.4 leads to a net current. Imagine, for instance, a temperature oscillation. With energy expressed in units of kT, a variation in temperature implies an oscillation of the barrier height E. Because of the difference in relaxation times on the slopes on either side of the barrier, a net current will result [55–58]. Recently, ever more examples have been found of nature exploiting ratchet effects for the purpose of regulation [59].

Researchers have meanwhile also succeeded in making artificial channels. Cone-shaped (and therefore anisotropic) channels form when a heavy ion is shot through an artificial membrane [60,61]. The I–V characteristic for the current of different types of ions has subsequently been recorded. It has even been experimentally shown that net charge transfer results when a zero-average field is imposed on such an artificial channel. The channel is thus made to behave like a kind of pump that converts an AC input into a DC output [62].

Imagine a number of identical anisotropic channels in a vesicle with an otherwise impermeable membrane. Next, put a large number of such vesicles in a beaker with an ionic solution. Any nonequilibrium fluctuation from the environment, or any ''signal'' for that matter, will now be picked up and converted into an electrochemical potential. The convection caused by a temperature gradient will heat up and cool down the vesicles and lead to their electrically charging up. The electric component of an ELF electromagnetic field will do the same thing. The beaker could thus be a battery that recharges by harnessing any incoming nonequilibrium fluctuation. This mechanism might, moreover, have played a role in the emergence of early prokaryotic life.

The Fourier spectrum of the noise that is associated with processes that dissipate energy is not white. Nonequilibrium noise appears to have higher amplitudes at lower frequencies; in other words, it exhibits an intensity that decreases with frequency. The so-called $1/f$ noise was first studied in the 1920s in the very nonequilibrium context of thermionic vacuum tube amplifiers [37]. In current scientific discourse the term ''$1/f$ noise'' actually applies to all noises that have spectral densities behaving like $1/f^{\alpha}$, where α ranges from about 0.5 to about 1.5. Especially in electrical devices, such noise is very commonly and easily observed. It is also known as ''excess noise'' or ''flicker noise.'' In a log–log plot the $1/f^{\alpha}$ behavior usually extends over several frequency decades.

In the 1930s, it was proposed that the flicker noise originated from a variable number of electrons present in the conduction band. Electrons would shuttle between a free state and a bound state as in a chemical reaction. Let the relaxation time of that reaction be $1/\lambda$. This leads to a simple exponential relaxation $N(t) = N_0 \exp[-\lambda t]$ after any kind of fluctuation that has a magnitude N_0. The Fourier transform of the exponential decay is easily found:

$$F(\omega) = N_0 \int_{t=0}^{\infty} \exp\left[-(\lambda + \mathrm{i}\omega)t\right] \mathrm{d}t = \frac{N_0}{\lambda + \mathrm{i}\omega} \tag{7.8}$$

For the power spectral density, $S(\omega) = \|F(\omega)\|^2$, we find:

$$S(\omega) \propto \frac{1}{\lambda^2 + \omega^2} \tag{7.9}$$

where the proportionality constant involves the magnitudes of the fluctuations as well as the rates at which fluctuations occur. The power spectral density is a useful quantity as it describes how the energy in the noise is distributed over the different frequencies. $S(\omega)\mathrm{d}\omega$ is proportional to the amount of power that the noise carries between the frequencies ω and $\omega + \mathrm{d}\omega$. Equation 7.8 describes a so-called Lorentzian power spectrum. With a log scale for the frequency, the resulting curve is a sigmoid. At high ω, $S(\omega)$ behaves like $1/\omega^2$. As better data became available, it was found that a better fit was obtained when a distribution of infinitely many relaxation times was assumed [63]. Take, for instance, a uniform distribution of relaxation times between λ_1 and λ_2. With Equation 7.9 this leads to:

$$S(\omega) \propto \frac{1}{\lambda_2 - \lambda_1} \int_{\lambda_1}^{\lambda_2} \frac{1}{\lambda^2 + \omega^2} \mathrm{d}\lambda = \frac{1}{\omega(\lambda_2 - \lambda_1)} \left\{ \arctan\frac{\lambda_2}{\omega} - \arctan\frac{\lambda_1}{\omega} \right\} \tag{7.10}$$

It is easy to check that on $\lambda_1 < \omega < \lambda_2$ this $S(\omega)$ is approximately proportional to $1/(\omega(\lambda_2 - \lambda_1))$. This $S(\omega)$ is, moreover, roughly constant for $\omega < \lambda_1$ and drops off like $1/\omega^2$ when $\omega > \lambda_2$.

If we let, between λ_1 and λ_2, the relaxation rates contribute proportional to $\lambda^{-\beta}$, we can actually get any $1/f^{\alpha}$ dependence that we want, since

$$S(\omega) \propto \int_{\lambda_1}^{\lambda_2} \frac{1}{\lambda^{\beta}(\lambda^2 + \omega^2)} \mathrm{d}\lambda \propto \frac{1}{\omega^{1+\beta}} \quad \text{for } \lambda_1 < \omega < \lambda_2 \tag{7.11}$$

At $\omega < \lambda_1$, this spectrum would again flatten out.

In experimental practice with electrical resistors and amplifiers the $1/f^{\alpha}$ behavior has been observed to extend over more than six frequency decades with no noticeable flattening at low-frequency [64].

$1/f^{\alpha}$ spectra have been observed in nature in a wide variety of systems: electrocardiac waves [65], the variation of sea levels [66], tardiness at work [67], etc. An essential feature of $1/f^{\alpha}$ noise is that it exhibits self similarity, that is, if one magnifies both time and space with the appropriate factor, the noise pattern is indistinguishable from the original one. So the noise does not have a characteristic timescale or length scale. $1/f$ noise is often seen as a signature of the fractal character of nature.

In 1987, Bak et al. [68] proposed a model for a universal mechanism behind $1/f$ noise. In their landmark paper they illustrated the concept of ''self-organized criticality'' with a sandpile model. When a sandpile has an inclination steeper than a critical angle θ, avalanches will occur that bring the pile back to the critical angle. When sand is added to the pile in a random fashion, these avalanches do not exhibit a characteristic size, nor do they appear after regular time intervals. Instead, there are bigger avalanches that are relatively rare and smaller avalanches that occur more frequently. The size distribution follows a power law in the frequency f. For instance, in one day there can be one avalanche involving more than 1000 grains, 10 involving more than 100 grains, 100 avalanches involving more than 10 grains, and so on. The picture that emerges is one of a system that is sitting on the critical edge between two phases and is ''organizing'' avalanches to stay there [69]. The most commonly cited real-life example of self-organized criticality is the Gutenberg–Richter power law for earthquakes. It appears that every year, on average, there is one earthquake larger than magnitude 8, 10 earthquakes larger than magnitude 7, and 100 earthquakes larger than magnitude 6. Self-organized criticality is an attractive theory. It proposes a simple mechanism and predicts power laws that can be easily verified or falsified. It has been utilized in a wide variety of contexts [69]. It has, for instance, been applied to evolutionary theory [70] and has been used to explain frequency-size distributions of forest fires [71].

How truly universally applicable self-organized criticality is and to what extent its claims may be unwarranted are matters that are still very much under debate. The $1/f$ proportionality for earthquakes applies only between magnitudes 5 and 8. Even for the archetypal sandpile, things turn out to be more involved upon close inspection than self-organized criticality suggests. Accurate measurements [72–74] on real sandpiles showed that in many cases there is no $1/f$ pattern in the avalanches. It turns out that system parameters, like the grain size and the rate of sand addition, determine to a large extent what kind of spectrum eventually emerges. The entire concept of self-organized criticality collapses, of course, if fine tuning by the experimentalist is crucial for the $1/f$ spectrum to materialize. All in all, $1/f$ noise is not as universal as first thought, and the dynamics behind nonequilibrium noise are usually best unraveled with *ad hoc* models.

The node of Ranvier is where the action potential for myelinated nerve cells is generated [75]. There is a high concentration of ion channels in the node of Ranvier, and in the days before patch clamp, it was a good place to record membrane electrical activity. In the mid-1960s, Verveen and Derksen measured 5–10 min of cell membrane voltage noise at a Ranvier node of an unstimulated nerve cell [76,77]. The resulting power spectrum showed two decades, between 10 Hz and 1000 Hz, of $1/f$ noise (see Figure 7.5). This $1/f$ noise, they found, was much larger in magnitude than what Nyquist's $4kTR$ formula (cf. Equation 7.5) would predict. Following the explanation for $1/f$ noise in ordinary resistors (cf. Equation 7.10 and Equation 7.11), Verveen and Derksen suggested that an ion channel could, from time to time, get ''clogged up.'' The wide distribution of waiting times (i.e., the λs in Equation 7.8 through Equation 7.11) before getting unclogged would then give rise to the $1/f$ spectrum [78].

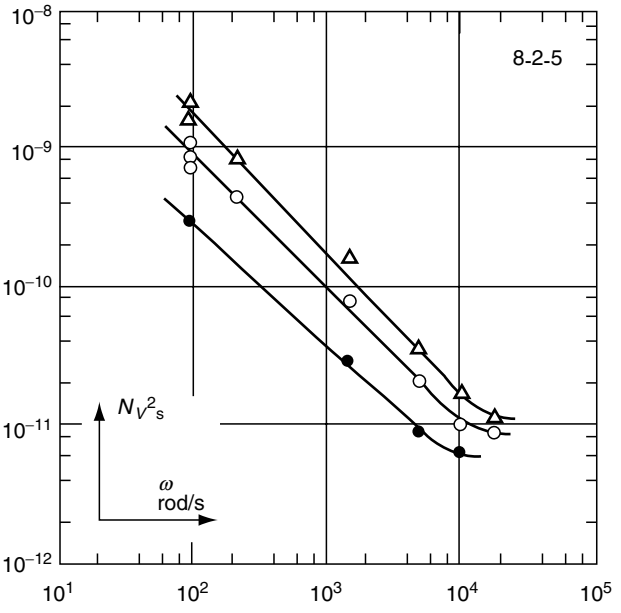

FIGURE 7.5
The voltage noise spectral densities from the frog node of Ranvier at room temperature at rest (open circles), at 10-mV depolarization (open triangles), and at 10-mV hyperpolarization (filled circles) [76,77]. (© Dutch Physiological Society. With permission.)

In the last two decades, single-channel recordings have shown how, even without stimulus, ion channels open and close repeatedly [40,75]. The kinetics behind the openings and closings is still very much a matter of debate. Modeling an ion channel as a two-state molecule with an open and a closed state and chemical steps with constant rates connecting these states appears not to account for the data in many cases. Electrophysiologists have commonly resorted to explaining the nonexponential distributions of open and closed times with a kinetic scheme that contains more than two states. With such an approach any distribution of open and closed times can always be fitted with a kinetic scheme [79–81]. It is just a matter of coming up with sufficiently many parameters (i.e., states and rates) to fit the data. In chemical kinetics the transitions are always assumed to be Markov transitions, that is, the probability of moving from a state 1 to a state 2 is constant and does not depend on the time that the molecule has been in state 1. A channel that is making such Markov transitions between a finite number of states always exhibits a power density spectrum that is a sum of Lorentzians. The number of characteristic times in the spectrum will always be one less than the number of states. If the characteristic times are sufficiently far apart, the power density spectrum will exhibit a number of identifiable plateaus when plotted on the customary logarithmic scale. The inflection points between the plateaus occur at the inverses of the characteristic times.

An alternative approach, foreshadowed by the aforementioned suggestion of Verveen and Derksen, has been to model the open to closed transition rates of an ion channel as time dependent, for instance $k(t) \propto t^{-\mu}$, where $0 < \mu < 1$ [82–85]. The exponent μ is taken to be smaller than unity to make $\int_{\tau}^{\infty} k(t)\, dt$ diverge for all $\tau > 0$ and thus guarantee the inevitability of an eventual transition. The proportionality $k(t) \propto t^{-\mu}$ leads to a decreasing transition probability, that is, the channel is ''stabilizing in its openess,'' as more time is spent in the open state. There is ample justification for the use of open–closed transition rates that vary in time. A protein has many degrees of freedom and is subject to many equilibrium and nonequilibrium fluctuations. If an intramolecular rearrangement, like a transition between an open and a closed state, can be modeled as the crossing of an

activation barrier, then that barrier will most likely not be fixed and stationary. A fluctuating barrier implies fluctuating open–closed transition rates. We could thus get the infinitely many relaxation rates that give rise to the $1/f$ power density spectra of Equation 7.10 and Equation 7.11. Under physiological conditions an ion channel is trafficking ions in an electric field of tens of megavolts per meter and comparable chemical gradients. This is a very nonequilibrium setup, and it has been conjectured that the channel operates as a self-organized critical structure. One authoritative textbook [65] states it as follows:

> A channel protein may be a self-organizing critical system. The channel protein consists of many pieces that interact with their neighbors. The energy added to the protein from the environment causes local strains that are spread throughout the structure. If these distortions spread faster than the time it takes for the structure to thermally relax, then the channel protein may be a self organizing critical system. If that is the case, then the fluctuations in the channel structure will be due to a global organization of the local interactions between many small interacting pieces of the channel protein. The fractal scaling would then be due to the fact the channel structure is poised at a phase transition between its open and closed conformational shapes.

Over the past few years increasing amounts of data have been gathered with ever more accurate technology. Recently, the $1/f$ power spectral density of a nerve cell that Verveen and Derksen discovered was more accurately rerecorded [86]. But through careful subsequent experimentation and computer simulations, these researchers were also able to show how the apparent $1/f$ result comes about as the sum of a number of Lorentzian contributions. Each type of channel has its own Lorentzian, and because of close characteristic times the sum of the individual sigmoids appears like a smoothly decreasing $1/f$ curve.

For a single channel, things often turn out to be much more intricate than simple $1/f$ versus Markov kinetics. In single-channel recordings of a bacterial ion channel it was found that actual channel openings and closings follow Markov kinetics and lead to Lorentzian contributions to the ultimate net power spectrum [87]. The $1/f$ noise that is present in the power spectrum originates from transitions between open states of a slightly different (about 1–5%) conductance. The rates of these miniconductance transitions appeared to be independent of the transmembrane voltage. The small transitions in conductance have been conjectured to be due to small clusters within the channel's structure moving in and out of the lining of the pore [87]. A cluster can cause a partial flow constriction when it sticks out into the pore. Following this idea, the apparent $1/f$ behavior can be attributed to many different clusters moving in and out with equally many different relaxation times. The voltage independence comes about because these clusters are either uncharged or the external electric field is somehow screened. Noise in synthetic channels has also been studied [88]. There it was found that potassium currents through a one-state, permanently open channel exhibit $1/f^2$ noise. An artificial channel that can open and close, on the other hand, was found to exhibit $1/f$ noise when the externally applied voltage is in the right regime. With this latter artificial channel there is good ground to attribute the open–closed transitions to the movement of ''dangling ends'' of polymers in the pore's lining. So the result supports the ''moving cluster'' for the mechanism behind $1/f$ noise in channels.

There appears to be no simple theory that can convincingly bring all manifestations of $1/f$ noise under one common denominator. All the indications are that an *ad hoc* approach to nonequilibrium noise phenomena is still the most fruitful one.

In ordinary resistors the amount of $1/f$ noise grows linearly with the dissipated power W. If we take $S(\omega)\,\mathrm{d}\omega$ to denote the power in energy per unit of time (watts) in an interval $\mathrm{d}\omega$, then we have for the power spectral density:

$$S(\omega) = \frac{gW}{f} \tag{7.12}$$

Here, g is a dimensionless constant the value of which depends on the type of resistor.

Nyquist noise is simple in that the net value of the resistance R fully determines the noise amplitude. With $1/f$ noise a more complex situation arises. Experimentally, the constant g (cf. Equation 7.12) turns out to be proportional to the volume-to-power ratio [89]. In Figure 7.6 the four resistors in design (b) are identical to the one resistor in design (a). It is obvious that (a) and (b) will have the same net resistance and therefore the same amount of Nyquist noise. Design (a), however, will exhibit four times as much $1/f$ noise as design (b). Design (b) is quieter because the energy dissipation is distributed over a larger volume. Generally, we have $g \propto 1/V$, where V denotes the resistor's volume. The gW in Equation 7.12 can be expressed as $g_\mathrm{e}w$, where g_e is the g-value for a single elementary charge carrier in the resistor and w is the energy dissipated in the volume of such a single, independent charge carrier.

Pumps and carriers move ions one by one. Imagine a single pump or carrier that moves ions across the membrane at a rate ν. During a small time interval $\mathrm{d}t$ there is a probability $p = \nu\,\mathrm{d}t$ that an ion is transported. We take $\mathrm{d}t$ to be sufficiently small so that the probability of more than one ion being transported during $\mathrm{d}t$ is negligible. We also take the duration of the catalytic cycle, that is, the ''processing'' time for an ion going through the membrane, to be negligible in comparison to the time between catalytic cycles. If we were not to make the latter assumption, we would simply have to multiply by the probability that an average channel is available for transport when we want to express the transport rate. For the average number of ions $\langle n\rangle_{\mathrm{d}t}$ transported by the channel in time $\mathrm{d}t$, we now have $\langle n\rangle_{\mathrm{d}t} = 1 \cdot p + 0 \cdot (1-p) = p$. For the variance we have $\sigma_{\mathrm{d}t} = \langle n^2\rangle - \langle n\rangle^2 = 1^2 \cdot p - (1 \cdot p)^2 = p(1-p)$. For M subsequent timesteps and $M\,\mathrm{d}t = T$, the variances add up, and we have $\langle n\rangle_T = Mp$ and $\sigma_T = Mp(1-p)$. So the standard deviation, $\sqrt{\sigma_T}$, works out to be proportional to $\sqrt{M}$. Over time the standard deviation becomes more and more negligible compared to the average. For sufficiently small $\mathrm{d}t$ we can take $1-p$ to be equal to 1, and we then have a variance that equals the average.

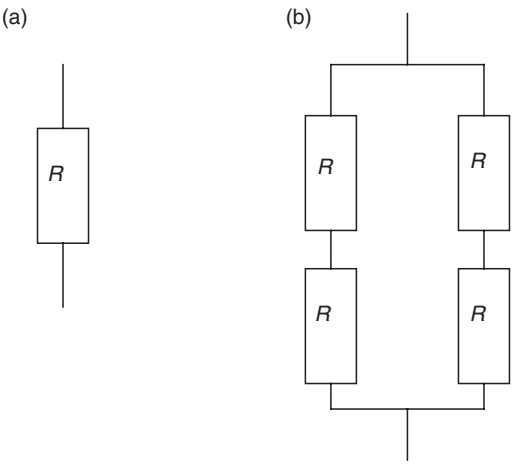

FIGURE 7.6
Design (a) and design (b) both have a net resistance R. They are different in that design (b) actually consists of two parallel resistors of $2R$. Designs (a) and (b) will exhibit the same amount of equilibrium noise, as it is only the net resistance (cf. Equation 7.5) that determines the equilibrium noise amplitude. It appears, however, that design (a) has four times as much power spectral density as design (b). The amount of nonequilibrium noise is proportional to the current density.

In the textbook by DeFelice [89] it is shown how the power spectral density of the process above amounts to $S(f) = 2\sigma_T/T = 2\nu$. The frequency-independent power spectrum can be intuited as follows. If the actual transport time through the membrane is small, then we can conceive of the transmembrane current as delta function-like pulses occurring at a rate ν. The Fourier transform of a Dirac delta function is a flat spectrum. In order to go from particle current to electrical current we must, to obtain the current power spectral density, multiply with the square of the charge of the involved ion. Taking this to be the elementary charge e, we find

$$S_i(f) = 2\nu e^2 = 2e\langle i\rangle \tag{7.13}$$

Here, $\langle i\rangle = e\nu$ denotes the average current through one pump.

Next, we let $\langle I\rangle$ denote the total transmembrane current due to pumps of a particular ion through the entire cell surface. We then have for the total current power spectral density:

$$S_I^{\mathrm{pu}}(f) = 2e\langle I\rangle \tag{7.14}$$

For a living cell in a steady state, for each kind of ion, there are just as many ions going in as there are going out, that is, there is just as much uphill transport through pumps as there is downhill flow through ion channels. So we have the same current $\langle I\rangle$ uphill as well as downhill. Below, we will first show that the downhill flow through the channels generates much more nonequilibrium noise than the uphill flow through the pumps. We will then show how the channel noise far exceeds the Johnson–Nyquist equilibrium noise.

Ion channels stay open for an average time of about $\tau_{\mathrm{op}} = 10^{-3}$ sec, and during that time there is a current of about 10^7 ions per sec (i.e., about 1 pA). So the equivalent of the elementary charge mentioned in the previous paragraph is now $N = 10^4$ ions.

However, before we blindly substitute Ne for e in Equation 7.14 to obtain the current power spectral density generated by the channel population of a cell, we have to take another source of variance into account. The channel-open time of about a millisecond is an average. If we view opening and closing of a channel as simple chemical steps between an open and a closed state, then the millisecond is the average of an exponential distribution of open times. For an exponential distribution the average open time equals the standard deviation in the open time. So the standard deviation ΔN equals N itself. The associated variance has to be added in. So we have $S_I^{\mathrm{ch}}(f) \approx 2\,\nu e^2\,(N^2 + (\Delta N)^2)$. The rate ν now represents the number of channel openings per unit of time. So we get for the current power spectral density produced by the channels:

$$S_I^{\mathrm{ch}} \approx 4Ne\langle I\rangle \tag{7.15}$$

So the channel contribution to the total nonequilibrium current noise is about 10^4 times as large as the contribution of the pumps. For the total current power spectral density, S_I^{noneq}, due to nonequilibrium currents, we thus neglect the pump contribution.

The above Equation 7.15 constitutes $S_I^{\mathrm{ch}}(0)$. At higher frequencies, when f approaches the average open time τ_{op} of the channel, $S_I^{\mathrm{ch}}(f)$ will decrease. The characteristic inverse time for a channel is $f_* = \tau_{\mathrm{op}}^{-1} + \tau_{\mathrm{cl}}^{-1}$, where τ_{cl} is the average closed time of the channel. With only one type of channel present in a cell, there will be a sigmoidally shaped, Lorentzian noise spectrum with an inflection point at $f = f_*$. With many types of channels for different kinds of ions present it is indeed possible to obtain a $1/f$ spectrum over several decades as the sum of Lorentzians [86].

To obtain the voltage power spectral density, we have to multiply $S_I^{\text{noneq}}(f)$ by R^2, where R represents the electrical resistance of the entire cell membrane. We let the cell surface area measure A. So we have $S_V^{\text{noneq}}(0) \approx 4\,Ne\,\langle I\rangle\,R^2$. The equilibrium Nyquist voltage noise across the same cell membrane is $S_V^{\text{eq}}(f) \approx 4kTR$. This is white noise and has the same strength at all frequencies. We thus obtain the following formula at $f = 0$ for the ratio $\theta(0)$ of the nonequilibrium noise and the equilibrium noise:

$$\theta(0) \approx \frac{Ne\langle I\rangle R}{kT} \tag{7.16}$$

The transmembrane current $\langle I\rangle$ is proportional to the cell surface A. The resistance R is inversely proportional to A. So eventually, the cell surface area and the cell geometry in general cancel out of the equation.

Data for the steady-state Na^+ flux through several types of cell membranes (e.g., rat soleus, sheep purkinje, squid axon, guinea pig auricles, and frog sartorius) are available [90]. That flux is about 50 pmol/(cm^2 sec). The vast majority of transmembrane ion transport is carried out by Na,K-ATPase, which transports two K^+ ions for every three Na^+ ions. We assume Na^+ and K^+ transport to therefore be about equal. After multiplying by Faraday's constant (the number of coulombs in a mole, i.e., about 10^5), we get a total current of about $\langle I\rangle \approx 10\ \mu A/cm^2$. The resistance of a cell membrane varies from 10^3 Ω cm^2 (squid axon) to 7×10^3 Ω cm^2 (mammalian cardiac cell). We thus find for $\theta(0)$ a value of about 5000.

Based on experimental data, it has been estimated that at 1 Hz the $1/f$ noise in the frog node of Ranvier is about a thousand times larger than thermal noise [91]. This is consistent with our estimate. Experimentally, it turns out that the power spectral density is constant from $f = 0$ up to about somewhere between 1 and 10 Hz [86,89]. At that point, the power spectral density starts to fall off as $1/f$. This means that we reach $\theta(f) = 1$, that is, the equilibrium and nonequilibrium noise being equal, somewhere near 10^4 Hz. Figure 7.5, in which the horizontal axis is in radians per second, indeed shows flattening between 10^3 and 10^4 Hz. At the 50- and 60-Hz power line frequencies, the nonequilibrium voltage noise is expected to exceed the equilibrium voltage noise by a factor of at least 10^2.

However, we should pause before taking the value of θ and employ it to incorporate nonequilibrium noise in the evaluation of a signal-to-noise ratio. As we saw earlier in this section, nonequilibrium noise may be a way to transduce energy from one stored form to another. So a signal can come in the form of a piece of nonequilibrium noise. With this gray area between signal and noise, it may no longer be straightforward to calculate a signal-to-noise ratio. There has been a natural selection toward high signal-to-noise ratios for signals whose detection has been important for the survival of the organism for many millennia. But what the signal-to-noise ratios and detection thresholds are for ELF and microwave radiation, which are relatively new phenomena in the environment, and how nonequilibrium noise figures in all of this is still open to conjecture and debate.

7.7 Chemical Noise

Chemical noise consists of both fundamental chemical noise (stochastic variations in net or accumulated amounts of a particular ion or molecule) and nonfundamental changes in chemical amount (molecular number) due to influences other than the applied field. We again adopt a recent discussion [12] in which an arbitrary biological system is considered.

In the discussion, attention focuses on weakly interacting fields that can create small chemical changes, but much of the approach is also relevant to strongly interacting fields, for example, those causing cell membrane electroporation (see Chapter 9 on electroporation in Ref. [127]). To begin, consider a small physical perturbation of the biological system due to the interaction of a local electromagnetic field, $\vec{F}_{\text{local}}(\vec{r}, t)$, that may vary from site to site within the volume of the biological system. In general, $\vec{F}_{\text{local}}$ may have a complicated dependence of its magnitude and direction on time and position, such that a formal prescription for calculating the field-induced molecular change due to an exposure is

$$\bar{n}_S = \int_{t=0}^{t=t_{\text{exp}}} \int_{\text{system volume}} J_0(t') f_{\text{bpm}}(\vec{F}_{\text{local}}(\vec{r},t')) \, dV \, dt' \tag{7.17}$$

We regard $\bar{n}_S$ as a molecular change signal. It is the primary consequence of the field exposure for the case where only one process, or one step in a cascade, is altered. Integration is carried out over the entire biological system volume and over the time comprising the exposure, t_{exp} (or control). This yields the accumulated, total chemical (molecular) change due to the applied field during the exposure. Other changes in the same ionic or molecular species may result from competing influences, for example, temperature variations, during t_{exp}.

The applied field interacts through one or more of a limited class of biophysical mechanisms. Here, *biophysical mechanism* means a class of interactions by which the field alters an ongoing biochemical rate (transport or reaction), with the rate arising from nonequilibrium processes dependent on metabolism. Examples of known biophysical mechanisms involving electric fields are heating (most biochemical processes have a nonzero temperature dependence), voltage-gated channels, electroconformational coupling of membrane enzymes, electroporation, and iontophoresis (mainly electrophoresis, but in some cases also electroosmosis). Examples involving magnetic fields are radical-pair reactions and twisting of magnetic material (magnetite or contaminant magnetic particles). As used here, a biophysical mechanism modulates an ongoing biochemical process, and both the coupling strength and the magnitude of the basal rate are important.

For a particular type of biophysical mechanism (bpm), the function f_{bpm} $(\vec{F}_{\text{local}}$ $(t))$ describes the instantaneous alteration of the basal rate, J_0, which itself can vary in time [92]. The local field can be computed numerically at the tissue level (millimeter scale; see Chapter 11 on dosimetry, this volume) [93–99] and at the cellular level [100,101]. The time and position dependence of $\vec{F}_{\text{local}}$ $(\vec{r},t)$ is often simple, namely, a constant magnitude (steady or DC) field, a constant amplitude periodic (AC) field, or at high frequencies a spatially decaying amplitude field due to power absorption. Environmental and occupational fields can be much more complicated, such that piecewise continuous representations may be needed.

If a weakly coupled physical perturbation alters the basal rate of a biochemical process (transport or reaction), the total chemical (molecular) change, expressed as the number of molecules, is

$$\bar{n} = \bar{n}_0 + \bar{n}_S \tag{7.18}$$

where $\bar{n}_0$ is the basal change during an exposure (sensing) time t_{exp}, and $\bar{n}_S$ is the (much smaller) molecular change due to the field exposure [22,45,92,102]. As noted above, $\bar{n}_S$ can be regarded as a molecular change signal. The basal process is far from equilibrium,

driven by free-energy differences associated with metabolism. The largest field-induced molecular change occurs for a steady (DC) field exposure [22,102]:

$$\bar{n}_S = K_{\text{bpm,dc}} F_0 \; J_0 \; t_{\text{exp}} \tag{7.19}$$

where $K_{\text{bpm,dc}}$ describes the alteration of the basal rate by the steady field, here of magnitude F_0. Equation 7.19 is the DC version of the case of a weakly coupled periodic perturbation, previously described for the case of an extracellular electric field [45,92], namely,

$$\bar{n}_S = K_{\text{bpm,ac}} F_0^2 \; J_0 \; t_{\text{exp}} \tag{7.20}$$

where $K_{\text{bpm,ac}}$ describes the coupling that leads to rectification of the ongoing rate [45]. For basal rates with more complicated time dependence, Equation 7.17 may need to be evaluated numerically, but the same basic ideas apply. Equation 7.20 is valid for long exposures, involving a large number of cycles of the periodic field. Basal rates that can be altered by weakly interacting electromagnetic fields by definition involve small interaction energies, so that thermal fluctuations and chemical free-energy differences result in nonzero basal rates. A zero basal rate with an extremely large activation or interaction energy cannot, therefore, be expected to be changed to a measurable nonzero rate by a weakly interacting field.

A generalized, molecular change-based signal-to-noise ratio can be constructed by estimating the ratio of primary molecular change to the combined competing changes for the same molecular (ionic) species. We consider the simplest case of the field altering the rate at one step in a single pathway but note that in principle the present analysis can be extended to include multiple steps involving more than one biochemical pathway. We further assume that this biochemical has its rate through the pathway altered slightly by a physical perturbation, here an electromagnetic field. But competing influences can also alter the rate. Such influences include temperature variations, normal physiological concentration variations, changes in hormones and other regulating biochemicals, and mechanical perturbations of cells and tissues. Competing molecular changes can also be created by a background electromagnetic field, for example, normal electrical activity within the human body or by movement in the earth's magnetic field, interacting through the same biophysical mechanism. Such competition goes beyond fundamental chemical noise (molecular shot noise). Nonionizing influences can only modulate ongoing processes, and therefore such influences cannot (essentially by definition) introduce foreign molecules. This has the important consequence that competing molecular changes may arise from several sources (Table 7.1).

TABLE 7.1

Quantities Employed in Generalized Chemical Noise

Symbol	Molecular Change	Source
S	$\bar{n}_S$	Field-induced molecular change signal
N	$\sqrt{\bar{n}} \approx \sqrt{\bar{n}_0}$	Molecular shot noise (fundamental)
V	$\bar{n}_V$	Molecular change due to temperature variations
C	$\bar{n}_C$	Molecular change due to concentration variations
I	$\bar{n}_M$	Molecular change due to mechanical interference
B	$\bar{n}_B$	Molecular change due to background fields

A generalized signal-to-noise ratio $(S/N)_{\text{gen}}$, can thus be considered. The field-induced molecular change signal, S, is thereby quantitatively compared to the several sources of competing molecular changes for the same biochemical (molecule or ion), yielding

$$(S/N)_{\text{gen}} = \frac{S}{f_{\text{com}}(N,V,C,I,B)} \tag{7.21}$$

The various competing molecular changes, which may or may not be independent, are combined to give the total competing molecular change, f_{com}. Important simplifications can be made if the various competing molecular changes can be approximated as independent and random around their mean values. In this case, f_{com} can be approximated as

$$f_{\text{com}}(N,V,C,I,B) \approx [N^2 + V^2 + C^2 + I^2 + B^2]^{1/2} \tag{7.22}$$

Alternatively, emphasizing the changes in terms of numbers of molecules,

$$f_{\text{com}}(N,V,C,I,B) \approx [\bar{n}_0 + (\Delta n_V)^2 + (\Delta n_C)^2 + (\Delta n_M)^2 + (\Delta n_B)^2]^{1/2} \tag{7.23}$$

All significant sources of competing molecular change are directly relevant.

Consistent with experimental treatment of errors as random, here we consider the special case that all the important competing molecular changes can be approximated as independent and random variations around their mean value, as this allows the competing changes to be added in quadrature (Equation 7.22). This leads to a general molecular change-based signal-to-noise ratio that involves Gaussian distributions, namely,

$$(S/N)_{\text{gen}} \approx \frac{S}{[N^2 + V^2 + C^2 + I^2 + B^2]^{1/2}} \tag{7.24}$$

Each of these competing molecular changes is discussed briefly below, with reference to Table 7.1.

As indicated in Table 7.1, $N = \sqrt{\bar{n}} \approx \sqrt{\bar{n}_0}$ is the competing molecular change due to fundamental stochastic variations in biochemical reaction and transport processes [15,45,92], which provides a fundamental, minimum molecular change noise. Fundamental chemical noise is increasingly recognized as important to understanding other aspects of biological systems, such as the circadian clock [103,104], control of genetic circuits [105,106], and bacterial chemotaxis [107].

Temperature variations within the volume of the biological system are generally expected to result in altered rates. When integrated over the system volume and over the exposure time, a contribution to the end-point molecular change is expected, because most biochemical processes have nonzero temperature dependence. Thus, $V = \bar{n}_v$ is the resulting, competing molecular change due to temperature variations [15]. Human core body temperature has daily variations of more than 1°C [108–113], and there are even larger variations in the extremities. Often *in vitro* electric and magnetic field experiments use feedback control, for instance, in temperature-regulated exposure chambers, but these typically have variations greater than about 0.01°C at one or a few temperature measurement sites. Temperature variations within the biological system itself are often inferred,

preferably by numerical models that can reasonably predict the temperature through the biological system by first predicting the specific absorption rate. During the exposure time, interfering temperature variation can be significant. To allow correction for temperature variations, the biological system should be characterized for its temperature sensitivity, and each particular apparatus should be characterized for its temperature variations for control and exposed conditions. As an example, an investigation first reporting athermal effects [114] was subsequently found to have temperature variation $\sim 0.1^{\circ}$C at temperature measurement sites [115]. Without thermal modeling of the exposure systems and the biological systems, however, larger temperature changes away from the measurement site cannot be ruled out. It is the temperature change and variation over the entire volume containing cells (or other specimens) that need to be quantitatively understood. Temperature measurement at one site, typically somewhere along the perimeter or boundary of a temperature-regulated apparatus, is generally insufficient. The measured biochemical quantity should also be characterized for its temperature sensitivity for the biological system studied, so that the expected V can be determined, to address the basic specificity question of whether an observed change is due to the field or to temperature changes [116].

Changes in concentration of biochemicals involved in a process are well known to alter the rate of a process. Relevant chemical species include substrates, products, inhibitors, etc. The competing molecular change due to one or more interfering concentration changes is $C = \bar{n}_{\mathrm{C}}$. In this case, a significant difference may exist for *in vitro* and *in vivo* experiments. Usually, only small, slow changes of chemical concentrations are expected *in vitro*, occurring, for example, through absorption or release of molecules (ions) from glass- and plasticware, spontaneous chemical decomposition, binding to cellular constituents, or evaporation. Uptake or release of interfering biochemicals from a biological preparation could be the predominant source, particularly if cells grow (taking up molecules) or die (releasing molecules). *In vivo* concentration variations are relatively large, because of normal physiologic variations. For example, Ca^{2+} concentration varies in humans by more than 1% over a day [117,118]. Unless buffered, these normal biochemical variations also compete with the field-induced molecular change.

Movement of tissue *in vivo* and vibration of an experimental apparatus containing a biological system can also create a mechanically induced molecular change, $I = \bar{n}_{\mathrm{M}}$, that competes with a molecular change signal. In this case, the competing molecular change is due to interference of mechanical stress and strain [119,120], often present at high levels in living humans [11,121,122] but at low levels for *in vitro* experiments. *In vitro* apparatus can have quite different mechanical properties and isolation from ambient vibrations. Indeed, it has been found in some experiments that mechanical vibrations create effects larger than the field exposure [123]. Tissues *in vivo* experience significant mechanical deformation, but there is the least strain expected within the bone marrow and the brain [120]. This may be relevant to the ''contact current hypothesis,'' which suggests that currents in the bone marrow may be important in exposures of children [124–126].

Background fields can, of course, also couple to biochemical processes through the same biophysical mechanisms as the applied field. Background field-induced molecular change competes, and is denoted by $B = \bar{n}_B$. Examples of background electromagnetic fields include the endogenous electrical fields generated within the body by cardiac, muscular, and neural activity and the sampling of different field values (local anomalies) in the ambient magnetic field as mobile humans move about in their environment. *In vitro* background fields will depend on the particular experimental environment, are usually small and constant, and are often measured.

7.8 Interpretation of Experiments

Specificity is fundamentally important to interpret experiments, as one wants to know what agent is responsible for the observed change(s). This is particularly relevant to experiments that find small changes in biological systems that are exposed to small electromagnetic fields. A basic challenge is to show that other influences are not responsible. Because it is well known that most biochemical processes have a significant temperature dependence, the approximate temperature sensitivity of the observed quantity should be determined or known, and some bound should be established for temperature drift or variations in the experiment. However, as already noted, even big changes can have more than one candidate cause. Both tissue electroporation and tissue movement can, for instance, underlie the changes in molecular uptake associated with large field pulses. For this reason, signal-to-noise ratio considerations should be preceeded by establishing field specificity, which can be much more difficult than observing a change associated with a field exposure. To establish specificity, a number of issues must be considered, many of which will be discussed next.

Many experiments determine quantities related to biochemical change. Exceptions are experiments that determine physical quantities such as voltages and currents, temperature changes, and magnetic particle rotation. However, electrical measurements are the most frequent physical measurement. These are incredibly important to systems of excitable cells, with experimental preparations ranging from isolated cells to electrophysiologic measurements on humans. Accumulation of charge might be measured, but probably as a voltage on a capacitance. Signal-to-noise ratio issues are still important, of course, but usually there is an important distinction: voltages and currents (rarely charge) are readily measured continuously.

A further distinction is that most experiments involving exposures to small fields use long exposure times (many seconds to hours or even days). Such experiments commonly determine biochemical quantities directly, for example, enzyme activity, or indirectly, for example, fluorescence emission from fluorescent indicators of intracellular calcium concentration. In this broad case, consideration of generalized chemical noise is relevant. Following the discussion in a recent paper [12], both the magnitude of the field perturbation and the nature and magnitude of chemical competition need to be understood. Such analysis should explicitly estimate the coupling to ongoing, far from equilibrium, metabolically driven biochemical processes and should quantitatively determine molecular changes due to competing influences. Only then can the analysis distinguish idealized conditions from *in vitro* conditions and *in vivo* conditions and then determine whether reported effects can be explained by known biophysical mechanisms.

In vivo there are several kinds of noise, and it is important to distinguish between them. Equilibrium noise comes about as a consequence of Brownian motion, that is, the random movement of molecules at finite temperature. At equilibrium, every degree of freedom takes on the same amount of energy, and equilibrium noise is therefore easy to evaluate. For a signal to exceed the equilibrium noise band, the quantitative criteria are often readily derived. Such baseline criteria can be useful when assessing the electroreception and magnetoreception that many organisms exhibit. But the nonequilibrium nature of life brings in nonequilibrium noise. When a primary molecular change is amplified through a biochemical cascade, ''amplifier noise'' is inevitable. Nonequilibrium noise appears whenever energy is dissipated, that is, when work is done. In many biological contexts the nonequilibrium noise is much more intense than the equilibrium noise. A serious complication is constituted by the fact that nonequilibrium noise, unlike equilibrium noise, is also able to perform work, that is, be a power source for an energetically uphill

process. Many biological processes may rely on the energy transduction that can be accomplished through nonequilibrium noise. The analysis of such situations poses challenges as the noise may be a signal and the signal may be noise. There is no easy general ''common denominator'' theory for nonequilibrium noise like there is for equilibrium *kT*-noise.

In a recent discussion [12], it is argued that experimental measurements can be plausibly related quantitatively to an underlying primary molecular change because of a field exposure operating through a biophysical mechanism. It is further argued that only the uncertainty in this change propagates through biochemical amplification and therefore dominates the measurement uncertainty. A more complete approach would involve traditional, independent determination of the instrumental or assay error (quantitative characterization of the experimental measurement system). After removal of the ''instrumental noise,'' the generalized signal-to-noise ratio $(S/N)_{\text{gen}}$, could be revised upward. This would allow interpretation (correction) of experimental error to estimate the uncertainty in the measured quantity itself. Assessment of combinations of biophysical mechanism models and particular exposure can then be carried out, using the most field-sensitive versions of theoretical models for the candidate biophysical mechanisms. The criterion $(S/N)_{\text{gen}} \leq 0.1$ is a very conservative basis for ruling out a particular class of biophysical mechanism for a given field exposure. Similarly, the criterion $(S/N)_{\text{gen}} \geq 10$ is a conservative basis for ruling in a candidate biophysical mechanism for a given exposure, retaining that biophysical mechanism hypothesis for further evaluation. This approach provides a quantitative basis for rejecting or accepting hypothetical biophysical mechanisms as candidate explanations for an experimental measurement.

The traditional choice $(S/N)_{\text{gen}} \approx 1$ is a useful but somewhat arbitrary dividing line, which indicates conditions for which an effect might appear. $(S/N)_{\text{gen}} \leq 0.1$ and $(S/N)_{\text{gen}} \geq 10$ provide criteria for stronger conclusions, allowing rejection or provisional retention of a biophysical mechanism hypothesis. This approach to interpreting experiments thus provides a general method for carrying out theoretical assessment of reported weak field exposure effects. This approach can distinguish relatively quiet *in vitro* conditions from *in vivo* conditions containing more and larger influences of competing molecular change. This in turn allows quantitative estimates of whether an *in vitro* result is relevant to *in vivo* conditions.

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8

Biological Effects of Static Magnetic Fields

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CONTENTS

8.1 Introduction

In ancient times, magnetism, especially permanent magnets, were a symbol of mystique because of the magnetic force that remains even after numerous attractions of iron. Although William Gilbert was called the pioneer of modern magnetics, he was surprised by the magnetism associated with living organisms. Magnetism, in contrast to transient static electricity, has been used as an explanation for various invisible effects and is expected to possess miraculous healing powers. Although people have been using magnetism for healing purposes without any scientific evidence, there have not been significant problems concerning the side effects of magnetism. As permanent magnets have improved in quality and achieved higher magnetic strength, magnetism has become more commonly used in modern medicine. For example, magnetism is commonly used in the correction of dentures.

In the society today there are many sources of electromagnetic fields. Humans are exposed daily to man-made and naturally originated fields. During the past decade, questions about whether the exposure to electromagnetic fields may be linked to adverse health effects have been raised. Although the interaction of electromagnetic fields with biological systems has been investigated, there are no biophysical mechanisms that can explain many of the observed biological effects of low-level of magnetic fields. Proposed mechanisms include effects on currents, direct forces on biomagnetic materials, effects on free radicals, ion cyclotron resonance, charge transfer processes, stochastic resonance, etc.

Recent developments in medical instrumentation such as magnetic resonance imaging (MRI) and transcranial magnetic stimulation (TMS) have raised questions as to whether or not strong (in the tesla range) magnetic fields influence human health. Medical applications of weak (1–200 mT) magnetic fields for the purpose of pain reduction and tissue healing have also been studied for many years. Therapeutic applications of permanent magnets and other magnetic devices have recently been expanded to various areas such as treatment of pain and diseases like rheumatoid arthritis and cancer.

The objective of this chapter is to describe some of the more recent information on biological effects and medical applications of static magnetic fields. This chapter consists of four sections. Each section has a comprehensive review of a recent topic of interest. A short summary of the mechanism of static magnetic field action on biological systems is described in the second section, which includes a brief review of well-known mechanisms that are discussed before mentioning the interactions of weak static magnetic fields with biological systems. The third section reviews and summarizes more recent *in vivo* and *in vitro* experimental results of the effects of static magnetic fields, including near-zero magnetic fields, geomagnetic fields, and MRI fields. The fourth section covers special topics including magnetic sensing, magnetite, and plant response to magnetic fields. In parallel with the comprehensive review of biological effects, the development and medical application of the static magnetic field phenomena are introduced in the fifth section and reviewed with emphasis on the applications that are currently under investigation.

8.2 Mechanisms of Biological Effects of Static Magnetic Fields

The biological effects of static magnetic fields are not well understood. Magnetic fields exert a force on moving charged particles at right angles to both the field and the velocity, $\vec{F} = q\vec{v} \times \vec{B}$, where $\vec{F}$ is the force, q is the charge, $\vec{v}$ is the velocity, and $\vec{B}$ is the magnetic flux density. In vacuum, the magnetic flux density is given by $\vec{B} = \mu_0 \vec{H}$, where $\vec{H}$ is the magnetic field strength and μ_0 is the magnetic permeability of a vacuum. (In this section

we will be careful to distinguish between $\vec{B}$ and $\vec{H}$, although in subsequent sections we will be less careful, using ''magnetic field'' as a general term that often is used to describe flux density.) Additionally, these fields exert a torque on particles with both fixed and induced magnetic dipole moments. This torque tends to align the dipoles along the magnetic flux density and is given by $\vec{T} = \vec{M} \times \vec{H}$ where $\vec{M}$ is the magnetic dipole moment. For paramagnetic and diamagnetic materials, $\vec{M}$ is proportional to the magnetic flux density. The magnetic susceptibility, χ, is given by the equation, $\vec{M} = \chi \vec{H}$, where $\vec{H}$ is the local value of the magnetic field strength and χ is dimensionless. All materials may be mainly divided into three categories based on their susceptibility values. Materials with negative susceptibility are called diamagnetic. Materials with positive values are referred to as paramagnetic. Materials with large susceptibility include both ferro- and ferrimagnetic materials. Recognition of the role of diamagnetic, paramagnetic, and ferro- or ferrimagnetic materials in the body helps in the understanding the underlying mechanisms of biomagnetic effects.

Table 8.1 shows three types of well-known mechanisms of the biological effects of magnetic fields including time-varying magnetic fields. As shown in Table 8.1, there are two basic mechanisms of static magnetic fields: first, the magnetic torques on objects and second, the mechanical force effects. A radical pair mechanism is also proposed.

When biological materials or systems are exposed to a spatially homogenous magnetic field, they tend to rotate to a stable direction, which is determined by the anisotropy of magnetic susceptibility of the materials and magnetic torque acting on the materials, as described by the following equation:

$$T = -\frac{1}{2\mu_0} B^2 \Delta\chi \sin 2\theta$$

where B is the magnetic flux density, $\Delta\chi$ is the anisotropy of magnetic susceptability of the materials, θ is the angle between the direction of the magnetic field and the long axis of the materials, and μ_0 is the magnetic permeability of a vacuum. The magnetic orientation of diamagnetic materials such as fibrin and collagen can be observed and explained by this principle (Torbet et al., 1981).

Next, when biological materials or systems are exposed to a spatially inhomogenous magnetic field, the materials or systems tend to move along the direction of the steepest

TABLE 8.1

Well-Known Mechanisms of the Biological Effects of Magnetic Fields

1. Time-varying magnetic field	
Eddy currents $J = -\sigma \frac{B}{t}$	Nerve stimulation
Heat SAR $= \sigma \frac{E^2}{\rho}$	Thermal effects
2. Static magnetic fields	
a. Homogenous magnetic field Magnetic torque $T = -\frac{1}{2\mu_0} B^2 \Delta \chi \sin 2\theta$	Magnetic orientation of biological cells
b. Inhomogenous magnetic field Magnetic force $F = \frac{\chi}{\mu_0} (\text{grad } B) B$	Parting of water by magnetic fields (Moses effect)
3. Multiplication of magnetic fields and other energy Photochemical reactions with radical pairs Singlet–triplet intersystem crossing	Yield effect of cage product and escape product

gradient of magnetic force. The magnetic force acting on the materials is proportional to the multiplication of the magnetic flux density B, the gradient of the magnetic flux density B (grad B), and the magnetic susceptability χ of the materials, as described by the following equation:

$$F = \frac{\chi}{\mu_0}(\text{grad}B)B$$

where μ_0 is the magnetic permeability in a vacuum.

Dramatic demonstrations of these forces can be seen when water is parted by magnetic fields using magnetic field exposures of 4–8 T with a gradient of 50 T/m (Ueno and Iwasaka, 1994a,b). Magnetic levitation of diamagnetic materials such as wood and other organic materials, is realized in magnetic fields of more than 20 T (Beaugnon and Tournier, 1991). This phenomenon can also be explained by the principles of magnetic force.

Oxygen is a paramagnetic molecule, and its behavior under magnetic field gradients has an important role both as a gas and when dissolved in solution. The blockage and disturbance of gas flow by magnetic fields have been observed (Ueno and Harada, 1987). This phenomenon, called a magnetic curtain, can be explained by the action of magnetic force on a paramagnetic molecule. The magnetic curtain in this example is a wall of oxygen or air. Experimentation with this principle has demonstrated the quenching of burning candle flames (Ueno, 1989), where the interception of oxygen by the magnetic curtain has a quenching effect on the flames. As a second example, when a human subject is positioned inside a space shielded by the magnetic curtain, one may expect the respiratory function, evaporation of water molecules, body temperature, blood circulation, and other physiological functions to be disturbed or modulated.

The effect of static magnetic fields on water vaporization rate was investigated (Nakagawa et al., 1999). This study demonstrated that the water vaporization rate was found to be significantly influenced when both air and oxygen were in the presence of magnetic fields, and the observed effect was dependent on the field–field gradient product rather than on the B field itself. It should be noted that this magneto-enhancement of vaporization might be the indirect cause of certain physiologic effects on living organisms.

For example, skin temperature decreases in rats exposed to magnetic fields have been observed (Ichioka et al., 2003). This observation can be explained in terms of the effects of the magnetic field on air convection. That is, high magnetic field gradients (135–140 T^2/m) push the diamagnetic water molecules toward the magnet bore. This increases the movement of water molecules in the air around the animal body and the vaporization rate. The heat of vaporization leads to a decrease in skin temperature. The decrease in the blood flow of the skin microcirculation is assumed to be a secondary change to the decrease in skin temperature.

Oxygen dissolved in water is also affected by magnetic fields. Changes in dissolved oxygen concentration were observed for magnetic field exposures on the order of 1 T (Ueno and Harada, 1982; Hirota et al., 2000; Kishioka et al., 2000). The changes in oxygen concentration are accelerated or regulated by gas transport of oxygen and water molecules inside and outside the water surface.

The magnetic field effects for large fields can be explained by these well-known mechanisms. With ever-increasing evidence indicating that weak static magnetic fields have profound effects on biological systems, a number of mechanisms for the action of these static magnetic fields, including geomagnetic fields, on biological systems have been proposed.

Possible biomagnetic and chemical effects can be expected when biological systems are exposed to both static magnetic fields and other forms of energy such as light and

radiation (Ueno and Harada, 1986). Photochemical reactions produced by a radical pair intermediate can be expected to show magnetic field effects that arise from an electron Zeeman interaction, electron-nuclear hyperfine interaction, or a hyperfine interaction mechanism including an electron-exchange interaction in a radical pair intermediate (Hata, 1976; Schulten et al., 1976; Tanimoto et al., 1976; Nagakura and Molin, 1992; Natarajan and Grissom, 1996; Hayashi, 2004).

The magnetic field effect observed with radical pair recombination is one of the well-known mechanisms by which magnetic fields interact with biological systems. Throughout the past decades there have been several experimental results describing the effects of magnetic fields on radical pair recombination. Mohtat et al. (1998) examined the behavior of radical pairs derived by hydrogen abstraction of triplet benzophenone and some of its derivatives from bovine serum albumin, human serum albumin, and calf thymus DNA. The magnetic field strength was as high as 150 mT with durations as long as 10 μs. This result indicated that radical pair behavior is sensitive to magnetic fields, and this effect can be interpreted by using the theory of free radical recombination. Using the triplet state of benzophenone as a convenient source of pairs, Eveson et al. (2000) examined the effects of weak (>1 mT) magnetic fields on radical recombination reactions in micells. They found that the concentration of free radicals escaping from the micelle was both affected and depended on the conditions surrounding the radical pair.

Timmel and Till discussed the weak magnetic field effects on free radical recombination reactions (Till et al., 1998; Timmel et al., 1998). Vink and Woodward (2004) described the effects of a weak magnetic field, 21 mT, on the recombination reaction of neutral free radicals in isotropic solution.

Ritz et al. (2002) reviewed the physiological basis of animal magnetoreception. They suggested that there was a link between photoreception and magnetoreception, from their findings in behavioral and theoretical studies. Migratory birds have the ability to sense the geomagnetic field and use it as a source of compass information. The candidates for a biophysical mechanism of this magnetoreception are magnetite and magnetically sensitive chemical reactions in animals. Ritz et al. (2000) postulated the possibility that magnetoreception involves radical pair processes as a biophysical mechanism.

8.3 Experimental Studies on Static Magnetic Field Effects

This section focuses on *in vivo* and *in vitro* studies of the effects of static magnetic fields. It covers the field effects observed on behavior, the cardiovascular system, reproductive system, cellular and tissue development, the neuroendocrine system, and the magneto-mechanical system, utilizing molecular, cellular, tissue, and cell-free systems.

8.3.1 *In Vivo* Studies

8.3.1.1 Animal Behavior: Recognition and Analgesia

Scientific interest in behavioral changes has led to the development of a psychology of learning that studies the effects of various external stimuli, and this research has further led to the development of behavioral pharmacology to observe the effects of drugs on the central nervous system. There have been several investigations for studying the effects of magnetic fields on behavior and the central nervous system using techniques developed

specifically in these research fields. Behavioral research directed toward the effects of magnetic exposure of living organisms mainly addresses two questions: whether magnetic fields are sensed and avoided and whether magnetic fields have any influence on the functions of leaning and memory. Magnetic field experiments designed to address both questions have been conducted using several indicators, such as open-field behavior, operant behavior, and spontaneous motor activity, as tools of observation and measurement. (See also Chapter 4 on behavioral effects by Johnston and D'Andrea.)

8.3.1.1.1 Animal Behavior and Recognition

Nikolskaya et al. (1996) investigated the influence of inhomogeneity of natural magnetic fields on rat cognition with regard to whether or not magnetic fields could serve as an informational factor for cognition. Under three natural magnetic field conditions, 37 $\pm$ 2 μT (condition 1; horizontal component (N–S) is 14 μT, and vertical 34 μT), 16–118 μT (condition 2), and 55–240 μT (condition 3), rats were subjected to a food-operant behavior study. All rats in conditions 2 and 3 were unable to form operant behavior, while rats in condition 1 demonstrated the behavior. Using the combination of an original behavioral model and a multiple alternative maze, an impact of Opilong, which is an analog of dermorphine and μ-receptor agonist, on rat sensitivity to 38 $\pm$ 2 μT, in the static magnetic field has been investigated by the same authors (Nikolskaya et al., 1999). They concluded that chemical modulation of the opioid system in rats induced both an increased magnetic field sensitivity and an allowed perception of magnetic field parameters. In the following study (Nikolskaya and Echenko, 2002), it was reported that cognitive activity in the natural magnetic field of 38 μT caused an increase of ethanol intake in 34.8% of rats.

During the 1980s, Liboff (1985) argued favorably for the combined effects of static (DC) with extremely low-frequency (ELF) magnetic fields (see also Chapter 9 resonance phenomena by Liboff on). A surprising effect was observed at the ELF magnetic field frequency close to the cyclotron frequency of a calcium ion. Thomas et al. (1986) reported the disruption of operant behavior in rats after exposure to low-intensity magnetic fields. The protocol developed by them in the report has been reexamined by Stern et al. (1996) in a two-part experiment. In the first part, the vertical component of the static field was reduced to 0.0261 μT. In the second part, both the horizontal and the vertical components were matched to those used by Thomas et al. The results obtained in these experiments were found to be inconsistent with the results reported by Thomas et al. Effects of the combination of static (DC) and AC magnetic fields at the cyclotron frequency on rat open-field behavior have been investigated (Zhadin et al., 1999). Levels of locomotor and exploratory activities were decreased after exposure to DC and AC magnetic fields at the calcium cyclotron frequency, whereas field exposure at the magnesium cyclotron frequency increased levels of these activities.

Studies have been conducted to determine whether rats could acquire a two-choice discrimination based on a specified discrimination stimulus (Creim et al., 2002). The specified discriminative stimulus used in this study was tested both in ambient illumination as well as in a combination of an oscillatory field of 50 μT at 60 Hz and a static field of 26 μT. The results demonstrated that rats were able to discriminate between two-choice tasks easily during the period of changing illumination and that the presence or absence of the static and oscillatory fields had no observed effect on these findings.

Tsuji et al. (1996) evaluated physiological consummatory behavior by observing intakes of food and water and changes in the body weight using BALB/c mice exposed to magnetic field levels of 5 T for a period of 24 and 48 h. Exposure to a 5-T magnetic field for 48 h suppressed eating and drinking behavior. The decreased body weight, the increased blood urea nitrogen (BUN) level, and the slightly increased BUN–Cr ratio

observed in this experiment might be attributed to the loss of body fluid secondary to decreased food and water intake.

For the purpose of observing changes caused by magnetic field exposure, MRI systems and application of their high-strength static magnetic fields have been useful and widely used to obtain intact images. There have been three reports describing the behavioral effects observed as a result of high-strength static magnetic field exposure of rats and mice. Using a conditioned taste aversion technique, it was shown that rats developed a conditioned taste aversion after exposure to a high magnetic field of 9.4 T for 30 min (Nolte et al., 1998). Following this report, similar experiments were carried out. Restrained rats and both unrestrained and restrained mice were exposed to magnetic fields of 7 and 14 T generated by superconducting magnets (Houpt et al., 2003). In the report, it was found that exposure of rats to high magnetic fields suppressed rearing and locomotor circling and induced conditioned taste aversion and expression of c-Fos in vestibular neclei. The rat's orientation in magnetic fields is a key factor for the direction of circling. Similar results were obtained with mice (Lockwood et al., 2003). All tested mice showed development of conditioned taste aversion, and a significant number showed tight circling and rearing suppression. Effects were observed more significantly in unrestrained mice than in restrained mice. Snyder et al. (2000) have identified brain stem regions that were activated by exposure to static magnetic field levels of 9.4 T for 30 min, of restrained rats, by using a c-Fos immunohistochemisty detection assay. Increased expression of c-Fos and neural activation in visceral and vestibular nuclei by magnetic field exposure have been reported. It has been suggested that the neural activation response might be a factor in promoting conditioned taste aversion learning.

Superconducting high magnetic field exposures of 7 T have been reported to have reduced the trehalase enzyme activity in honey bees (Kefuss et al., 1999). There were no changes found in the level of fatty acids, triacyglycerols, and steroids in this study.

8.3.1.1.2 Analgesia

Effects of a hypogeomagnetic environment with a flux density of 4 μT inside a Mu-metal box on stress-induced analgesia in C57 male mice have been investigated (Del Seppia et al., 2000). This study consisted of three consecutive parts: (1) maintaining the mice under various magnetic exposure conditions: hypogeomagnetic, altered magnetic field, and Earth's geomagnetic field of 46 μT for 90 min; (2) immobilizing the animals in a tube for 30 min under each exposure condition; and (3) recording nociceptive responses of the restraint-stressed mice as the latency of front-paw lifting to hot-plate stimulus. Stress-induced analgesia was significantly reduced in the animal group exposed to the hypogeomagnetic field, and this result was comparable with that in the mice exposed to altered magnetic fields or treated with prototypic opiate antagonist naloxone. It has been suggested that the exposure period in a hypogeomagnetic environment might be responsible for the inhibition of stress-induced analgesia. They also demonstrated that exposure to altered magnetic fields induce more rapid habituation to a novel environment (open field) (Del Seppia et al., 2003). The experiment was carried out to investigate effects of irregularly varying (<1 Hz), 20–70-μT or regular 37-Hz, 80-$\mu T_{p\text{-}p}$ magnetic fields with a 2-h exposure of mice. The nociceptive response was measured by a hot-plate test and showed that the nociceptive sensitivity was significantly greater in magnetically treated mice than in controls.

Various sensing-transduction mechanisms have been proposed to explain the biological effects of magnetic fields. Prato et al. (1996a). showed inhibitory effects of 60-Hz magnetic fields at levels of 299 $\pm$ 1 $\mu T_{p\text{-}p}$ and static magnetic fields at levels of 78 $\pm$ 1 μT on opioid-mediated analgesia in the land snail, *Cepaea nemoralis*. It has been reported that

the effects were dependent on the relative direction of both the weak static and the 60-Hz magnetic field, as well as on the presence of light. In a following study, indirect and direct mechanisms of ELF magnetic fields on an endogenous opioid peptide-mediated analgesic response have been proposed. It was shown that the energy transduction mechanism did not involve induced electric currents or magnetite (Prato et al., 1996b), and the results indicated that a direct magnetic field detection mechanism was consistent with the parametric resonance model. In a later study to reexamine the results obtained and further clarify the role of light, it was found that reduction of the opioid-induced analgesia by magnetic field exposure was enhanced by the presence of light. It was reported that the reduction rate of analgesia was not dependent on ELF frequency; however, the effect of the ELF magnetic field was in fact mediated by direct magnetic field detection.

In order to detect static magnetic field-induced functional changes in brain tissue, Veliks et al. (2004) carried out an investigation to identify the effects of static magnetic fields on rat brain structures using heart rate and heart rhythm as physiologic indicators. Rats put under ketamine–xylazine anesthesia were exposed to magnetic field levels of 100 mT for 15 min. Before and after the exposure, an electrocardiogram was recorded for analysis of heart rate and heart rhythm. Static magnetic fields were found to evoke changes in both heart rate and heart rhythm in 80% of the subject animals.

McLean et al. (2003b) examined the effects of inhomogenous static magnetic fields, alone or in combination with the chemical agent phenytoin (PHT), on audiogenic seizures (AGS) in DBA/2 mice. In experimental studies where the static magnetic fields ranged from 0.26 to 10.5 mT, with a field gradient ranging between 0.012 and 0.48 T/m, seizure severity decreased as the magnetic flux density and exposure duration period increased. It was found that the magnetic field pretreatment enhanced the effect of PHT, and it was also found that a static magnetic field alone had some anticonvulsant effects as well. Further investigation is required to clarify the anticonvulsant effects of magnetic fields in AGS.

8.3.1.2 Reproduction and Development

The effects of static magnetic fields, including MRI fields (static, gradient, and RF), on fertility, the developing embryo, and the fetus have been investigated. There have been a series of reports describing the effects of 10- and 35-day exposures to a magnetic field level of 0.7 T on mice, in terms of sperm motility, maturation, and production and morphological and developmental changes (Tablado et al., 1996, 1998, 2000). In the first report, mice were exposed to a magnetic field level of 0.7 T for time periods between 1 and 24 h/d, over 35 d. It was found that sperm motility, maturation, and production were not affected. Two years later, it was reported that the size of sperm heads was still intact; however, the animals that had undergone continuous exposure demonstrated increased sperm head abnormality. In a study by Tablado et al. of magnetic effects during developmental changes, experiments were carried out to investigate the *in utero* exposure effects from magnetic field levels of 0.5 to 0.7 T on testis and epididymis development in mice. After mating, female mice were exposed from day 7 of gestation until the day of birth. Results showed that there were no significant differences between exposed and sham-exposed animals in terms of body weight gain of dam, litter size, body weight of male pups, and testis–epididymus weight gain of pups up to 35 d of age. In addition, there were no detectable changes found during a histopathological evaluation of the testis and epididymis of pups.

Narra et al. (1996) reported the biological effects of a static magnetic field on spermatogenesis and embryogenesis in Swiss Webster mice. Male and pregnant female mice were exposed to a magnetic field level of 1.5 T for 30 min. There was no increase in sperm head shape abnormality and no reduction in testicular sperm numbers; however, a decreased survival rate of preimplantation embryos was indicated.

It has been reported that there were no harmful effects detected in a static magnetic field of 4.7 T on ICR mice (Okazaki et al., 2001). Pregnant ICR mice were exposed to the field from days 7.5–9.5 of gestation and sacrificed on day 18.5 of gestation. There were no significant differences in the incidence of prenatal death or malformations between the exposed and control groups. The investigation has been conducted for potential adverse effects of a 10-week exposure to a 9.4-T magnetic field on the development of male and female rats as well as their offspring (High et al., 2000). All rats were exposed to 9.4 T for 3 h twice a week with an intermittent duration of 5 week on, 2 week off, and 5 week on. The results demonstrate hematological, biochemical, pathological, and behavioral changes in both adults and their offspring; however, there were no adverse effects observed in either male or female adult rats, as well as in their offspring.

Effects of long duration and high magnetic field exposure on fetal growth and postnatal development in mice have been investigated (Magin et al., 2000). One group of mice was exposed for 9 h on day 9 or on day 12 postcoitus (or both) to MRI conditions (static magnetic field of 4 T with 5-T/s gradient and whole-body SAR of 0.2 W/kg at 170 MHz). A second group was exposed to a combination of ultrasound and MRI fields. There were no significant changes in fetal growth in animals exposed to MRI or ultrasound fields individually. The average fetal weight of animals exposed to combined fields was lower than that of the other group. Carnes et al. (1996) investigated the effects of static magnetic field levels of 4.7 T, which is equivalent to the level used in MRI, on fetus, adult growth, and testicular development in mice.The 8-h exposure was carried out on day 9 or day 12 of gestation (or both). Effects of the combined application of 1 MHz ultrasound on day 9 and MRI on day 12 was also investigated. The average fetal weight of the exposed groups was found to be less than that of the control groups. It was found that the postpartum death rate was higher after the MRI exposure, and sperm production was reduced; however, no changes were detected in embryonic death rate, sex ratio, body weight at day 50, spleen weight, and seminal vesicle weight.

Jove et al. (1999) studied the effects of static magnetic field levels of 18 and 36 mT on the development of chick embryo, including the pineal gland. They found that static magnetic fields affected the development and growth of embryos, and this effect was dependent not only on the intensity but also on the length of exposure time. Ruggiero et al. (2004) reported the effects of a 3-h exposure to a magnetic field level of 0.2 T generated by a clinically used MRI system on the angiogenesis of chick embryo. Angiogenesis was evaluated using a chick embryo chorioallantoic membrane assay. Results indicated that static magnetic field exposure inhibited angiogenesis in chick embryo. Effects of a uniform static magnetic field of 29 mT on cell migration and differentiation in the cerebellum of chick embryo have been studied (Espinar et al., 1997). The cerebella of chick embryos was exposed to the magnetic field on 6 d of incubation and sacrificed at day 13 of incubation. Results showed that static magnetic field exposure could induce irreversible developmental effects on cell migration and differentiation. Clear signs of cell degenerations and delay in the process of neuronal differentiation were indicated.

There have been a series of reports describing the effects of static magnetic field on fish embryos (Formicki and Winnicki, 1996, 1998; Winnicki et al., 1996; Formicki et al. 1997; Formicki and Perkowski, 1998). First, it was reported that during a prolonged transportation of fertilized salmonid eggs and trout (*Salmo trutta* L. and *Oncorhynchus mykiss*), a magnetic field of 4 mT lowered the mortality rate and enhanced the conservation condition (Winnicki et al., 1996). Effects of static magnetic fields ranging from 50 to 70 mT on the cardiac muscle activity of carp (*Cyprinus carpio* L.) embryos and larvae have been investigated (Formicki and Winnicki, 1996). An increase in heart rate was observed after exposure to these fields. Effects from both the strength and the direction of the geomagnetic field and static magnetic fields of 0.5 and 1 mT on the orientation of trout embryo

(*S. trutta*) and rainbow trout (*O. mykiss*) have also been investigated. Results have shown that the embryos were sensitive to the static magnetic fields, with a preference for a certain field direction. Further investigation has been conducted to clarify the response of fish embryos and larvae from the same type of trout to a static magnetic field (Formicki and Winnicki, 1998). Eggs were placed in magnetic fields during the period from fertilization to hatching. The exposure of eggs resulted in slower embryonic development; thus, eggs were incubated for a prolonged period of time. Embryos of rainbow trout (*O. mykiss*) and trout (*S. trutta*) exhibited orientation both in the natural magnetic field and in artificial magnetic fields of 0.5 and 1 mT. In a supplementary paper, Formicki and Perkowski (1998) showed the effects of static magnetic fields of 5 and 10 mT on the gas exchange in rainbow trout (*O. mykiss*) embryos. An increase of oxygen uptake was observed. It was determined that the impact of magnetic field exposure on the respiratory system was significant in the periods of advanced morphogenesis.

It has been reported that the exposure to static magnetic fields of 10–100 mT could alter the early embryonic development in two species of sea urchin embryo, *Lytechinus pictus* and *Strongylocebtrotus purpuratus* (Levin and Ernst, 1997). Results suggested that static magnetic fields delayed the onset of mitosis in both species. A static magnetic field of 30 mT caused an eightfold increase in the incidence of exogastrulation in one species. Static magnetic field effects of 4 and 8 mT and effects of exposure to 60-Hz AC magnetic fields of 6 and 8 mT on the first division of two sea urchin embryos, *Sphaerechinus granularis* and *Paracentrotus lividus*, have been studied (Pagnac et al., 1998). No differences were found in the time of the first cleavage in both exposures.

In a static magnetic field of 35 mT, the fruit fly (*Drosophila melanogaster*) was reared through several generations to investigate the width and length variability of both wings (Stamenkovic-Radak et al., 2001). In the second-generation exposure, there was a significant difference between sexes in the context of directional change of wing size variability. In the sixth generation, the differences in wing size between the magnetic field exposure group and control groups showed the same directional pattern in both sexes. Pan and Liu (2004) reported the effects of high static magnetic fields of 9.4 and 14.1 T on the hatching behavior of fresh mosquito eggs. Hatching was delayed, and the delay time depended on the intensity of the magnetic field.

Effects of exposure to high static magnetic field with levels up to 16.7 T on the first three cleavages of *Xenopus laevis* embryos have been investigated (Denegre et al., 1998). Results have indicated that cleavage furrows aligned parallel to the magnetic field. The most significant effects on the second and third cleavages have been observed in homogenous fields, not in the gradient fields. It has been suggested that this phenomenon was caused by interactions between the magnetic fields and the diamagnetic materials in the *Xenopus* embryo. Further studies have shown that after exposure to static magnetic fields of 17–22 T during either or both of the first two cell cycles, the third cell cycle mitotic apparatus at metaphase could be induced, and the third cleavage furrows aligned perpendicular to their nominal orientations (Valles, 2002; Valles et al., 2002). Valles et al. (1997) investigated the magnetic field gradient levitation (MFGL) as a technique for simulating low gravity for biological systems.They levitated living biological specimens, embryos of the frog *X. laevis*, using a large inhomogenous magnetic field. MFGL of embryos reduced the body forces and gravity-induced stress on them.

8.3.1.3 Circulatory System Effects

Recently, effects of static magnetic field applications on the circulatory system have been reviewed in experimental animals (Tenforde, 2005) and in humans (Chakeres and de Vocht, 2005; Crozier and Liu, 2005; van Rongen, 2005). Most of the studies have been

related to MRI systems, and it has been reported that in MRI-related studies using strengths of up to 8 T, there were little or no significant changes in cardiovascular and circulatory parameters. In contrast, it was found that moderate-intensity static magnetic fields ranging from 1 to 350 mT can have significant circulatory system effects, most notably on cutaneous microcirculation and arterial blood pressure.

8.3.1.3.1 Microcirculation

Ohkubo and Xu (1997) studied the acute effects of 1–10-mT static magnetic fields applied for 10 min on the microcirculatory changes in conscious rabbits using a rabbit ear chamber (REC) and microphotoelectric plethysmography (MPPG). The static magnetic fields induced biphasic changes in vasomotion in a non-dose-dependent manner. Static magnetic fields suppressed vasomotion when the vascular tone was high, while the same level fields enhanced vasomotion when the tone was low. To clarify these effects, the same group, Okano et al. (1999), investigated the effect of a 1-mT static magnetic field for 10 min on microcirculation in conscious rabbits using pharmacological manipulation together with REC and MPPG. The results showed that the static magnetic field enhanced vasodilatation and increased vasomotion under norepinephrine, which induced high vascular tone and, in contrast, induced vasoconstriction and decreased vasomotion under acetylcholine, which induced low vascular tone.

These studies are strongly supported by another independent study that examined the effect of a moderate-intensity static magnetic field on microcirculation, suggesting that the static magnetic field could modulate the biphasic responses of relatively smaller-diameter blood vessels (arterioles). Morris and Skalak (2005) studied the acute effect of a 70-mT static magnetic field for 15 min on the diameter of microvessels in rat skeletal muscle placed under pentobarbital anesthesia, using intravital microscopy. This study suggested that the static magnetic field could modulate microvascular tone in a restorative fashion, thereby acting to normalize the tone.

Gmitrov and colleagues reported the acute effects of 250–350 mT static magnetic field exposures for a time period of up to 80 min on microcirculation within cutaneous tissue of the rabbit ear lobe placed under pentobarbital anesthesia using REC and MPPG (Gmitrov and Ohkubo, 1999a,b; Gmitrov et al., 2002). They demonstrated that application of static magnetic fields to the carotid sinus baroreceptor region for a period of 65–80 min increased microcirculation. The static magnetic fields suppressed or recovered a Ca^{2+} channel blocker, verapamil, which reduced microcirculation.

Xu et al. (1998) observed the subchronic effects of a 180-mT static magnetic field, with length of exposure times for up to 4 weeks, on cutaneous microcirculation in conscious rabbits, using REC and MPPG. The static magnetic field significantly increased the long-lasting vasodilatation and enhanced the vasomotion. The same authors found that exposure to static magnetic fields at 1 mT or higher for 10 min enhanced microcirculation and increased peak blood velocity (Xu et al., 2000).

Mayrovitz et al. (2001, 2005) investigated the effects of static magnetic fields with strengths as high as 100 mT and exposure periods of up to 36 min on skin blood flow in humans, using a laser-Doppler flowmeter. They showed that the static magnetic fields have no significant effect on the normal, unstressed circulation or vasoconstrictive response in conjunction with skin temperature. Steyn et al. (2000) also indicated that there are no effects observed on blood flow in horses after exposure to static magnetic fields.

In a series of studies that observed the effects of ultrastrong (>5 T) static magnetic field exposure, Ichioka et al. (1998, 2000) investigated the acute effect of an 8-T static magnetic field exposure for a period of 5 min on blood flow in rat by using a laser-Doppler flowmeter and thermistor-derived measurements.They demonstrated that blood flow

and skin temperature decreased during the field exposure, through the movement of water vapor over the animal and the decreased humidity in the air.

8.3.1.3.2 Blood Pressure

Gmitrov and colleagues studied the influence of both a 350-mT static magnetic field and geomagnetic field activity on mean arterial blood pressure (MAP) in pentobarbital-anesthetized rabbits (Gmitrov and Ohkubo, 2002; Gmitrov et al., 2002). Application of the static magnetic field to the baroreceptor region for 65–80 min decreased MAP. In testing geomagnetic field applications, they found that there was a positive correlation of this field's activity with MAP, and this result implied that magnetic storms could increase the incidence of severe cardiovascular events.

Okano and Ohkubo (2001) examined the acute effect of a 1-mT static magnetic field applied for 30 min on pharmacologically altered blood pressure in conscious rabbits. It was found that (1) the static magnetic field reduced the vasodilatation effect from enhanced vasomotion and antagonized the reduction of blood pressure under a Ca^{2+} channel blocker, nicardipine, which induced low vascular tone, and (2) the static magnetic field attenuated vasoconstriction and suppressed the elevation of blood pressure while under the influence of a nitric oxide (NO) synthase inhibitor, L-NAME, which induced high vascular tone. However, two of their experiments, which were carried out under normal conditions without pharmacological drugs, showed that static magnetic fields did not induce any significant effects on hemodynamics and blood pressure (Okano and Ohkubo, 2001, 2003a). With regard to these undetectable effects, Muehsam and Pilla (1996) speculated that physiologically significant bioresponses to therapeutic signals appear to occur only when the physiologic state of the target system is far from homeostasis.

In contrast to the experiments done without pharmacological manipulation, Okano and Ohkubo (2003a) found that exposure to a 5.5-mT static magnetic field for 30 min caused the suppression of norepinephrine- or L-NAME-induced vasoconstriction and hypertension in rabbits. Furthermore, they tested exposures of 5–10-mT static magnetic fields for a period of several weeks on the development of hypertension in spontaneously hypertensive rats (Okano and Ohkubo, 2003b; Okano et al., 2005a). Experimental results indicated that the static magnetic fields suppressed and retarded the development of hypertension because of the reduction in plasma levels of both angiotesin II and aldosterone together with lower levels of NO metabolites (NO_x).

In addition, the antihypotensive effects of static magnetic fields on reserpine-induced hypotensive rats were investigated (Okano et al., 2005b). The result suggested that exposure to a 25-mT static magnetic field for several weeks suppressed the reserpine-induced hypotension and bradykinesia through the inhibition of norepinephrine depletion.

Saunders (2005) commented that most of these studies were undertaken in the context of the potential therapeutic effects of static magnetic field on various disorders. Further studies with some independent replications are required even if the effects of static magnetic field on both blood flow and blood pressure indicate possible medical applications.

8.3.1.4 Neuroendocrine, Visual, and Neurophysiological Systems

Effects of static magnetic field exposures of 0.05 μT to 80 mT, and 7 T on the level of melatonin in rat have been examined (Kroeker et al., 1996). The first experimental exposure using field strengths of up to 80 mT for 12 h/d and 8 d showed no significant changes in night-time pineal and serum melatonin levels, as did the second experimental exposure using 7 T for 45 min. The visual system of the fruit fly (*D. melanogaster*) was

investigated after an exposure to a zero magnetic field (Creanga et al., 2002). Adults from pupae maintained in a zero magnetic field for 20 h were used for the electroretinogram. A significant increase in sensitivity of neural cells from the first optic ganglion was indicated.

Osuga and Tatsuoka (1999) tested the effects of a 1.5-T static magnetic field by using an MRI system application on neuroconduction in a partially active nerve in the bullfrog (*Rana catesbeiana*). The action potential and nerve impedance measurements indicated that a field strength of 1.5 T had no effect on neuroconduction; therefore, it was determined that neuroconduction in damaged nerves was not affected by the exposure.

8.3.1.5 Magneto-Mechanical Systems

Testorf et al. (2002) studied the influence of homogenous static magnetic fields of 8 and 14 T on melanophore aggregation in black tetra (*Gymnocorymbus ternetzi*). The result showed no significant field effects on the aggregation after exposure to magnetic fields.

Effects of a 0.2-T static magnetic field on a normal human neuronal cell culture, FNC-B4, has been investigated with MCF-7 and WEHI-3 cells as controls (Pacini et al., 1999b). FNC-B4 cells changed their morphology after the exposure. Cells became elongated and formed vortexes, while controls did not show any alteration. The morphological changes in MRC-5 fibroblasts were evaluated as well (Pate et al., 2003). The cells were screened for cell mobility, cell distribution, and cellular morphology (size, shape, lysis, and background). These cells were exposed to both a static magnetic field and a pulsating magnetic field for a period of 0, 24, 48, and 72 h. Although the static magnetic field-exposed cells showed cell membrane damage and morphological change, as well as other interesting findings that were included in the report, this report may not be useful because it did not provide essential dosimetric data, such as strength of the field.

Danielyan et al. (1999) examined the effects of a 0.2-T static magnetic field on binding of ouabain-H^3, which is a specific inhibitor of Na^+-K^+-ATP-ase, in normal glandular breast tissue and in cancerous breast tissue. The static magnetic field-induced decrease of binding was considered as evidence for the dehydration effect of the field. This study has indicated that the static magnetic field tested could influence the cancer cell's metabolism through cell hydration changes. They investigated the effects of a 0.2-T static magnetic field on the hydration of rat tissues (Danielyan and Ayrapetyan, 1999). They assumed that the target for magnetic field action was the structured water of the cell. Decreases in hydration and adaptation of brain, liver, and spleen and an increase in the case of kidney were observed.

8.3.1.6 Musculoskeletal System

Yan et al. (1998) investigated the effects of static magnetic fields on bone formation of rat femurs. They implanted magnetized samarium cobalt rods with a field strength of 180 mT into rat femurs. The bone mineral density (BMD) and bone calcium content were measured 12 weeks after implantation. Results indicated that the femurs adjacent to the magnetized specimens had significantly higher BMD and calcium content. However, BMD and calcium content levels were found to be normal in both magnetized and unmagnetized specimen groups. The same research group further studied the effects of a 180-mT static magnetic field on bone formation, using an ischemic rat femur model (Xu et al., 2001). It was reported that the enhancement of the femoral bone formation was due to the improved blood circulation in the femur.

Satow et al. (2001) observed the effect of a 0.65-T static magnetic field on muscle tension in the neuromuscular preparation of the sartorius muscle of bullfrog (*R. catesbeiana*). The

tension development was obtained by stimulation of the sciatic nerve or of the sartorius muscle itself for a duration of 30 min. A decrease in muscle tension was observed. The results indicated that application of the static magnetic field was responsible for tension development.

8.3.2 Tissue, Molecular, and Cellular Studies

8.3.2.1 DNA and Chromatin

The exposure of isolated rat lymphocytes to a static magnetic field of 7 mT for 3 h did not increase the number of damaged cells (Zmyslony et al, 2000). Although incubation with 10 μg/ml $FeCl_2$ did not cause DNA damage, the number of damaged cells increased when the $FeCl_2$-incubated lymphocytes were simultaneously exposed to the field. A hypothesis for these observations was that the number of reactive oxygen species generated by iron ions in cells might increase after the exposure to the magnetic field (Jajte et al., 2002).

Binhi et al. (2001) have reported the effect of a weak static magnetic field on *Escherichia coli* K12 AB1157 cells, by using anomalous viscosity time dependence (AVTD) assay methods. The AVTD changes were found when the cells were exposed to static magnetic field levels up to 110 μT. These results were consistent with the calculations of individual rotations of the ion–protein complexes Ca^{2+}, Mg^{2+}, and Zn^{2+}, provided that all complexes rotated at the same speed. They suggested that the rotation for all ion–protein complexes is on the same carrier, such as DNA.

The effect of a zero magnetic field on the conformation of chromatin in human VH-10 fibroblasts and lymphocytes was investigated by the AVTD method (Belyaev et al., 1997). A decrease in the AVTD peaks was observed within 40–80 min of exposure to fibroblasts, and this decrease was transient, disappearing 120 min after the beginning of exposure. A similar effect of zero field was observed when cells were exposed for 20 min and kept at an ambient field. They concluded that both zero field and γ-rays caused hypercondensation and decondensation of chromatin. Zero field effects were more significant in the beginning of the G_1-phase than in the G_0-phase in human lymphocytes.

Okuda et al. (1998) evaluated the effects of a 6.34-T static magnetic field on the instability of microsatellite repetitive sequences in DNA mismatch repair (MMR)-proficient and MMR-deficient cell lines, HeLa S3, and HCT116, respectively. After exposure to the field, both cell lines exhibited no significant microsatellite sequence changes. This result suggested that the static magnetic field might not induce the genetic changes in microsatellite sequences.

8.3.2.2 Cell Growth, Cell Proliferation, and Cell Cycle

Potenza et al. (2004b) showed that *E. coli* cell growth and gene expression were affected by a static magnetic field exposure level of 300 mT. Cell proliferation at the stationary phase was increased by exposure to those cells growing in a modified medium culture containing glutamic acid; however, cell proliferation was not affected in those cells growing in traditional Luria–Bertani (LB) medium. Gene expression differences were estimated by differential display assays using arbitrary primers, and four genes were found to be responsive to the static magnetic field. One clone, expressed only in the exposed cells, corresponded to a putative transposase. Potenza et al. suggested that the static magnetic field exposure might stimulate transposition activity.

Stansell et al. (2001) reported that antibiotic (piperacillin) resistance of the clinically isolated *E. coli* was increased by the heterogenous static magnetic field exposure level of

8–60 mT for 45 min. They suggested the observation may be unique to the particular strain of *E. coli* or the specific antibiotic used. They did not suggest any mechanistic implication for this observation.

Poiata et al. (2003) reported zero magnetic field effect on the antibiotic resistance of *E. coli* strains isolated from human subjects. They used 26 *E. coli* strains and 5 different antibiotics, ampicillin, ceftazidine, tetracycline, ofloxacin, and kanamycin. Approximately one third of the tested strains was sensitive to the zero field treatment. Minimum inhibitory concentrations (MICs) of each antibiotic for some strains were decreased by zero magnetic field exposure, while the MICs for other strains were increased by the exposure. Their mechanistic hypothesis, based on magnetic particles, did not support these observations.

Ruiz-Gomez et al. (2004) showed that growth of the haploid yeast strain *Saccharomyces cerevisiae*, a eukaryotic cell, was not affected by exposure to static magnetic field levels of 0.35 and 2.45 mT.

Effects of a 0.2-T static magnetic field, generated by MRI alone or in combination with vitamin D treatment, on cell damage and proliferation in the human breast cancer cell MCF-7, human neuronal cell FNC-B4, and murine leukemia cell WEHI-3 have been investigated (Pacini et al., 1999a). Three-hour exposures to the 0.2 T field had no effect on the cell colony formation number in all three cell lines. Results demonstrated that [^{3}H] thymidine incorporation level decreased in MCF-7 and FNC-B4 cells, while no changes were observed in WEHI-3. It was also demonstrated that the treatment of cells using vitamin D had a permanent antiproliferative effect.

Long-term effects on proliferation of human fetal lung fibroblast (HFLF) cells of repetitive exposure to a 1.5-T static magnetic field with exposure periods of 1 h/d for 3 weeks have been investigated (Wiskirchen et al., 1999). Results showed no changes in clonogenic activity, DNA synthesis, cell cycle, and proliferation kinetics. In a following paper, effects of static magnetic field levels of 0.2, 1.0, or 1.5 T on the cell cycle in both synchronized and nonsynchronized HFLF cells were evaluated (Wiskirchen et al., 2000). The exposure condition was 1 h/d for 5 consecutive days. Results showed no significant differences in cell cycle events between synchronized and nonsynchronized cells.

A series of research studies on growth enhancement by strong inhomogenous static magnetic fields have been reported. Tsuchiya et al. (1996) showed that the growth of *E. coli* was affected by both a strong homogenous static magnetic field strength of 7 T and inhomogenous field strengths of 5.2–6.1 or 3.2–6.7 T. In the stationary phase, the cell number under a high magnetic field was about two to three times higher than that of a control. The effect of the inhomogenous field was much stronger than that of the homogenous field. They also showed that the transcription activity of *E. coli* was enhanced by the strong inhomogenous static magnetic field levels of 5.2–6.1 T (Tsuchiya et al., 1999). The transcription levels of the *rpoS*, gene which encodes sigma factor of RNA polymerase, was increased in the stationary phase by the static magnetic field exposure. This transcription factor is specifically activated during the stationary phase and plays an important role in the transcription control of other genes in the stationary phase.

Horiuchi et al. (2001) showed that *E. coli* cell death in the stationary phase was suppressed by strong inhomogenous static magnetic field levels of 5.2–6.1 T with a gradient of 24 T/m and that the suppression was dependent on the addition of amino acids to the LB medium. The addition of glutamic acid enhanced cell death as pH increased in the stationary phase, and cell death was dramatically suppressed by the field exposure. At the same time, *rpoS* gene expression was increased 20% by the field exposure. They suggested that the increase of *rpoS* gene expression in the stationary phase by the field exposure might be related to the base resistance because the *rpoS*-disrupted strain showed a lower base resistance than the wild-type strain (Ishizaki et al., 2001). It has

been shown that the medium supernatant, when used after the static magnetic field exposure, could enhance the suppression of cell death (Horiuchi et al., 2002). The pH of the medium after the static magnetic field exposure was only slightly different from that of the control (by a factor of 0.07 pH), and pH-adjusted medium from both exposed and control supernatants still had the suppression effect characteristics from the exposure to static magnetic fields. It has been suggested that other factors also were involved in the full suppression effect of cell death by the field exposure.

The growth advantage in stationary phase (GASP) phenomenon is described as follows. When *E. coli* cells grown for 10 d (aged culture) and *E. coli* cells grown only for 1 d (young culture) were mixed, the cell number of the young culture decreased, and the population of the young culture was taken over by the aged culture, and eventually only aged cells predominantly survived in the system. It has been found that the GASP phenomenon disappeared with the exposure to strong inhomogenous static magnetic field levels of 5.2–6.1 T (Okuno et al., 2001). They suggested that the disruption of the GASP phenomenon might be related to an effect on the *rpoS* gene by the static magnetic field exposure.

Gray et al. (2000) evaluated static electric and magnetic field effects on the action enhancement of the chemotherapeutic agent adriamycin in transplanted mammary adenocarcinoma in female B6C3F1 mice. Treatment consisted of using 10 mg/kg of adriamycin in combination with a 4-h exposure to a 110-mT field. Tumor regression in the groups exposed to a static magnetic field was greater than in the group treated with adriamycin only.

Tanioka et al. (1996) evaluated the effects of a 6.34-T static magnetic field on proliferation and metastatic activity in the B16 melanoma and EL-4 T-lymphoma cell lines. Cell cultures were incubated in the presence of magnetic fields for 12, 24, 36, or 48 h at 37°C. It was found that the proliferative and the metastatic activities of both cell lines were promoted under certain conditions.

Tofani et al. (2003) exposed immunocompetent mice bearing either the murine Lewis lung carcinoma or the B16 melanotic melanomas to static field levels of 3 and 4 mT and treated them with two commonly used anticancer drugs, cisplatin and cyclophosphamide, respectively. The survival time of mice treated with cisplatin and exposure to the magnetic fields was significantly longer than that of mice treated only with cisplatin or only exposed to the magnetic fields, surpassing that of mice treated with 10 mg/kg i.p. of the drug and showing that the magnetic field acts synergically with the pharmacological treatment. When mice treated with cyclophosphamide were exposed to the magnetic field, no synergic effects were observed. No clinical signs or toxicity were seen in any of the mice exposed to the magnetic field alone or along with cisplatin or cyclophosphamide treatment.

Raylman et al. (1996) studied the effects of exposure to a static magnetic field of 7 T for 64 h on cell viability in three malignant human cell lines, melanoma (HTB 63), ovarian carcinoma (HTB 77IP3), and lymphoma (Raji; CCL86). It has been reported that the static field exposure reduced the viable cell count and appeared to inhibit cell growth.

Using two types of mammalian cells, mouse leukemia cells P388 and Chinese hamster fibroblast cells V79, Sakurai et al. (1999) tested the effects on cell growth patterns of exposure to a 7-T static magnetic field for up to 5 d. No significant magnetic field effects on cells were found.

In a series of papers (Kula, 1996; Kula and Drozbz, 1996a,b), the magnetic field effects on cultured fibroblasts isolated from the BALB/c mouse have been investigated. The fibroblast cultures were exposed to a static magnetic field of 0.49 T and a 50-Hz AC magnetic field of 0.02 T for a time period of 2–64 min/d over four consecutive days. The following parameters were studied: the dynamics of culture growth; protein content;

thymidine incorporation; Zn, Fe, and Cu ion content; the activity of superoxide dismutase (SOD) and catalase (CT); and glycosaminoglycan metabolism. The static magnetic field exposure had no effect on both the vital functions and glycosaminoglycan metabolism and did not show any changes in the free-radical process in fibroblasts. Kula et al. (2000) further evaluated the activities of SOD, CT, glutathione peroxidase, and malondialdehyde (MDA) in the livers and kidneys of rats exposed to a static magnetic field of 0.49 T and a 50-Hz AC field of 0.018 T. While the 50-Hz magnetic field was found to influence free-radical processes in both liver and kidney tissue, the static magnetic field showed no effects. Magnetic field effects on the lipid peroxidation product, MDA, in mouse subcellular fibroblast have been evaluated by the same protocol in a previous report (Kula et al., 2002). It was found that exposure to a static magnetic field caused no changes in peroxidation of membrane structures.

Effects with a combination of static and alternating magnetic fields on cell attachment and induction of apoptosis in rat tendon fibroblast and rat bone marrow (RBM) osteoprogenitor cells have been reported (Blumenthal et al., 1997). Experiments utilized 60-and 1000-Hz AC magnetic fields of up to 0.25 mT_{p-p} and static magnetic fields of up to 0.25 mT. It was found that AC fields and static magnetic fields tested with various combinations of field strengths and frequencies resulted in extensive detachment of preattached cells and prevented the normal attachment of cells not previously attached to substrates. Results suggested significant alterations in cell metabolism and cytoskeleton structure after the exposure.

Blanchard and Blackman (1994) proposed the ion parametric resonance (IPR) model for the prediction of the interaction between magnetic fields and biological systems (see also Chapter 9 on resonance phenomena by Liboff). According to the IPR model, the relationships among the strength of a static magnetic field, the AC magnetic field frequency, and the charge-to-mass ratio of ions of biological relevance were important key factors. Blackman et al. (1996) tested the influence of magnetic fields on neurite outgrowth in PC-12 cells and showed that the PC-12 cell response to perpendicular AC and static magnetic fields was distinct and predictably different from that found for parallel AC and static magnetic fields. It has been reported that the response to perpendicular fields was dominant in an intensity-dependent nonlinear manner.

The effects of the combination of AC and static magnetic fields on the behavior of Friend erythroleukemia cells have been studied (Eremenko et al., 1996). The combined fields were a geomagnetic field of 45 μT, together with a 70-μT field at 50 Hz which was produced in a solenoid coil, and 20-nT DC and 2.5-pT AC fields in a magnetically shielded room. It was found that the culture growth cycle of cells was slightly accelerated inside the solenoid, and the degree of acceleration appeared to depend on sensitivity of the cell cycle to the magnetic field. On the other hand, it was found that the culture growth cycle of cells inside the magnetically shielded room was slightly decreased.

Effects of a static magnetic field exposure of 10 T for up to 4 d on the rate of cell growth or cell cycle distribution in Chinese hamster ovary (CHO-K1) cells have been investigated (Nakahara et al., 2002). The exposure to the static magnetic field alone did not affect micronucleus formation. In x-ray irradiated cells, exposure to the 10-T static magnetic field resulted in a significant increase in micronucleus formation. Buemi et al. (2001) examined the effects of a 0.5-mT static magnetic field on the cell proliferation and cell death balance in monkey renal cells (VERO) and in rat cortical astrocyte cells. After 6 d of exposure to the magnetic field, they observed the effects on cell proliferation and cell death balance and suggested that the effects might vary depending on the cell type. Magnetic fields may also have a nephropathogenic effect.

Tofani et al. (2001) investigated the role of magnetic field characteristics on the growth of WiDr human colon adenocarcinoma, MCF-7 human breast adenocarcinoma,

and MRC-5 embryonal lung fibroblast. Cell death induction was observed with a magnetic field exposure of greater than 1 mT when the combined static magnetic field and 50-Hz magnetic field was applied. The report showed that significant tumor growth inhibition appeared when the total field strength was greater than 3.59 mT.

Schiffer et al. (2003) studied the effects of four different types of magnetic field applications on the cell cycle progression in two different tumor cell lines, the human acute myeloid leukemia cell HL-60 and the mouse lymphoma cell EA2. The four types of magnetic field applications used were (1) the static magnetic field of 1.5 and 7.05 T, (2) the magnetic gradient field with ± 10 and ± 100 mT/m at 100 Hz; (3) the pulsed high frequency magnetic field (5.8 μT at 63.6 MHz); and (4) the combination of (1)–(3). The exposure duration ranged from 1 to 24 h. Cell cycle fractions at G_0/G_1, S, and G_2/M phases were analyzed by flow cytometry. Cell cycle analysis did not show differences between the exposed and control cells. In conclusion, during MRI, no influence of magnetic field on cell cycle progression was observed in these cell lines.

8.3.2.3 Cell Membrane and Cell Metabolic Activity

Chignell et al. (1998) studied the effects of static magnetic fields of 25–150 mT on the photohemolysis of human erythrocytes by ketoprofen. An application of a static magnetic field during UV (>300 nm) irradiation of ketoprofen and erythrocytes significantly decreased the time required for photohemolysis. It has been suggested that the magnetic field increases the concentration and lifetime of free radicals that escape from the radical pair.

Chionna et al. (2005) investigated the effects of a 6-mT static magnetic field, applied for 24 h, on cell shape, cell surface sugar residue, cytoskeleton, and apoptosis in the hepatic transformed cell line Hep G2. Significant modifications of cell shape and surface by the field exposure have been observed. The exposed cells were found to be elongated, with many irregular microvilli randomly distributed on the cell surface. The shape of the cells was found to be less flat at the end of the exposure, although the morphology of the organelles remained unmodified throughout the exposure period. It has been reported that cell proliferation was partially affected. Results suggested that the static magnetic field caused a time-dependent biological effect on Hep G2 cells.

Sonnier et al. (2000) found that there were no effects from the exposure of static magnetic field levels of 0.1, 0.5, 5, or 7.5 mT, applied for 5 sec, on resting potential in cultured neuroblastoma cells. They also used the patch-clamp technique to measure transmembrane Na^+, K^+ currents in neuroblastoma cells SH-Sy5Y exposed to static magnetic fields of up to 7.5 mT (Sonnier et al., 2003). The magnetic field exposure did not result in detectable changes in any of the action potential parameters.

Trabulsi et al. (1996) measured the excitatory postsynaptic potential (EPSP) after the exposure of a mouse hippocampal slice to static magnetic field levels of 2–3 mT and 8–10 mT for a period of 20 min. They observed biphasic effects at 2–3 mT and depression of EPSP at 8–10 mT. It has been suggested that changes in intracellular Ca^{2+} concentration were responsible for these effects. Isolated *Helix aspersa* neurons were exposed to static magnetic field levels of 0.07–0.7 T, and their action potential was measured (Azanza and del Moral, 1996). A decrease in the spike depolarization voltage has been observed, and it has been attributed to desensitization of the membrane Na^+-K^+-ATP-ase pumps through an anisotropic diamagnetism reorientation.

Wieraszko (2000) studied the effect of 2–3-mT static magnetic fields applied for 20 min on the evoked potential response in B57/J56 mice hippocampal slices. Results, which were based on measurements of hippocampal function, showed both an alteration of the evoked potential and an effect on the influence of dantrolene, an inhibitor of intracellular Ca^{2+} channels.

The voltage-activated calcium channel function in cultured GH3 cells has been investigated (Rosen, 1996). A static magnetic field of 120 mT was applied for 150 sec. Reversible changes in calcium channel function were observed and were found to be temperature dependent. Results indicated that these changes were a result of alterations in the membrane proper because of the magnetically induced deformation.

Using the whole-cell patch-clamp technique, voltage-activated Na^+ channels in GH3 cells were examined (Rosen, 2003). The effects of exposure to a static magnetic field of 125 mT for 150 sec on voltage-gated Na^+ channel kinetics included a slight shift in the current–voltage relationship, a 5% reduction in peak current, and an increase in the activation time constant, τ_m, during and at least 100 sec after the exposure to the field. Significant changes were only observed at 35°C and 37°C. It was suggested that the temperature dependence factor that affected this process was probably due to the greater ease with which the liquid crystal membrane was deformed. Results suggested that the changes might be due to the reorientation of diamagnetic anisotropic molecules in the membrane. Hinch et al. (2005) showed the effects of static magnetic fields on action potential propagation and excitation recovery in nerve. At a field level of 125 mT, which was the same condition previously used by Rosen, they did not observe major changes in the electrical functioning of neurons.

Aldinucci et al. (2003a,b) investigated the effects of a 4.75-T static magnetic field exposure applied for 1 h, and also a 1-h exposure using combined fields of 4.75 T with a pulsed field of 0.7 mT, on proinflammatory cytokines, in human peripheral blood mononuclear cells (PBMCs) and Jurkat cells. They measured Ca^{2+}, proliferation, and the eventual production of proinflammatory cytokines. The static magnetic field exposure alone did not show any effects on the physiologic behavior of normal lymphocytes; however, the combined static and alternating magnetic field exposure contributed synergistically to the increase of $[Ca^{2+}]_i$. The exposure of PBMCs was carried out in a static magnetic field of 10 T (Onodera et al., 2003). It was reported that the magnetic field exposure reduced the viability of phytohemagglutinin (PHA)-activated T cells in both CD4+ and CD8+ subclasses. Sabo et al. (2002) observed a decrease in the metabolic activity of human promyelocytic leukemic cells HL-60 when exposed to a field of 1 T for 72 h. The decrease was also observed in the presence of antineoplastic drugs, which included 5-fluorouracil, cisplatin, doxorubicin, and vincristine.

Miyamoto et al. (1996) studied the effects of strong 6-T homogenous magnetic fields on both active and passive Rb^+ influx into HeLa cells. Using field exposures of 1.6 T and lower, and of 2.0 T, at various temperatures did not cause any changes in active or passive Rb^+ influxes.

Mouse islet of Langerhans cells have a very regular oscillation of calcium concentration. Madec et al. (2003) showed no effects of combined AC and static magnetic fields on these calcium oscillations in mouse islet of Langerhans.

8.3.2.4 Gene Expression and Signal Transduction

Fanelli et al. (1999) found a decrease of apoptosis in the human cell lines U937 and CEM, following exposure to a static magnetic field of 600 μT. It was suggested that the protective antiapoptotic effect was due to cellular modifications from the static field exposure, which affected the ability of the cell to enhance Ca^{2+} influx from the extracellular medium. Cohly et al. (2003) examined the effects of a 0.618-mT static magnetic field on a human osteoblast cell line (MG-63) culture, in terms of proliferation, proline uptake, and gene expression. Results showed that the exposure might be detrimental to bone formation.

Mnaimneh et al. (1996) investigated the effects of static magnetic field levels from 1 to 100 mT and also an AC field of 1.6 mT delivered at 1 Hz on NO production by murine

BCG-activated macrophages. No significant differences were observed in NO levels after a 14-h exposure.

Brief exposure effects from a static magnetic field of 100 mT for 15 min on protein expression in cultured rat primary hippocampal cells have been reported (Hirai et al., 2002). Expression of DNA binding activator protein-1 (AP-1), neural marker protein (MAP2), and neural differentiation marker protein (GAP-43, c-Fos, Fos-B, Fra-2, c-Jun, Jun-B, and Jun-D) were examined. Cytoplasmic Ca^{2+} and lactate dehydrogenase activities were also analyzed. It was found that exposure to the static field increased AP-1 DNA binding through expression of Fra-2, c-Jun, and Jun-D in immature cultured hippocampal neurons.

Flipo et al. (1998) examined *in vitro* effects of the static magnetic field levels of 2.5–150 mT applied for 24 h on the mitogen response to concanavalin A, phagocytosis, apoptosis, and Ca^{2+} influx in C57Bl/6 murine macrophages, spleen lymphocytes, and thymic cells. The exposure resulted in a decrease of phagocytosis, an inhibition of mitogenic response in lymphocytes, and a marked increase of apoptosis in thymic cells.

Salerno et al. (1999) measured *in vitro* expressions of activation markers and interleukin release in human PBMCs after exposure to a static magnetic field of 0.5 T for 24 h. They observed that the expression of CD69 at 0.5 T was reduced after PHA stimulation. Increases in interferon-γ and interleukin 4L (IL-4L) releases were observed; however, no changes in tumor necrosis factor α (TNF-α), IL-6, and IL-10 releases were observed.

Effects of a static magnetic field of 1.5 T applied for 240 min on human L-132 cells have been investigated (Guisasola et al., 2002). Heat shock proteins hsp70, hsp27, and their corresponding messenger RNAs (mRNAs), along with cyclic AMP and Ca^{2+} ions were analyzed. No field exposure effects were observed.

Effects of the exposure of HL-60 cells to a 6-T spatially inhomogenous magnetic field with a strong gradient of 41.7 T/m and to a spatially homogenous magnetic field of 10 T have been studied (Hirose et al., 2003b). The expression of c-Jun protein increased in HL-60 cells after exposure to the 6-T static magnetic field for 24, 36, 48, and 72 h.

Using budding yeast (*S. cerevisiae*) as a model for an *in vitro* biological test system, Ikehata et al. (2003) examined the genome-wide gene expression profile of yeast cells after exposure to 5- and 10-T fields for periods of 2 and 24 h. Exposure to static magnetic fields did not affect gene expression. Slight changes in the expression of several genes were observed after exposure to 14 T for 24 h.

8.3.2.5 Genotoxicity

Previous studies have shown that static magnetic fields alone did not have a lethal effect on cell growth and survival under normal culture conditions, regardless of the strength of the magnetic field applied. Effects of 5-h exposures of HL-60 cells to 6-mT static magnetic fields, with or without camptothecin, which is a DNA topoisomerase I inhibitor, have been investigated (Teodori et al., 2002). Results indicated that the field exposure did not cause apoptogenic or necrogenic effects. It was reported that exposure to the static magnetic field alone or with camptothecin did not affect cell viability.

Potenza et al. (2004a) showed that the conformation of plasmid DNA was altered by exposure to static magnetic fields of 250 mT. Various DNA point mutations were found, while no DNA degradation was observed. It was shown that the DNA degradation from H_2O_2 was accelerated by simultaneous field exposure; however, the plasmid DNA in *E. coli* cells exposed to the same static magnetic field did not show any alteration. They suggested that the magnetic field could change DNA stability directly or by activating the reactivity of oxidant radicals. It has also been suggested that the genotoxic effect could be minimized in living organisms by the presence of protective cellular responses, such as the DNA repair system and the buffering action of heat shock proteins.

In order to reveal the genetic effects of a 0.6-T static magnetic field, mutagen-sensitive mutants of the fruit fly (*D. melanogaster*) were used for the somatic cell test (Koana et al., 1995). It was shown that the exposure resulted in damaging effects in larval cellular DNA, and somatic cells without normal DNA repair functions failed to continue cell division, which resulted in developmental lethality of mutant larvae. The genotoxic activity of the field exposure was estimated to be the same as that of UV irradiation with 0.14 mJ/m^2/sec. Further study has been conducted with *D. melanogaster* using a wing spot test to estimate possible mutagenic or carcinogenic activity of the static magnetic field (Koana et al., 1997). A DNA repair defective mutation *mei-41*^{D5} was introduced into the conventional *mwh/flr* test system to enhance mutant spot frequency. Third-instar larvae were exposed to a field of 5 T for 24 h. It was shown that the exposure significantly enhanced the somatic recombination, and the recombination was found to be suppressed by supplementation of vitamin E. Results indicated that the magnetic field enhanced the genotoxic effects of spontaneously produced free radicals (Takashima et al., 2004).

In a report describing the investigations of whether static magnetic fields have cytogenetic effects in BALB/c AnNCrj male mouse bone marrow cells, Suzuki et al. (2001) indicated that the frequency of micronuclei was significantly increased by exposure to a 3-T field for 48 and 72 or a 4.7-T field for 24, 48, and 72 h. The increase in micronucleus frequency was shown to be dose dependent.

Micronuclei in cells have been used as an indicator of DNA damage. A study for *in vitro* assessment of the effects of a 4.7-T static magnetic field on the frequency of micronucleated cells in the Chinese hamster CHL/IU cell line with preexisting damage induced by exposure to mitomycin C (MMC) has been carried out (Okonogi et al., 1996). Results indicated a decrease in the frequency of micronuclei formation after 6 h of exposure and also the influence of the static magnetic field on the DNA damage stage produced by MMC.

An *E. coli* mutation assay has been carried out to assess the mutagenic effects of strong static magnetic fields (Zhang et al., 2003). Results obtained with a wild-type *E. coli* strain GC4468 and several derivatives, which were defective in DNA repair enzymes or redox-regulating enzymes, showed no effects of the exposure in terms of the survival rate of cells. On the other hand, the mutation frequency was significantly increased by exposure to the 9-T static magnetic field for 24 h in *soxR* and *sodAsodB* mutants, which were defective in their defense mechanism against oxidative stress. Results indicated that static magnetic fields induced mutations by increasing the production of intracellular superoxide radicals.

Ikehata et al. (1999) reported that 2- and 5-T static magnetic fields did not have mutagenic potential in a bacterial mutation test using *Salmonella typhimurium* (TA98, TA100, TA1535, and TA1537) and *E. coli* (WP2 *uvrA*) strains. They also reported that the exposure resulted in an increased mutation rate of the WP2 *uvrA* strain when induced by the agents *N*-ethyl-*N*′- nitro-*N*-nitrosoguanidine (ENNG), *N*-methyl-*N*′-nitro-*N*-nitrosoguanidine (MNNG), ethylmethanesulfonate (EMS), 4-nitroquinoline-*N*-oxide (4NQO), 2-amino-3-methyl-3*H*-imidazo-[4,5-*f*]-quinoline (IQ), and 2-(2-furyl)-3-(5-nitro-2-fulyl) acrylamide (AF-2). The mutagenicities of 2-aminoanthracene (2-AA), 9-aminoacridine (9-AA), *N*-4-aminocytidine, and 2-acetoamidofluorene (2-AAF) were not affected by the exposure. The bacterial growth did not change after the exposure. They suggested that the mechanism of these effects might be related to *in vitro* interactions between the chemicals and DNA and to repair systems in the test strains.

8.3.2.6 Cell-Free System, Free Radical, Enzyme Activity

Markov and Pilla (1994, 1997) studied the Ca^{2+}/calmodulin-dependent myosin phosphorylation and observed magnetic field effects of 44-μT, ambient, and 200-μT vertical fields for 5 min on the Ca^{2+} binding property. Phosphorylation increased up to at 200 μT

depending on the [Ca^{2+}] concentration. The magnetic field effect disappeared as [Ca^{2+}] approached saturation for calmodulin. They emphasized that very small alterations in ambient level static magnetic fields are sufficient to have a profound effect on a cell-free enzyme system. In an attempt to replicate the results of Markov and Pilla, Coulton et al. (2000) saw no effects on myosin phosphoration in a cell-free system in vertical static magnetic fields up to 400 μT. As a result, in this experiment, no effects of static magnetic fields on the calcium/calmodulin binding property were observed. Engstrom et al. (2002) investigated the effects of nonuniform static magnetic fields of 0.7–87 mT with a gradient of 0.4–20 T/m for a period of 5 min on myosin phosphorylation and reported that the magnetic field exerted an influence on the rate of myosin phosphorylation. Increased phosphorylation was observed. It can be seen that the magnetic field gradients played a specific role in this experiment. Liboff et al. (2003) investigated the effect of a 30-min exposure to a static magnetic field of 20 μT on calmodulin-dependent cyclic nucleotide phosphodiesterase activity in cell-free systems and reported that the activity was altered in comparison to zero magnetic field exposures.

After studying the theoretical background of a cell-free system—Ca^{2+}/calmodulin-dependent myosin light chain phosphorylation reaction—Markov (2004a,b) designed experiments to test the effects of a pulsed radio frequency (RF) field, pulsating magnetic fields, gradient magnetic fields, and homogenous static magnetic fields on this cell-free system. He suggested that the magnetic fields affect the cell-free enzyme system by modulating ion–protein interactions.

Watanabe et al. (1997) measured and evaluated lipid peroxidation in the liver, kidneys, heart, lung, and brain of 8-week-old male BALB/c mice. The mice were exposed to 3.0- and 4.7-T fields for 3–48 h. The lipid peroxidation level in the liver was increased after exposure to the 4.7-T field. In kidney, heart, lung, and brain, no changes in the level of lipid peroxidation were observed compared to the control. The exposure to the 3.0-T field showed no alteration of the lipid peroxide level in all the tissues. The combination of CCl_4 administration and 4.7-T field exposure increased the lipid peroxidation level in the liver. It was concluded that the exposure to high static magnetic fields could induce the increase of lipid peroxidation levels in the liver of mice and could enhance the hepatotoxicity caused by CCl_4 injection.

Using fireflies, *Hotaria parvula* and *Luciola cruciata*, as bioluminescence systems, Iwasaka and Ueno (1998a) studied the effects of 8- and 14-T static magnetic fields on the emission of light. They showed that changes in the emission intensities under a magnetic field were related to the change in certain biochemical systems of the firefly, systems such as the enzymatic process of luciferase and the excited singlet state responsible for subsequent light emission.

Zhadin et al. (1998) have undertaken experiments that investigated the combined action of static and AC magnetic fields on ionic current in aqueous glutamic acid solution. Results showed that the combined parallel static and AC magnetic field causes a rapid change in the ionic current flow when the AC frequency is equal to the cyclotron frequency.

During the last few years, Brocklehurst and McLauchlan (1996) discussed the free radical mechanism involved in the observed effects of environmental electromagnetic fields on biological systems. Grissom and Natarajan (1997) summarized the theory of magnetic field effects on chemical and enzymatic reactions. Magnetic field effects have been used as a powerful technique to study enzymatic and chemical reactions with radical pair intermediates. They suggested that the coenzyme B_{12}-dependent enzymes with radical pair intermediates are well suited for the study of this effect. Taoka et al. (1997) tested the magnetic field effects on coenzyme B_{12}-dependent enzymes. The end point was that ethanolamine ammonia lyase and human enzyme

methylmalonyl–coenzyme A mutase catalyze coenzyme B_{12}-dependent rearrangement reactions. While the end point was affected, the authors speculate that the change would have little physiological significance.

Eichwald and Walleczek (1996) showed a model for magnetic field effects on radical pair recombination in enzyme kinetics. The magnetic field effects in radical pair chemistry have been reviewed (Grissom, 1995; Brocklehurst, 2002; see also Chapter 6 on free radicals by Engström).

8.4 Miscellaneous

8.4.1 Biological Sensing and Magnetite

Many studies have suggested that the magnetic field is an important marker for animal navigation and spatial discrimination (Wiltschko and Wiltschko, 1995). The blind mole-rat (*Spalax ehrenbergi*) was used as a model to examine the possibility of the perception and use of magnetic fields in their orientation in space (Kimchi and Terkel, 2001). Experiments were performed in an eight-arm maze under Earth's natural and artificial magnetic fields. Results showed that the blind mole-rat was able to perceive and use Earth's magnetic field to orient in space. Kimchi and Terkel showed that blind mole-rats spontaneously preferred to place their nests toward the south of the magnetic North. Deutchlander et al. (2003) showed that Siberian hamsters (*Phodopus sungorus*) used directional information from the magnetic field to set a position for their nests. In contrast to blind mole-rats, the directional preference for nest position demonstrated by Siberian hamsters appeared to be a learned response.

Since the neural substrate subserving magnetic orientation is not known, the combination of two techniques, a behavioral test for magnetic compass orientation and an immunocytochemical visualization of the transcription factor c-Fos as a neuronal activity marker, has been used to investigate magnetoreception in the mole rat (*Crytomys anselli*) (Nemec et al., 2001). Nemec et al. found that the superior colliculus of the hypothalamus contained neurons that would respond to magnetic stimuli, and thus determined the involvement of a specific mammalian brain structure in magnetoreception.

Edmond (1996) showed that a very sensitive magnetic compass is formed by the incorporation of a small quantity of ferromagnetic, single-domain crystals, such as magnetite, within a nematic liquid crystal. Winklhofer et al. (2001) localized high concentrations of Fe^{3+} in the upper-beak skin of homing pigeons (*Columba livia*), and identified the materials of magnetite nanocrystals as the core of a magnetic field receptor.

Lohman et al. (2001) found that hatchling loggerhead sea turtles (*Caretta caretta*), when they were exposed to magnetic fields found in three widely separated oceanic regions, swam in the direction that would help to keep them within the currents of the North Atlantic gyre and facilitate their migratory pathway. It was found that young loggerheads used a guidance system of magnetic fields to assist in their navigation.

Although the mechanism of magnetoreception has not been clearly identified, geomagnetic orientation has been well recognized. A biophysical model has shown that changes in the wavelength of light can influence magnetic field orientation through the interaction between the geomagnetic field and photoreceptors. Deutschlander et al. (1999a) found that light-dependent orientation in the newt (*Notophthalmus viridescens*), was mediated by extraocular photoreceptors located in the pineal complex or deeper in the brain. Using newts, Phillips et al. (2001, 2002b) showed the role of photoreceptors in magnetic compass

orientation and the magnetic inclination for deriving map information. They investigated the possibility that the fixed-axis response of the newts was mediated by a magnetoreception mechanism involving single-domain particles of magnetite (Phillips et al., 2002a).

There are several explanations for the magnetic sensitivity in fish. The aquatic animal might perceive an electric voltage induced by the water current or by its own movement in the geomagnetic fields. Elasmobranch fish such as sharks, skates, and rays are known to possess a sensitivity to the induced electric field through the sensory organs called the ampullae of Lorenzini.

Yano et al. (1997) studied the migrating behavior of the chum salmon (*Oncorhynchus keta*) fitted with a magnet to investigate the role of magnetic compass orientation in the North Pacific off the coast of Kushiro, Hokkaido. The magnetic field strength was about 0.6 mT around the head area, with polarity changes every 11.25 min. There were no effects observed on the movement of salmon.

Effects of electric and magnetic fields have been observed in the behavior of marine animals and freshwater and terrestrial species. In addition, there are a growing number of questions concerning the effect on aquatic ecosystems of the growing spread of artificial techniques such as underwater sea DC cables. There are many underwater DC cables under various seas all over the world, which carry electrical currents (see also Chapter 1 on fields in the environment by Mild and Greenebaum). These electric currents induce static magnetic fields with intensities up to 3.5 mT around cables on the sea bottom, where there are many invertebrate and vertebrate species. Research has been carried out to examine whether the exposure to magnetic fields of 3.7 mT for several weeks could influence the survival rate and fitness of common benthic animals of the Baltic Sea (Bochert and Zettler, 2004). The investigation was carried out on the crustacean (*Crangon crangon*, *Rhithropanopeus harrisii*, and *Saduria entomon*); the mussel (*Mytilus edulis*); and the flounder (*Planthichthys flesus*). Results showed no differences between experimental and control animals. Since this is the first study for investigating the effects of static magnetic fields generated by sea-positioned DC cables, on aquatic organisms and marine benthic animals, further studies are required.

In a study to confirm the magnetite-based detection mechanism in rainbow trout (*O. mykiss*), magnetic crystals in the area of olfactory lamellae were found, and the arrangement of several magnetic crystals in a chain of about 1 μm has been confirmed (Diebel et al., 2000).

It was shown that magnetizable material abolishes the behavior of bobolink (*Dolichonyx oryzivorus*) by blocking the ophthalmic branch of the trigeminal nerve (Beason and Semm, 1996). The result was consistent with the hypothesis that magnetite is a constituent of the magnetoreceptors associated with the ophthalmic nerve.

It is suggested that migratory birds, amphibians, and reptiles may have the ability to sense the geomagnetic field and use it as a source of compass information. Phillips (1996) presented a graphical model that predicts qualitatively the changes in the direction of homing orientation. Munro et al. (1997) investigated the effect of pulse remagnetization on the orientation of inexperienced, juvenile migrant birds, such as the Australian silvereye (*Zosterops l. lateralis*). The ability of juvenile birds to maintain their normal magnetic orientation after pulse application indicated that the pulse does not impair the magnetic compass. On the other hand, the deflection observed in adult birds after pulse treatment appeared to reflect ''false'' map information, which leads to a change in course. This is consistent with evidence that the magnetic compass involves light-dependent magnetoreception mechanisms.

Wiltschko and Wiltschko (2001) studied the behavior of European robins (*Erithacus rubecula*), under monochromatic light of various wavelengths and intensities to investigate magnetoreception. At a quantal flux of 7×10^{15} quanta/sec/m^2, the birds were well

oriented in their migratory direction under 424 nm blue, 510 nm turquoise, and 565 nm green, whereas they were disoriented under 590 nm yellow. Changes in behavior depended on increasing the light intensity. This finding suggested that light-dependent magnetoreception may involve receptors and a neuronal pathway of its own.

Ritz et al. (2000) postulated the possibility that magnetoreception involves radical pair processes as a biophysical mechanism. They first considered a system of radical pairs as a model for the magnetic sensory organ and evaluated the influence of the geomagnetic field on radical pair systems. European robins (*E. rubecula*), were used in this study, and the results showed the disruption of magnetic orientation behavior of robins when exposed to a vertically aligned broadband field of 0.1–10 MHz and 0.085 μT or the single frequency of 7 MHz and 0.47 μT, together with the geomagnetic field (Ritz et al., 2004). The disorientation observed was found to depend on the angle between the 7-MHz oscillating field and the geomagnetic field. The robins oriented in the migratory direction when the oscillating field was parallel to the geomagnetic field. The author suggested a magnetic compass based on a radical pair mechanism, due to the resonance effect on singlet–triplet transitions in the oscillating fields.

Fuller suggested the significance of the time constants of magnetic field sensitivity in animals (Fuller and Dobson, 2005). Conditioning experiments have had great success in the analysis of animal sensory physiology. Wiltschko and Wiltschko (1996) commented that the conditioning technique did not appear to be suitable for testing magnetic sensitivity.

Some insects are able to respond to magnetic fields, especially the geomagnetic field. Mosquitoes were tested for the presence of remanent ferromagnetic material and their behavioral response to magnetic fields. Most mosquitoes, when placed in a uniform static magnetic field of 0.1 mT, moved around until they were oriented parallel to the field. It was reported that a significant remanence found on the surface of both living and dead mosquitoes might be due to attraction of ferromagnetic dust onto the body (Strickman et al., 2000). It is well-known that magnetic fields influence honey bee behavior, moth navigation, beetle larvae, the behavior of hatchling loggerhead sea turtles, migration of birds, etc. Slowik et al. (1997b) speculated that the red imported fire ant (*Solenopsis invicta*) might use magnetic field information in their nesting activities and in orientation, since their first observation suggested that fire ant workers moved as a colony toward the magnetic field. In a second paper, Slowik et al. (1997a) suggested the presence of small amounts of ferromagnetic material in fire ants.

Many review papers have been published during the last few years. Deuschlander et al. (1999b) and Wiltschko and Wiltschko (2002) reviewed the light-dependent magnetoreception in animals. Lohmann and Johnsen (2000) described the difference between a magnetic directional sense and a magnetic map sense and reviewed the three hypotheses of vertebrate magnetoreception.

8.4.2 Plant Growth, Response, and Magnetotropism

The enhancement of plant growth using various magnetic field applications has been reported by many researchers (Phirke et al., 1996). Effects of magnetic fields on seed germination, crop growth, physiological response, sporulation, water uptake, and rate of seed have been studied; however, there has been no consistency in results among the various reports.

Studies directed toward investigating the effects of magnetic field treatment on seeds and water in terms of the rate and percentage of germination of rice (*Oryza sativa* L.) and on the length and weight of germinating barley (*Hordeum vulgare* L.) and wheat (*Triticum aestivum* L.) have been carried out (Carbonell et al., 2000; Martinez et al., 2000, 2002). The

field strength ranged from 125 to 250 mT depending on the research strategies. Results by Carbonell et al. showed that the rate and percentage of germination increased after chronic exposure to 150-mT fields. Magnetically treated water was found to improve the germination of rice seeds. Martinez et al. (2000) showed that the magnetic field increased the length and weight of barley seed, and the degree of this effect depended on the duration of exposure. Effects of magnetic biostimulation on the initial growth stages of wheat, with an exposure duration of 0, 1, 10, 20 min, 1 h, 24 h, and chronic exposure were investigated (Martinez et al., 2002). In the report, they defined the magnetic doses in terms of magnetic field energy density (J/m^3). An increase in plant height had been observed as the magnetic dose increased; thus, it was suggested that the stimulatory effects might be related to the amount of magnetic field energy. Florez et al. (2004) investigated the effects of 125- and 250-mT static magnetic fields on the germination and the initial growth stages of rice seeds (*O. sativa* L.). The seeds were exposed to the magnetic fields for various time durations, and the germination time was found to be shortened when the seeds were exposed to these fields. The seeds' maximum length and weight were obtained for the chronic exposure. It was shown that magnetic treatments, when applied under specific conditions, affected germination and the first stage of growth.

Piatti et al. (2002) investigated the effects of inhomogenous static magnetic fields ranging between 6 and 10 mT on the growth and viability of the plant-growing bacteria *Serratia marcescens*, barley callus cells (*Hordeum vulgare*), and blackberry (*Rubus fructiosus*). While there was no field effect observed on blackberry cells, it was found that the exposure reduced the number of bacterial cells and lowered both the number and the viability of barley cells. Diamagnetic susceptibility and root growth response to magnetic field exposure on three plant species, *Lens culinaris*, *Glycine soja*, and *T. aestivum* were investigated (Penuelas et al., 2004). Magnetic fields of 17.6 mT reduced root growth in all three plants. The field strength of 2.1 mT had no significant effect on reduction in the cereal *T. aestivum*.

Among the many studies that examined gradient magnetic field effects on various engineering, biological, and physicochemical phenomena, a study of effects of gradient magnetic fields of up to 10 T on the germination and growing process of cucumber (*Cucumis sativus* L.) was carried out (Hirota et al., 1999). It was found that the shoot germinated toward the field center, whereas the root grew in the opposite direction of the shoot. This observation seemed to be a result of the magnetic force influencing the geotaxis of the cucumber.

After calculating the magnetic field dependence of the ionic current density across the cellular membrane, Reina and colleagues examined the effects of 0–10 mT static magnetic fields on the amount and rate of water absorption in the lettuce seed cell membrane (*Lactuca sativa*) in order to compare the calculated and experimental results (Reina and Pascual, 2001; Reina et al., 2001). Theoretical calculations showed that the static magnetic field induced changes in the ionic concentration and in the osmotic pressure, which regulates the entrance of water into the seeds. The magnetic field exposure was 10 min in a Helmholtz coil, and this was carried out immediately before placing the seeds in water inside a climatized room. The investigators demonstrated a close correlation between their theoretical calculations and the actual experimental results. It was shown that exposure to the static magnetic fields altered the water absorption in seeds, which may possibly explain the change of germination rate. Adair (2002) discussed and questioned these results. Amyan and Ayrapetyan (2004) investigated changes in the wet and dry weight of barley seed after treatment by static magnetic field levels of 1.25, 2.50, and 3.75 mT. Seed treatment was carried out in cold (4°C) and warm (20°C) distilled water. After pretreatment by the fields, the seeds were incubated for 72 h. Results suggested that effects depend on not only the field strength but also the incubation time period.

Growth and sporulation of phytopathogenic microscopic fungi have been investigated under exposure to a static magnetic field that ranged from 0.1 to 1 mT (Nagy, 2004). It was

shown that the growth was decreased by the magnetic field exposures. Increases in the number of developed conidia of *Alternaria alternata* and *Curvularia inaequalis* and a decrease in the number of *Fusarium oxysporum* conidia have been observed as well.

Effects of combined AC and DC magnetic fields on the germination of hornwort seed (*Cryptotaenia japonica* Hassk) have been reported by Kobayashi et al. (2004). They tested three directions of the AC magnetic field, which were vertical, parallel, and perpendicular to the direction of total geomagnetic field (DC). The frequency and strength of the AC magnetic fields ranged between 3.5 and 14 Hz and 500 and 750 μT. The total geomagnetic field was 50 μT. The seeds were exposed to the fields for 16 d at 24 h/d. The vertical AC magnetic field applied simultaneously with the DC field was found to promote the germination of seeds. Field level applications of 7 Hz, 750 μT and 14 Hz, 500 μT showed the maximum effects.

Effects of static magnetic fields ranging from 0 to 350 μT on gravitropic bending in the apical stem segments of flax seedlings (*Linum bienne*) have been investigated (Belova and Lednev, 2001). In comparison with the control group kept in a geomagnetic field of 46.5 μT, stimulation of the gravitropic bending was observed at $0 \leq B_{DC} \leq 2\,\mu T$ and $200 \leq B_{DC} \leq 350\,\mu T$, and inhibition was observed at $100 \leq B_{DC} \leq 170\,\mu T$.

Investigations of static magnetic field effects on the curvature of primary roots of radish seedling (*Raphanus sativus* L.) have been carried out (Yano et al., 2001). When radish roots were exposed to an inhomogenous static magnetic field, they responded to the south pole of the magnet. Trophic response was found at a field level of 13–68 mT with a gradient of 1.8–14.7 T/m. A small response to the north pole of the magnet was found as well.

Jovanic and Sarvan (2004) studied the effects of static magnetic fields on fluorescence spectra and leaf temperature in intact plant bean (*Phaseolus vulgaris* L.) The field strengths were as high as 160 mT, and the plant was grown for 3 weeks. It was reported that significant changes in fluorescence spectra and leaf temperature were induced after the field exposure. An increase of fluorescence intensity ratio and changes in leaf temperature ΔT were observed in parallel with increase in field intensity.

8.4.3 Magnetotaxis

There have been many studies reporting that magnetic fields affect the swimming behavior of *Paramecium*. A decrease in swimming velocity and an increase in the frequency of directional changes were observed after exposure to a magnetic field of 0.126 T during a motility study of *Paramecium* (Rosen and Rosen, 1990). Nakaoka et al. (2002) found that a typical ciliated protozoan, *Paramecium*, swam perpendicular to a static magnetic field of 0.68 T. It was suggested that the diamagnetic anisotropy of cellular components cilia and trichocysts was important for the magnetic orientation of their swimming.

Effects of horizontal magnetic fields on the movement of *Euglena gracilis* (ca. 50 μm in length) have been reported (Tanimoto et al., 2001). When the horizontal magnetic field with a gradient of ca. 400 T^2/m was applied, living *E. gracilis* moved to the higher field (positive magnetotaxis), whereas dead *E. gracilis* moved to the opposite, lower field. *E. gracilis* was found to be oriented perpendicularly to the magnetic field regardless of whether they were alive or dead. Thus, magnetotaxis of living *E. gracilis* may be explained by taking into account both the environmental inhomogenous magnetic forces and the magnetic orientation of *E. gracilis*. In contrast, magnetotaxis was not observed in a uniform magnetic field of 8 T. Effects of strong magnetic field gradient (max. 8 T, ca. 400 T^2/m) on the movement of *E. coli* have been investigated (Tanimoto et al., 2005). *E. coli* cells were placed in a 5 mm (diameter) × 150 mm (length) glass tube containing viscous media that flowed in the tube. The speed at zero field was 0.65 cm/h. The observed velocities of the movement from a high field (8 T) to a low field (1.5 T) and the movement in the opposite direction around

were 1.35 and 0.49 cm/h, respectively. Diamagnetic *E. coli* experienced a repulsive behavior to magnetic forces of increased magnetic gradient. Therefore, it has been speculated that the velocity of *E. coli* would be accelerated toward the direction of the lower-strength field, while it would be decelerated in the direction of the stronger fields. Results suggested the magnetic force specifically, could be an important mechanism of magnetic field effects when a low-frequency high magnetic field was applied, since the microorganism might respond to mechanical stress due to alternating magnetic forces.

8.4.4 Others

As an initial study for investigating the relationship between magnetic fields and amoebae, Berk et al. (1997) examined the inhibitory effects of static magnetic fields on the population growth of amoebae. They tested three species, *Acanthamoeba hatcheii*, *Acanthamoeba castellanii*, and *Acanthamoeba polyphaga*. Amoebae were exposed to magnetic field strengths of 71 and 106.5 mT with an exposure duration up to 72 h. Results showed that magnetic fields decreased the growth of all three potentially pathogenic ameba populations significantly within 72 h. It was reported that the inhibitory effect did not depend on the field strength, and it was shown that this research would be important and advantageous in the development of disinfection strategies for surface material, such as the surface of contact lenses.

Rai et al. (1997) investigated the effects of a 0.1-T static magnetic field on the electrical parameters of goat eye lens. Under magnetic field application, the complex impedance between real and imaginary parts was obtained in the form of a Cole–Cole plot. It was reported that the static magnetic field altered the current flow in the tissue.

Iwasaka and Ueno (1998b) investigated the effects of a static magnetic field of up to 14 T on the near-infrared spectrum of water molecules and glucose solutions. They demonstrated the possibility that the static magnetic field affected the formation of hydrogen bonds of water molecules and the hydration of glucose molecules.

Morariu et al. (2000) exposed human blood samples to zero magnetic fields for 72 h in order to observe the aging process of erythrocytes. The control samples were kept in a normal geomagnetic field. In a zero magnetic field, increases in the rate of Na^+ and Ca^{2+} influx, in the rate of K^+ outflow, and in homolysis were observed. Reduction in Na^+-K^+-ATPase and Ca^{2+}-ATPase activities has been observed in a zero magnetic field; thus, zero fields significantly accelerated the aging of erythocytes. Effects of zero magnetic fields were further investigated on Zn and Cu concentrations in the human blood serum during *in vitro* aging of blood with a 48-h exposure (Ciortea et al., 2001). Blood samples were collected from both healthy donors and chronic bronchial asthma (BA) patients. While the Zn concentration was not found to be affected by the zero magnetic field exposure, Cu concentration was found to be sensitive to this field. It was also reported that the aging effect appeared to be decelerated for most BA types.

8.5 Medical Applications

8.5.1 Biomagnetic Phenomena

Biomagnetic phenomena for different intensities of magnetic fields and their frequency are shown in Figure 8.1. It is important to know the intensities and frequencies of magnetic fields involved in biomagnetic phenomena while discussing the relationship

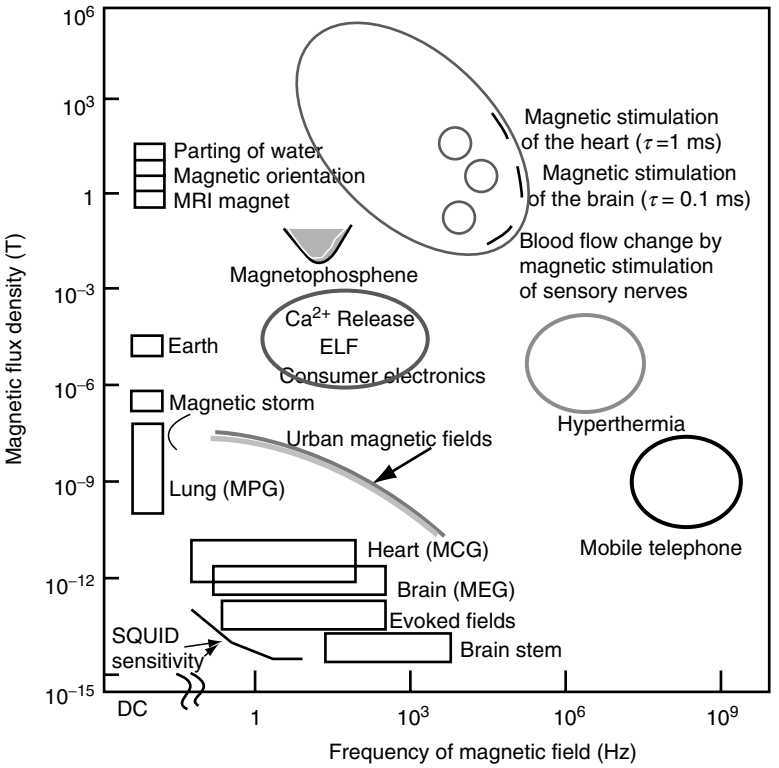

FIGURE 8.1
Biomagnetic phenomena for medical and therapeutic application.

between magnetism and living organisms. Regarding the effects of magnetism on living organisms, it should be realized that the actions of static and variable magnetic fields differ from each other in terms of the fundamental mechanism.

Studies on the biological effects of electromagnetic fields have resulted in significant developments in medical applications for electromagnetic fields, after the development of high-strength superconducting magnets. TMS, measurement of biomagnetic fields with the superconducting quantum interference device (SQUID), and MRI are the three mainstays of these medical applications. These techniques have also been leading the amazing progress in the understanding of the brain function. TMS locally stimulates the human cerebral cortex with millimeter-order spatial resolution from a figure-eight coil placed on the skull. A three-dimensional imaging of the brain neuron function has been enabled by utilization of SQUID in magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), and current-distribution MRI. Results from TMS and imaging studies indicate potential applications of biomagnetics in brain science and clinical neuropsychiatry.

In TMS, when a strong electric current is applied to a figure-eight coil positioned over the head for 0.1–0.2 ms, a pulsed magnetic field of 1 T is produced. This pulsed magnetic field generates eddy currents in the brain, which excite the targeted area of the nervous system.

Incidentally, unconscious and uncontrolled exposure of the brain to high-frequency electromagnetic waves has been increasing with the recent, rapid widespread use of cellular phones by the general public. Cellular phones in Japan are designed for operation with a frequency of 800 MHz and a microwave of 1.5 GHz (see Chapter 1 on environmental exposures by Mild and Greenebaum).

In biomagnetic measurements, MEG associated with auditory brain stem response is of the order of 10^{-15} T (1 fT), and it can be measured on the extremum of the sensitivity limitation of the SQUID gradiometer (Erne et al., 1988; Iramina and Ueno, 1995). In 10^{-12} T (1 pT)-order measurements, while α-wave spontaneous MEG can be detected without a signal-averaging technique, the technique is required to increase a signal-to-noise ratio (SNR) in order to detect various evoked responses and brain stem responses.

The recent development of noninvasive brain function measurement technologies, such as MEG and fMRI, has been contributing to the rapid progress in brain science research. Scientific discussions of mental problems such as thinking and psychomotor activities (e.g., joy, anger, sadness, and happiness) in terms of brain function became possible with the development of these new technologies.

In static magnetic fields of a few tesla, fibrin polymers, which are involved in blood coagulation, orient parallel to the magnetic fields in the course of polymerization (Yamagishi et al., 1989; Ueno et al., 1993). Furthermore, magnetic alteration of blood coagulation and dissolution processes by magnetic fields and magnetic orientation of biopolymers, such as fibrin and collagen, have been observed. These findings introduce a new aspect of biomagnetic applications in the regulation of living systems and biological materials.

8.5.2 Transcranial Magnetic Stimulation

TMS is the technique of locally applying magnetic stimulation by a strong pulsed magnetic field on the order of 1 T transcranially to the brain. When a strong electric current is applied to a figure-eight coil placed over the head for 150 μs, a pulsed magnetic field on the order of 1 T is produced that generates eddy currents in the brain, which excite the nervous system. The first study of magnetic stimulation in a human brain by Barker et al. (1985) utilized single coils; thus, localized magnetic stimulation of a targeted portion of the human brain was impossible. The localized vectorial magnetic stimulation of a human cortex using a figure-eight coil was developed by Ueno et al. (1978, 1986b, 1988, 1989, 1990a,b, 1991), which enabled stimulation of the motor cortex of a human brain at 5-mm resolution. Localized magnetic stimulation contributed to the creation of functional maps of the motor cortex related to hand and foot areas. An optimal direction of probe placement for the targeting of stimulating currents, which induce neural excitation in each functional area of the cortex, based on functional maps was observed, the so-called vectorial feature. Variations in the functional maps of the cortex with changes in orientation of the stimulating current were observed as well. It is proven that the vectorial feature allows for studies that reflect both functional and anatomical organizations of neural fibers in the brain. Localized magnetic nerve stimulation of the brain is suitable for investigations of brain function and construction without damaging any tissues.

Applications of TMS temporarily disturb brain function, which results in a virtual lesion in the brain. Zangaladze et al. (1999) showed that the disruption of the function of the occipital cortex with the use of focal TMS interferes with the tactile discrimination of grating orientation. Epstein et al. (2002) used TMS to investigate memory encoding and retrieval, particularly the role of the dorsolateral prefrontal cortex in associative memory for visual patterns. TMS disrupted associative learning of abstract patterns over the right frontal area, which suggests that the participating cortical networks may be lateralized in accordance with classic concepts of hemispheric specialization.

Traditionally, stimuli are applied at various scalp positions using a latitude- and longitude-based coordinate system referenced to Cz in the 10–20 international system at the vertex, while simultaneously, the amplitude of the motor evoked potentials generated in contralateral muscles is also measured (Ueno et al., 1989, 1990a). This gives a ''map'' of sites on the scalp from which responses can be obtained by each reference muscle.

Rothwell et al. (1987) revealed the enormous clinical importance of TMS, namely, for motor functional evaluation.

Recent developments in the navigated brain stimulation (NBS) stereotactic TMS devices allow noninvasive mapping of the spatial and temporal representation of any brain activity that reacts to magnetic stimuli (Krings et al., 2001), such as sensory, motor, language, and cognitive functions. Stereotactic TMS coil positioning and real-time visualization of the stimulating electromagnetic field effect using MRI allow precise replicability of stimulation parameters as well as accurate dose definition. Frameless NBS allows precise localization of a stimulation target in combination with other imaging modalities or by the use of anatomical landmarks. In a case where a brain tumor was resting adjacent to the precentral gyrus, the motor strip identified by TMS compared preoperative MRI and fMRI and revealed fine functional differences between results that were integrated on the navigation system. Distribution of the tumor margin and the motor cortex (both fMRI and TMS assisted) can be drawn on the patient's scalp using the navigation system. Skin incision, craniotomy, and operative approaches were considered from these results so as to avoid motor deterioration.

There has been no verification of which nerve cells are actually stimulated by TMS. There is one subject under discussion: whether a target neuron cell is directly stimulated by TMS (direct stimulation) or whether an interneuron is first stimulated and then a target neuron cell is stimulated indirectly (indirect stimulation). It is possible that alteration of eddy currents by heterogeneity of conductivity in the brain may affect the path of these currents and result in both neuronal excitation and excitatory directional changes at sites other than those targeted by the original intended direction of stimulation. Further investigation and analysis of TMS and construction of models using magnetic nerve stimulation are required to clarify how the relationship between a position of a coil and a site of stimulation can be affected by strength of stimulation, arrangement of neurons, heterogeneity of conductivity, and interneuronal participation. While a figure-eight coil is suitable for local stimulations at the surface of the cortex along the surface of the head, tridimensional localized stimulations are not possible with the coil at present.

Despite the problems described above related to TMS, there are high expectations for magnetic stimulation to contribute to a new era of brain science. A major and possibly very important future field of study is the application of TMS for obtaining therapeutic effects in neurological disorders. A number of animal studies testing the basic mechanisms of TMS-induced alterations of neurotrophic factors, gene expression, and changes in plasticity have been conducted (Fujiki and Stewart, 1997; Keck et al., 2000; Fujiki et al., 2003; Ogiue-Ikeda et al., 2003a).

There is strong evidence that the expression of certain genes such as the immediate early gene, astrocyte-specific glial fibrillary acidic protein mRNA (Fujiki and Stewart, 1997), and brain-derived neurotrophic factor is altered in response to repetitive TMS (rTMS). This indicates that the measurable effects of TMS reach the molecular and signaling levels. The most promising hypothesis is that magnetic field-induced neuroprotective or trophic factors may protect neurons from hypoxic insult (Fujiki et al., 2003). Long-duration rTMS modulates the monoamine neurotransmitter system in content and turnover and may also induce sprouting of mossy fibers in the hippocampus (Keck et al., 2000). Increased dopaminergic neurotransmission may contribute to the beneficial effects of rTMS in the treatment of affective disorders and Parkinson's disease.

The results of these studies provide strong evidence that noninvasive TMS can strongly modulate gene expression in neurons and astrocytes. Thus, TMS, originally used simply as a way to assess the function of descending motor tracts noninvasively, may in the end be used as a means to modulate gene expression and to induce restorative plasticity or tolerance against injury in the brain.

TMS does not cause any pain and requires no physical invasion of the body; therefore, it should become more important in functional, diagnostic, and therapeutic research of the brain. In brain functional research, application of magnetic stimulation for the temporary blockage or modification of the facultative information process and cognitive process of various sensory systems may be used to identify localization and connecting pathways of brain function. If a magnetic stimulation can effectively block and modify various sensory systems, it should be advantageous for pain treatment. Elucidation of the effects of magnetic stimulation on synaptic functions may lead to further research associated with brain plasticity. Further research for investigation of magnetic compensation and reconstruction of neuronal functions around damaged neurons may lead to the development of various magnetic field-based stimulation applications, including the treatment of depression, the prevention of dementia, and a safer and more effective magnetic pulse treatment, which may replace the current electroconvulsive therapy (ECT).

8.5.3 Magnetoencephalography

MEG measures the very weak magnetic fields of the order or 10^{-13} T (100 fT) generated by neuronal current flow, by the detection of magnetic signals measured by SQUID arrays. MEG can detect brain functions with high millisecond-order temporal resolution and high millimeter-order spatial resolution noninvasively; thus, it is useful for investigation of brain functions in humans, including higher brain functions such as memory and cognition. Since Cohen obtained a magnetoencephalogram for human α-waves with the use of a SQUID, a prototype developed by Zimmerman and Colleagues (1972), it was only until recently that the use of a whole-head MEG system that is able to carry out spontaneous measurement at multiple points has become practical (Squires, 1991; Ahonen et al., 1993; Vrva et al., 1993). In recent years, the whole-head MEG system has been incorporated into brain functional research all over the world and has accelerated progress in research.

Application of forward and inverse problems in MEG analysis is critical to estimate a localization of brain function. Ueno and Iramina (1991) measured MEG associated with short memory, cognition, and mental rotation in humans, constructed current-dipole and distributed intracerebral electrical source models, and carried out estimations for the localization of various brain functions during the processing of information. The electrical source of a visually evoked reaction with approximately 150 ms at latency localized in the primary visual cortex was described in a current-dipole model relatively well, while a distributed intracerebral electrical source model was more useful in estimation of the electrical source incident to a mental rotation with approximately 180 ms or higher at latency. In the distributed electrical source model, a chronological transition of electrical source groups from the occipital lobe area to the posterior temporal lobe area was captured. MEG is not only a tool for basic brain functional research, but is also applicable to medical research. Clinical applications of MEG include detection of epileptic spikes, measurements of slow waves associated with brain tumors and cerebrovascular diseases, and cerebroelectric activity of ELF induced by event-related potentials.

It is necessary to construct experimental paradigms that are able to perform more precise extraction of a specific brain function, allow understanding of brain function dynamics, and provide measuring techniques to assess the acquired information (Yoshida et al., 1995; Iwaki et al., 1999). It is also important to develop signal processing techniques for source determination of signals with very small SNRs and with distributed electrical sources, improve inverse problem approach methods, and construct suitable current source models (Ueno and Iramina, 1991; Iramina et al., 1994, 1995b). There are several factors to be taken into account in MEG inverse problem analysis: the shape of the head, heterogeneity of conductivity, alignment of neuron cells, interneurons, and

thalamocortical specific projection system. An ideal electrical source model possesses electrophysiological features of complex cranial nerve systems with consideration of these factors.

In a study on language-related brain activities, Kuriki et al. (1995, 1998) used MEG imaging to examine the temporal and topographical characteristics of neural activities in the comprehension of Japanese complex sentences with a clause structure. The Korean language was also used as an experimental language (Kwon et al., 2005). The Korean language has a subject–object–verb order structure, ending with a verb. Semantic and syntactic violations, that is, errors introduced in a sentence, can be made by altering a single word, that is, a verb, in an inappropriate manner. Neural activities in response to such a violation are measured as the response elicited by the final verb in the verb-ending sentence. This study is aimed to identify neural activities in the cerebral cortex that occur during a latency course, processing syntactic and semantic aspects of spoken sentences.

In another MEG study on music, Kuriki and colleagues used melodies to measure the responses that are elicited by an out-of-key tone in musical phrases (Hirata et al., 1999; Kuriki et al., 2005). The musical context is established by the sense of a key and melodic pitch sequence. The responses would reflect the perception of these restricted aspects of melody. The results of the present study should provide an understanding of the spatiotemporal characteristics of cortical activities involved in melody perception. MEG measurements were also performed for musical tones and chord stimuli for well-experienced musicians and nonmusicians. The principal purpose of this study was to explore how the brain activity reflected in late auditory evoked responses would behave when exposed to the successively presented tones and chords stimuli and also how the activity would vary according to experience of musical training.

Although there is still ambiguity in the analytical technique, MEG still attracts medical researchers because it can reflect the chronological change of source signals to that of magnetic fields. It is obvious that MEG will become an essential technique in human brain function research, since there is only one technique that is noninvasive with millisecond-order high temporal resolution, electroencephalography, available at this time for estimation of brain function localization,. Development of MEG with higher sensitivity and operativity, construction of an intracerebral electric source model, and improvement of inverse problem analysis may become more important.

8.5.4 Magnetic Resonance Imaging

Since Lauterber suggested a linear magnetic field gradient in 1973, MRI has been rapidly developed (Lauterbur, 1973). MRI utilizes fusion techniques of spatially uniform direct current magnetic fields, spatially gradient direct current magnetic fields, and RF electromagnetic fields. A guideline of static magnetic field exposure to a human body by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) suggests 2 T as the ceiling value for body parts, except for arms and legs, in occupational exposure. In the application of clinical MRI, although the exposure is carried out under supervision of doctors, the current exposure level is confirmed to be 2 T or less. It is not feasible to obtain resonance images, except from hydrogen atoms, in static magnetic fields at this strength.

The use of MRI conducted at high static magnetic field levels is fast growing (Robitaille et al., 1998). With the advent of the 8-T/80-cm MRI scanner (Schenck et al., 1992; Kangarlu et al., 1999) the safety of the static magnetic field became a paramount issue for MRI researchers. While the primary concern in high magnetic field MRI has been excessive RF deposition in human subjects (Kangarlu et al., 2003, 2005), the static magnetic field could equally cause alarm for its potential for interaction with biological cells and molecules. One concern regarding human exposure to a high static magnetic field is the

orientation of the molecules. Magnetohydrodynamics, which describes the interaction of moving charged particles with the magnetic field, has also raised concern with high magnetic field applications. Investigation of this effect with its possible consequences on human cognition has not received enough attention. As such, Chakeres et al. (2003) have recently conducted a series of studies on the effect of high static magnetic fields on human cognitive function. In spite of the availability and use of high magnetic field instrumentation for three decades, high magnetic field exposures of human subjects for extended periods of time have not been conducted. Such exposures did not pose a significant biological hazard at field strengths of up to 8 T as measured within the capability of their experimental design. In addition, human neuropsychological performance as a measure of any possible static magnetic field modification of cognition was not detected (Chakeres et al., 2003). To our knowledge, such a study has not been performed in the past at a field strength of 8 T for such an extended period of exposure time (Schenck et al., 1992; Kangarlu et al., 1999). In spite of the complex nature of an investigation of such effects, our present lack of observation of any detectable change in human cognition as related to high magnetic field exposure is an important reason for further research. In this regard, studies such as this could serve as a good starting point for *in vivo* characterization of static field effects in humans, in light of the rapidly expanding applications of high magnetic field MRI.

A time-varying magnetic field with sufficient intensity may be excitatory to peripheral nerve stimulation (PNS) (Ueno et al., 1986a; Barker, 1991; Sandrey et al., 2002; So et al., 2004). The physiologic mechanism is presumably due to interaction of neuronal structures with the induced electric field, rather than a direct physiologic effect of the magnetic field (Reilly, 1989).

Relatively early in the development of MRI, it was recognized that the pulsed gradient magnetic fields might induce PNS or cardiac stimulation (Reilly, 1991; Ueno et al., 1992). The pulsed gradients are of audio frequency, and they modulate the frequency and phase of the signal from the precessing magnetization as part of the MRI image reconstruction process. Reilly (1989) projected that a long-duration (>1 ms) pulse of induced electric field of 6.2 V would be sufficient to stimulate a 20-μm-diameter nerve fiber. The same amplitude of electric field was estimated to be the 1-percentile rank for stimulation of the human heart. Because of the much longer chronaxie for cardiac muscle, about 3 vs. 0.38 ms, the gradient field intensity, expressed in terms of the time derivative dB/dt of the magnetic field, required to achieve cardiac stimulation is far greater than that for PNS. The large projected values of dB/dt required for cardiac stimulation were confirmed in measurements in dogs by Mouchawar et al. (1992) and by Bourland et al. (1999), who reported that cardiac stimulation by pulsed gradient fields requires a dB/dt amplitude in excess of 2000 T/s for a 530-μs period. These values compare with representative dB/dt intensities of less than 100 T/s in an MRI system. For healthy patients, cardiac stimulation in MRI is avoided by a wide margin.

Mild PNS in MRI is not thought to be harmful, but painful stimulation should be avoided. To determine the population distribution for physiologic response to the time-varying gradient fields, the MRI safety group at Purdue University undertook a study with 84 human volunteers (Bourland et al., 1999; Nyenhuis et al., 2001). The volunteers were exposed to magnetic field patterns similar to those that would be experienced in a cylindrical bore MRI system. (Nyenhuis et al., 1997). The volunteers were asked to rate their responses to a gradient pulse sequence on a scale covering the range of 1 = onset of PNS, 5 = uncomfortable but acceptable for the duration of a scan, and 10 = intolerable. The duration of the dB/dt pulses ranged from 50 to 1000 μs, in order to determine parameters for the strength duration given by:

$$\frac{dB}{dt} = b\left(1 + \frac{c}{d}\right)$$

where b is rheobase for a long-duration pulse, c is chronaxie, and d is the pulse duration. The measured responses were well fit by a chronaxie of 380 μs. For onset of PNS (score = 1), the median rheobase b was found to be 18.8 T/s for the y-coil and 28.8 T/s for the z-coil. Median dB/dt intensities for scores of 5 and 10 were approximately 50% and 100% greater than the score = 1 values, respectively. From the population distribution, the lowest 1-percentile value for PNS (score = 1) was about half the median value, and the lowest 1-percentile for uncomfortable (score = 5) was approximately equal to the median of the PNS threshold.

den Boer et al. (2002) found good agreement among the Purdue and other studies for the PNS thresholds by the switched gradients. Accordingly, the results of these studies were used for determination of the allowable gradient field intensities in MRI, which were set to be 80% of the mean PNS threshold (IEC, 2002).

The values of chronaxie and rheobase in the Purdue study were determined for rectangular waveforms. Models based on the physiologic response to rectangular pulses can be used to predict the threshold intensities for nonrectangular waveforms (Havel et al., 1997; den Boer et al., 2002).

So et al. (2004) recently reported results of calculations incorporating a realistic human model of the rheobase electric field intensity for PNS in the Purdue study. The rheobase electric field intensities in subcutaneous fat ranged from 3.3 to 4.4 V/m for the different body models and coil configurations. These values are in reasonable agreement with a rheobase electric field of 5.36 V/m for PNS with a solenoidal coil enclosing the arm (Havel et al., 1997).

MRI of electrical phenomena in living bodies is potentially useful for quantitative evaluations of the biological effects of electromagnetic fields and for direct detection of neuronal electrical activities in the brain. Magnetic fields in an object cause a shift in the resonant frequency (Manassen et al., 1988; Sekino et al., 2004b) and a change in the phase of magnetic resonance signals (Joy et al., 1989). Spatial distributions of an externally applied magnetic field and electrical current can be estimated from these changes in magnetic resonance signals. These methods have use in certain medical applications, such as the imaging of current distributions in electrical defibrillation (Yoon et al., 2003).

The fMRI developed by Ogawa et al. (1992) utilizes a technology that reflects various magnetic features of hemoglobin in blood on magnetic resonance signal patterns. Tomograms of brain function can be obtained from information on localized blood flow in the brain. fMRI utilizes a blood oxygenation level dependent (BOLD) effect of localized blood flow on brain activation for indirect imaging of brain activities. However, no information on electrical conditions *in vivo* can be obtained with current MRI and fMRI systems.

Detection of electrical currents associated with neuronal or muscular electrical activities requires extremely high measurement sensitivity. The sensitivity for detecting weak magnetic fields in the human brain was estimated using numerical simulations (Hatada et al., 2005). The theoretical limit of sensitivity was approximately 10^{-8} T. The effect of neuronal electrical activities on magnetic resonance signals was investigated in several experimental studies (Kamei et al., 1999; Xiong et al., 2003). These studies potentially lead to a new method for visualizing brain function with a spatial resolution of millimeters and a temporal resolution of milliseconds.

Impedance-weighted magnetic resonance images were obtained during applications of external oscillating magnetic fields, which induce impedance-dependent eddy currents in a sample (Ueno and Iriguchi, 1998). In another study, spatial distribution of electrical impedance was obtained from the electrical current distributions by using an iterative algorithm (Khang et al., 2002). The apparent diffusion coefficient reflects electrical conductivity of a tissue, which enables an estimation of anisotropic conductivity of that tissue (Tuch et al., 2001; Sekino et al., 2004a). This method was applied to imaging of electrical

conductivity in the human brain. Several regions in the white matter, such as the corpus callosum and the internal capsule, exhibited high anisotropy in conductivity. The magnitude and phase of magnetic resonance signals are affected by permittivity (Sekino et al., 2005). A distinctive signal inhomogeneity arises in images of objects whose dimension is comparable to the wavelength of the electromagnetic fields at the resonant frequency. This phenomenon, dielectric resonance, particularly appears in scanners with high static fields.

Once high-quality current distribution MRI of the detailed distribution of electric source incident to brain neural activities becomes available, comparison of results of MRI and fMRI will show the relationship between brain neural activities associated with BOLD effects and neural current distributions, which may lead to various new observations of dynamics in brain function localizations.

Impedance MRI may not be applied widely in brain function research; however, high-quality impedance MRI for impedance and admittance *in vivo* may lead to development of a new research field of impedance physiology. It is obvious that the information of impedance distributions is important for studying magnetic stimulation and MEG inverse problems.

8.5.5 Magnetic Orientation for Tissue Engineering

In the last decade, it has become possible to create static magnetic fields of 10 T and higher. With this development, studies regarding magnetic effects on macromolecules have increased. These studies include investigations into the magnetic effects on fibrin, collagen, erythocytes, and platelets (Higashi et al., 1993a,b; Iwasaka and Ueno, 1994; Iwasaka et al., 1998; Iino and Okuda, 2001). Recent research on effects of strong static magnetic fields includes their impact on morphogenesis, cell adhesion, and apoptosis (Tofani et al., 2001).

When technology for generation of stronger magnetic fields becomes available in the future, magnetic orientation research will be subdivided into several areas. Effects of magnetic orientation on cell functions such as morphogenesis, adhesion, motility, proliferation, differentiation, and apoptosis may become one of the important areas of research.

Macromolecules such as fibrin and collagen are oriented by static magnetic fields of several tesla. Fibrin polymers are diamagnetic materials that are oriented in a magnetic field. Collagen fibers orient perpendicular to the magnetic field orientation (Torbet and Ronziere, 1984). Polymerization and dissolution of fibrin in homogenous magnetic fields of up to 14 T have been investigated (Iwasaka et al., 1998). It was shown that the magnetic orientation of fibrin fibers accelerated both the polymerization and the dissolution of fibrin fibers.

Magnetic orientation of cells is associated with magnetic anisotropy of proteins and lipids. Erythrocytes orient the disk surface parallel to magnetic fields because of magnetic anisotropy of the biomembrane lipid bilayer. However, halophillic bacteria orient their membrane plane vertical to magnetic fields even though the purple membrane has a similar membrane structure as the erythrocyte membrane (Neugebauer et al., 1977). The purple membrane contains a membrane-bound protein (bacteriorhodopsin) that contributes 75% to the membrane weight. Since the magnetic anisotropy of bacteriorhodopsin is larger than that of the lipid bilayer, halophillic bacteria posses a different magnetic orientation from erythrocytes. Therefore, magnetic orientation is determined by the quantity and the alignment of cell components that possess magnetic anisotropy.

Higashi et al. (1996) found that an orientation of glutaraldehyde-fixed erythrocytes in strong static magnetic fields up to 8 T was perpendicular to the field. The effect was attributed to the paramagnetism of membrane-bound hemoglobin. The rates of

sedimentation and aggregation of human erythrocytes in a homogenous magnetic field of 6.3 T have been studied (Iino, 1997; Iino and Okuda, 2001). It was reported that the cell aggregation accelerated the sedimentation rate. Results have suggested that the enhancement was especially significant in anisotropic erythocytes, and the increase in an intermembrane adhesive area might be due to the magnetic orientation of anisotropic erythrocytes.

DNA, which occupies most of the head portion in bovine sperm, may be involved in magnetic anisotropy and orientation determination of sperm. Cricket sperm with an acicular head part show the same magnetic orientation (vertical) as bovine sperm in magnetic fields of 0.09 T (Suzuki et al., 1995); this is because DNA, which is folded lengthwise, possesses large diamagnetic anisotropy. If DNA in the head part of bovine sperm is orderly aligned as in cricket sperm, the magnetic anisotropy may contribute to the magnetic orientation of sperm.

A significant feature of magnetic orientation of bovine sperm is the direction of orientation. Platelets orient parallel to magnetic fields because of the microtubules inside, which have a magnetic orientation parallel to the magnetic fields. Thus, bovine sperm without motility are assumed to orient parallel to magnetic fields as platelets do, since the tail (flagellum) consists of microtubules. On the contrary, the whole body of bovine sperm shows magnetic orientation vertical to magnetic fields, and the flat surface of the head also orients vertically to magnetic fields. A sperm with the tail removed shows the same orientation. Since it is impossible to obtain a tail without damaging flagellum, the magnetic orientation of a tail alone cannot be observed. In two separate experiments, Emura et al. (2001, 2003) studied the orientation of bull sperm cells and *Paramecium* cilia in static magnetic fields and measured their anisotropic diamagnetic susceptibility ($\Delta\chi$). Bovine sperm consists of a very flat head part (5 μm) and a long tail part (flagellum, 50 μm), which consists of microtubules. Compared to sperm of other species, the head, which contains DNA, is notably larger. The sperm showed an orientation perpendicular to the field of 1 T or lower. The diamagnetic cell components, such as cell membrane, DNA in the head, and microtubule in the tail, were thought to contribute to this orientation. It was observed that *Paramedium* cilia became oriented in parallel to the magnetic field at the strength of 8 T. The author suggested that $\Delta\chi$ for each was the quantitative index of the effect.

Iwasaka et al. (2003a) reported the effects of 14-T fields on assemblies of A7r5 smooth muscle cells. It was shown that the field affected the morphology of smooth muscle cell assemblies and the shapes of the cell colonies extended along the direction of the magnetic flux. They speculated that the mechanism was a diamagnetic torque force acting on cytoskeleton fibers, which are dynamically polymerizing and depolymerizing during cell division and cell migration. They also investigated the effects of the static magnetic field on the convection flow in a cell culture medium and on cell adhesion patterns (Iwasaka et al., 2003b). The mouse osteoblast cell line MC3T3-E1 and HeLa cell line were used in this study. The magnetic field of 6 T with a gradient of 60 T/m affected the convection of floating cell aggregations in a cell culture flask and reversibly changed the direction of convectional flow. After the exposure of MC3T3-E1 cells to the magnetic field of 8 T for 1 d, the thermal convectional flow in the medium was found to promote the cell orientation.

Iwasaka and Ueno (2003) examined the displacement of intracellular macromolecules under a static magnetic field of 14 T using linearly polarized light. The changes in polarized light intensity through the lamellar cell assembly under magnetic fields corresponded to the behavioral changes in cell components. They speculated that intracellular macromolecules rotated and showed a displacement due to diamagnetic torque forces during the exposure to the 14-T magnetic field for 2–3 h.

Matrix proteins provide a permissive environment for the orientation of cells, as demonstrated, for example, with the testing of smooth muscle cells and endothelial cells in collagen fibers under strong magnetic fields (Stefano and Tranquillo, 1993; Tranquillo et al., 1996).

Eguchi et al. (2003) observed the effect of a static magnetic field on orientation of Schwann cells. After a 60-h exposure, cultured Schwann cells from dissected sciatic nerves of neonatal rats oriented parallel to the field of 8 T, whereas Schwann cells suspended in a medium with collagen oriented perpendicular to the field after a 2-h exposure. It was suggested that magnetic field-oriented collagen fibers were the key factor in the orientation of Schwann cells.

Kotani et al. (2000) studied the effect of an 8-T magnetic field generated by a superconducting magnet on the orientation of osteoblasts alone and a mixture of osteoblasts and collagen. It was found that osteoblast cells oriented parallel to the magnetic field, but a mixture oriented perpendicular to the field.

Hirose et al. (2003a) investigated the preferred orientation of human glioblastoma cells A172 after exposure to a 10-T static magnetic field, in the presence or absence of collagen. It was found that A172 cells embedded in collagen gel oriented perpendicular to the direction of the static magnetic field.

By placing dorsal root ganglia (DRG) explants onto one end of magnetically aligned collagen gel formed into 4-mm-diameter rods, Dubey et al. (1999) developed an *in vitro* assay to study neurite elongation. The depth of neurite elongation from chick embryo DRG neurons into these aligned rods was found to be substantially greater than that under the control condition. The depth increased as the magnetic field strength increased, as did the collagen gel rod birefringence; collagen fibril aligned along the rod axis. These results may translate into an improved method of entubulation repair of transected peripheral nerves by directing and stimulating axonal growth through a tube filled with magnetically aligned collagen gel. The same research group later reported the improvement of peripheral nerve regeneration in mice after the treatment of magnetically aligned collagen gel filling of a collagen nerve guide (Ceballos et al., 1999). The hypothesis of this study was that contact guidance of regenerating axons or invading nonneuronal cells to the longitudinally aligned collagen fibrils would improve nerve regeneration. It was reported that mice exhibited regeneration with magnetically aligned collagen gel, including the appearance of nerve fascicle formation.

Application of magnetic orientation in the production of biologically functional materials and artificial organs has been started. By attaching aligned vascular smooth muscle cells and endothelial cells to artificial vascular walls in an orderly fashion, rheologically rational biological functions can be obtained. As techniques in bionics and biomaterials improve, application of magnetic orientation should expand.

8.5.6 Treatments of Pain, Cancer, and Other Diseases

Static magnetic fields or ELF-modulated static magnetic fields potentially have therapeutic effects on several diseases (see also Chapter 11 on medical applications of pulsed fields by Pilla). A static magnetic field in the 10-mT range blocks sensory neuron action potentials, which suggests that the magnetic field alleviates pain (Cavopol et al., 1995; McLean et al., 1995). To characterize the inhibitory effect of a static magnetic field, action potentials were elicited by intracellular application of 1-ms pulses of depolarizing current to the somata of mouse DRG neurons. During the control period, less than 5% of stimuli failed to elicit action potentials. During exposure to an approximate 11-mT static magnetic field produced by an array of four permanent center-charged magnets of alternating polarity, 66% of stimuli failed to elicit action potentials.

The efficacy of a nonpharmacologic, noninvasive static magnetic device was assessed for knee pain in patients with rheumatoid arthritis (Segal et al., 2001). Magnetic devices with four steep field gradients or one steep field gradient were taped to the knee of each subject for 1 week. Both devices demonstrated statistically significant pain reduction in comparison to baseline. Comparison between the two groups demonstrated a statistically insignificant difference.

Prato et al. (2005) reported effect of a magnetically shielded environment on opioid-induced analgesia. Mice were placed in a Mu-metal-lined box or an opaque Plexiglas box (sham condition) for 1 h/d for 10 consecutive days. Nociception was measured as the latency time to a foot lift/lick in response to an aversive thermal stimulus before and immediately after exposure. It was shown that mice can detect and will respond to the repeated absence of the ambient magnetic field, with the maximum analgesic response occurring over days 4–6 of exposure and returning to baseline thereafter. The effect was robust, independent of pre-exposure and intermittent testing, and seems to be opioid related, since the results obtained on day 5 were similar to those from a 5-mg/kg dose of morphine and were abolished with the opioid antagonist, naloxone.

Exposure to pulsed magnetic fields has been shown to have a therapeutic benefit in both animals (e.g., mice and snails) and humans. Shupak et al. (2004b) investigated the potential analgesic benefit of magnetic field exposure on sensory and pain thresholds following experimentally induced warm and hot sensations. Subjects were assigned to 30 min of magnetic field or sham exposure, between two sets of tests of sensory and pain thresholds and latencies at 1°C above and 2°C above pain thresholds. Results indicated that magnetic field exposure does not affect sensory thresholds. Pain thresholds were significantly increased following magnetic field exposure but not following sham exposure. A significant condition by gender interaction existed for postexposure pain thresholds. Taken together, these results indicate that magnetic field exposure does not affect basic human perception, but can increase pain thresholds in a manner indicative of an analgesic response.

Shupak et al. (2004a) showed an induction of analgesia in mice equivalent to a moderate dose of morphine (5 mg/kg) and the effect of both pulsed magnetic field (complex neuroelectromagnetic pulse, Cnp) exposure and morphine injection on some open-field activity. Cnp exposure was found to prolong the response latency to a nociceptive thermal stimulus (hot plate). Cnp plus morphine offset the increased movement activity found with morphine alone. These results suggest that pulsed magnetic fields can induce analgesic behavior in mice without the side effects often associated with opiates like morphine.

The effects of static and sinusoidal (AC) magnetic fields on myosin light chain phosphorylation were studied (Markov et al., 1993). In a cell-free preparation, exposure to DC (0–200 μT, vertically or horizontally controlled) or AC (16 Hz, 20.9 μT) magnetic fields significantly influenced myosin phosphorylation. Variations of the DC magnetic field (in the absence of AC components) were not only sufficient to alter the rate of phosphorylation but also gave the maximum effect.

The possibilities that magnetic fields cause antitumor activities *in vitro* (Tofani et al., 2001), *in vivo* (Tofani et al., 2002), and in human subjects (Ronchetto et al., 2004) have been investigated. *In vitro* experiments were carried out to study the role of magnetic field characteristics (intensity, frequency, and modulation) on two transformed cell lines (WiDr human colon adenocarcinoma and MCF-7 human breast adenocarcinoma) and one non-transformed cell line (MRC-5 embryonal lung fibroblast). Increase in cell death morphologically consistent with apoptosis was reported exclusively in the two transformed cell lines. Cell-death induction was observed with magnetic fields of more than 1 mT. Two different *in vivo* experiments were carried out on nude mice bearing a subcutaneous

human colon adenocarcinoma (WiDr). In the first experiment, a significant increase in survival time (31%) was obtained in mice exposed daily to 70 min of modulated magnetic fields (static with a superimposition of 50 Hz) having a time average total intensity of 5.5 mT. In the second independent experiment, when mice bearing tumors were exposed to the same treatment for four consecutive weeks, significant inhibition of tumor growth (40%) was reported, together with a decrement in tumor cell mitotic index and proliferative activity. Human patients with heavily pretreated advanced cancer were enrolled in a pilot study, in which they were exposed to static magnetic fields that were amplitude modulated by ELF. Toxicity was assessed according to WHO criteria. ECG, chest x-ray, physical examination, blood cell count, and complete blood chemistry were performed before and at the end of the treatment. The results indicated that magnetic fields can be safely administrated according to the magnetic field exposure schedules.

Recently, several studies tested the application of pulsed magnetic stimulation as a form of cancer therapy. In one case, use of magnetizable beads and pulsed magnetic stimulation enabled targeted-cell destruction *in vitro* (Ogiue-Ikeda et al., 2003b). The cells were combined with the beads by an antigen–antibody reaction (cell–bead–antibody complex), aggregated by a magnet, and stimulated by a magnetic stimulator. The viability of the aggregated and stimulated cell–bead–antibody complexes was significantly decreased, and the cells were destroyed by the penetration of the beads into the cells or by rupturing of the cells by the beads. In another study, exposure to a pulsed magnetic stimulation caused a decrease of tumor weight in mice B16-BL6 melanoma models and induced the increase of cytokine (TNF-α and IL-2) production (Yamaguchi et al., 2006). These studies show the potential therapeutic possibilities of pulsed magnetic stimulation in cancer treatment.

Basic studies for magnetic stimulation treatment of depression, which has the potential to replace ECT, and also, magnetic treatment for a wide range of clinical problems, such as Parkinson's disease and various kinds of pain, are in progress. It is important to recognize the safety of magnetic stimulation and the limitations of its usefulness.

8.6 Conclusion

Over the last two decades, various studies have been carried out to examine the effects of static magnetic fields, including MRI fields, on biological systems. This chapter consisted of two parts. The first part focused on recent experiments covering behavior, cardiovascular system responses, reproduction and development, genotoxicity, molecular and cellular systems, cell-free systems, free radical and enzyme activity, etc. The second part concentrated on the recent development of medical and therapeutic applications of static magnetic fields.

There are many studies that have been mentioned in this chapter. With exposure to about 1 T and above, there are no adverse effects on reproduction and development, genotoxicity, and molecular and cellular systems, and no consistent evidence on behavioral effects. However, several studies suggest that static magnetic fields in millitesla ranges may affect microcirculation and blood pressure, and furthermore, higher-strength static magnetic fields at levels up to 10 T may reduce skin blood flow and lead to change in skin temperature. These findings need to be confirmed in further studies.

Although there are so many experiments to test the effects of static magnetic fields on the biology of living systems, using *in vivo* and *in vitro* techniques, the International Agency for Research on Cancer (IARC) has stated that static magnetic fields are *not*

classifiable as to their carcinogenicity to humans by inconclusive carcinogenic evidence (IARC, 2002).

There are many experimental findings that suggest that animals use the static magnetic field, that is, the geomagnetic field for orientation, navigation, and migration. In order to establish the existence of a magnetoreception system in animals, Phillips argued that there are several key points that require further investigation: (1) establishing the lower limits of sensitivity to static magnetic, ELF, and RF fields in biological systems; (2) localizing specialized receptors responsible for sensing the geomagnetic field; (3) characterizing the underlying molecular and biophysical mechanisms; (4) identifying the regions of the brain involved in processing magnetic stimuli; and (5) understanding how the animal's perception of the magnetic field is physiologically processed for determining compass direction and spatial positioning (Phillips, 2005).

With the increasing exposure of humans to environmentally higher static magnetic fields generated from magnetic field equipment of higher capacity, it is necessary to investigate the possibilities of high static field effects on human biological and physiological processes.

There are an abundance of review papers and books published in recent years describing the possible physical and biological interactions of electromagnetic fields (Polk and Postow, 1986, 1997; Ueno, 1996; Andra and Nowak, 1998; Jin, 1999; Takebe et al., 1999; Lin, 2000; Shellock, 2001; Binhi, 2002; McLean et al., 2003a; Stavroulakis, 2003; Rosch and Markov, 2004). In addition, there have been many short reviews on the biological effects of static magnetic fields (Holden, 2005; Miyakoshi, 2005), since the physical interactions of static magnetic fields with living tissues were described (Schenck, 2005). In a report on the biological effects of exposure to MRI, an overview of the safety concerns regarding exposure to static magnetic fields, RF fields, and time-varying magnetic field gradients has been discussed (Formica and Silverstri, 2004). Application of novel high-throughput screening techniques for transcriptomics, proteomics, and metabolomics to determine *in vitro* effects of static magnetic fields have been suggested (Leszczynski, 2005). This report emphasized the research beyond screening that is required for the assessment of any possible health consequences. Possible physical mechanisms underlying the biological effects and interactions of zero-frequency (DC) and oscillating (AC) magnetic fields with biological matter have been reviewed (Binhi, 2001; Volpe, 2003). Effects of static and ELF electric and magnetic fields on human health have also been discussed (Repacholi and Greenebaum, 1999; McKinlay and Repacholi, 2005). Zhadin (2001) has introduced the Russian literature on the biological effects of DC and LF AC magnetic fields. These articles offer multidisciplinary information and knowledge for the understanding of magnetic field effects within living systems.

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9

The Ion Cyclotron Resonance Hypothesis

A.R. Liboff

CONTENTS

9.1 Introduction

9.1.1 General Remarks

Ion cyclotron resonance (ICR) is one among a number of possible mechanisms that have been advanced to explain observed interactions between weak low-frequency electromagnetic fields and biological systems. Despite the failure to find a reasonable physical explanation, there remains an impressive body of experimental evidence that can be taken as an empirical basis for this hypothesis. The ICR suggestion has proven fruitful in framing both experimental and theoretical work, despite the biophysical situation being far from the literal cyclotron resonance model of an isolated classical charged particle moving in a vacuum under the influence of a magnetic field.

The properties of the applied fields that are used in ICR experiments include linear or circular polarization, the presence of a finite magnetostatic field, frequencies ranging from a few to several hundred hertz, magnetic intensities ranging from about 1 μT to 1 mT, and,

most important, a directional constraint on the relative orientation of the time-varying electromagnetic field to the magnetostatic (DC) field. This orientation requires that time-varying magnetic fields be parallel to the DC field or, equivalently, that time-varying electric fields are perpendicular to the DC field.

The ICR hypothesis holds that the physiological activity of those ions implicated in cell signaling processes, including, among others, Ca^{2+}, Mg^{2+}, and K^{+}, can be altered when the ratio of applied signal frequency to the static magnetic field is equal to the ionic charge-to-mass ratio. This is expressed as

$$\omega/B = q/m \tag{9.1}$$

where the radial frequency $\omega = 2\pi f$, as measured in radians per second, is used instead of f, the frequency measured in hertz. In SI units, B is the DC field intensity measured in tesla, and q/m is the ratio of the ionic charge to mass, in coulombs per kilogram. For any given ionic species, the specific frequency that equals the product of B and q/m is called the cyclotronic frequency, ω_c.

The resonance concept is attractive for a number of reasons. There is a potential connection to interactions involving the Earth's magnetic field (geomagnetic field [GMF]). Further, the ICR mechanism may help provide the basis for at least some of the reports of low-frequency electromagnetic interactions that otherwise lack explanation. Finally, given the wide variety of biological systems in which ICR effects are observed, it is reasonable to ask if there are fundamental scientific questions connected to this phenomenon.

The ICR hypothesis has especial significance attached to magnetostatic fields whose intensity is of the order of the GMF (20–60 μT). This becomes apparent when the charge-to-mass ratios of key biological ions are substituted into Equation 9.1. These ratios range from about 2 to 8×10^6 C/kg, implying that a static magnetic field of 50 μT corresponds to resonance frequencies of the order of 10–100 Hz (Figure 9.1). Such frequencies could

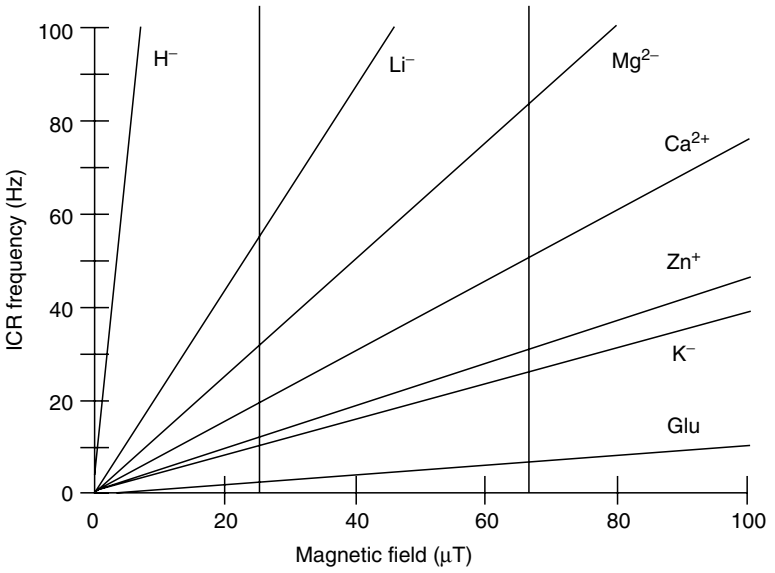

FIGURE 9.1
Ion cyclotron resonance frequencies for many biologically important ions in the Earth's magnetic field are in the ELF range.

TABLE 9.1

ICR Cation Possibilities

Ion	q/m (C/kg) $\times 10^{-6}$	f/B (Hz/μT)
H^+	95.76	15.241
Li^+	13.90	2.212
Mg^{2+}	7.937	1.263
H_3O^+	5.066	0.807
Ca^{2+}	4.814	0.766
Zn^{2+}	2.951	0.470
K^+	2.467	0.393
Arg^{2+}	1.235	0.197
Asn^+	0.838	0.133
Glu^+	0.747	0.119
Tyr^+	0.591	0.094

conceivably have physiological significance since they correspond approximately to the frequency range generated in the central nervous system [1]. This, coupled to the focus on the potential hazards attached to 50/60-Hz electromagnetic power delivery sources [2], has sparked study of the ICR hypothesis, in terms of both experiments specifically designed to test this hypothesis as well as theoretical models seeking an explanatory basis at the molecular level.

Some specific ions that have been implicated are listed in Table 9.1. Note that four polar amino acids and the hydronium ion are included. The ratios of frequency to DC magnetic field, as calculated from Equation 9.1, are shown in the right-hand column. This ratio can be regarded as an invariant characteristic for any given ion.

Although experimental evidence provides support for the ICR hypothesis [3], there is no widely accepted theoretical explanation. Indeed, because of constraints mainly arising from unfavorable damping conditions, there are strong arguments [4] against the occurrence in living tissue of any classical ICR mechanism [5], as occurs, say, for energetic charged particles moving in a vacuum under the influence of parallel static and AC magnetic fields. The circular and helical paths associated with such undamped motion are invariably the result of the Lorentz force, which imparts an acceleration **a** to a charged particle of mass m moving at velocity **v** in a magnetic field **B**:

$$\mathbf{a} = (q/m)(\mathbf{v} \times \mathbf{B}) \tag{9.2}$$

Nevertheless, arguments have been raised [6–11] that although the biological response may not correspond to the effects resulting from ICR-specific helical pathways of charged particles [4], the coupling is nevertheless a function of the ICR frequency as predicted by Equation 9.1. Although there has been no consistent experimental verification for any of these models, there is little question concerning the observed dependence on the cyclotron resonance frequency. Because the cyclotronic frequency is the common denominator in all these models, it is preferable to subsume all of them under the umbrella term ICR hypothesis.

The great variety of biosystems in which ICR effects have been observed implies a ubiquitous response that may have fundamental physiological significance. One can generalize this response R in terms of its functional dependence. From Equation 9.1, we can write

$$R = R(\omega, B, q/m) \tag{9.3}$$

Lednev [7] added a fourth variable, namely the intensity of the AC magnetic field, B_{AC}. Thus, the expanded expression for the response $R = R(\omega, B, B_{AC}, q/m)$, or, in terms of the two key variables,

$$R = R(\omega_c, B_{AC}) \tag{9.4}$$

There is no question as to the relevance of B_{AC} in studying the interactions between ICR field combinations and biological systems. However, it is not clear if the experimentally observed dependences on B_{AC} are a direct result of the underlying resonance mechanism, as has been suggested [7,9], or if there are other separate physiological factors that limit the levels of the AC field under which an ICR mechanism may be operative.

9.1.2 Background History

ICR was originally invoked [4] to explain an extraordinary set of observations by Blackman's group [12] indicating a strong dependence on the orientation of the magnetostatic field when studying the Ca-efflux model system [13]. The original discovery of the Ca-efflux effect [13] and subsequent studies [14–17] showed conclusively that the level of $_{45}Ca^{2+}$ efflux from preloaded chick brain was a nonlinear function of low-frequency (ca. 15 Hz) modulation signals when these brains were exposed to high-frequency carrier electric fields. Typically, this nonlinear signature (Figure 9.2), at first referred to as a ''window,'' has the appearance of a resonance curve. The Blackman experiment [12] discovered that this resonance signature appeared only when certain specific values of the vertical DC magnetic field were superposed on the system. In Table 9.2, ''Yes'' indicates the appearance of a resonance signature for a given combination of f and B.

In addition to Blackman's original set of results, a fourth column has been added in Table 9.2 to show the putative charge-to-mass ratio as determined from Equation 9.1. One sees that the sign of the magnetic field direction, either pointing up or down, does not affect the outcome. The specific combination of 15 Hz and 38 μT is positive, as is the combination of 30 Hz and 76 μT, suggesting that the ratio of frequency to field is involved as a key factor.

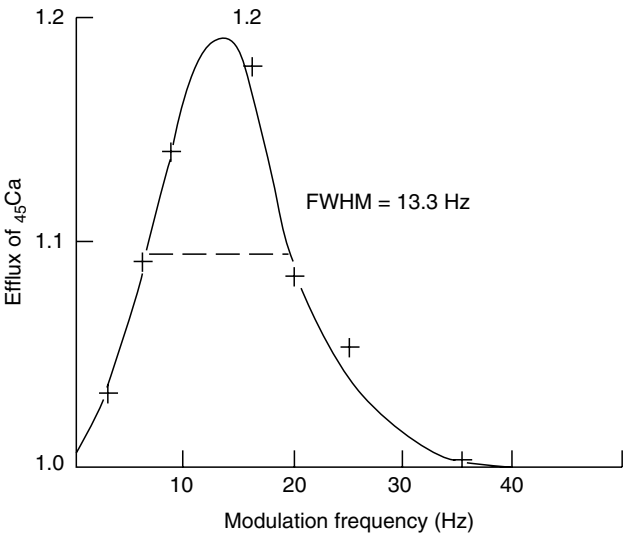

FIGURE 9.2
Comparison of shape of ''window'' data for Ca-efflux results [13] (seven points) with predicted resonance curve [18] (smooth curve). The best fit is for the charge-to-mass ratio for K^+, a magnetostatic field of 35.0 μT, and a collision time of 0.026 sec.

TABLE 9.2

Analysis of Blackman [12] Data

f (Hz)	B (μT)	Outcome	q/m (C/kg)
15	38	Yes	2.48×10^6
15	19	No	4.96×10^6
30	38	No	4.96×10^6
30	76	Yes	2.48×10^6
30	−76	Yes	2.48×10^6
30	50	No	3.77×10^6
30	25	Yes	7.54×10^6
30	−25	Yes	7.54×10^6
30	−83	No	2.27×10^6

Despite the fact that calcium was explicitly measured in this and the earlier Ca-efflux experiments, the data in Table 9.2 give reason to believe that the potassium ion was the primary target for the electromagnetic interactions. First, note that the charge-to-mass ratio of 2.48×10^6 C/kg is associated with positive outcomes. This ratio is less than 0.5% different from the q/m ratio for the potassium ion as shown in Table 9.1. The evidence linking K^+ to a positive outcome is further strengthened by examining the results obtained for the combination of 30 Hz and 25 μT. The positive outcome in this case suggests a q/m value of 7.54×10^6 C/kg, three times larger than the q/m ratio for K^+. In cyclotron resonance, one typically observes a set of resonance frequencies ω_n, where the fundamental at $n = 1$ is given in Equation 9.1, and the higher harmonic frequencies are restricted to the odd [19–21] harmonics $n = 3, 5, 7, \ldots$. The f/B ratio of 30/25 Hz/μT is nearly three times larger than the ratio 15/38 Hz/μT, again implying that the K^+ ion is interacting with the magnetic field, this time as a result of an excitation at the third harmonic.

There is further evidence that the K^+ ion is an important interactive factor in the nonlinear effects observed in the Ca-efflux experiments. McLeod and Liboff [18,22] derived the resonance signature for a charged particle as a function of frequency, showing that the relative conductivity, with and without the presence of an ion resonance field combination, is

$$\frac{\sigma_x}{\sigma_0} = \frac{(1 + (\omega_c + \omega)^2 \tau^2)}{\left(1 + [(\omega_c^2 - \omega^2)\tau^2]^2 + 4\omega^2\tau^2\right)} \tag{9.5}$$

This is a typical resonance expression that includes the effects of damping, expressed in terms of the collision time τ. By varying the choices of q/m ratios and collision times this expression can be directly compared to the results of Bawin and Adey [13], as shown in Figure 9.2. The smooth curve that best fits Equation 9.5 to the experimental points is also shown in Figure 9.2. This fitting procedure reveals that the most likely explanation for the data involves charged particles in cyclotron resonance with a q/m ratio equal to that of the potassium ion.

Thus, two independent sets of Ca-efflux data, one with DC magnetic fields applied as part of the experiment [12] and the other with the ambient magnetic field in the laboratory playing an unsuspected role [14], yield the same conclusion, that ICR stimulation of the K^+ ion results in the nonlinear resonance response.

9.2 Experimental Evidence

There is a surprisingly wide variety of biological systems in which ICR effects are observed. This suggests a heretofore unknown electromagnetic biological interaction. The model systems that have been examined in the literature can be conveniently divided into the categories of bone, cell culture, rat behavior, neural cell culture, diatom motility, complex biological systems, plants, and cell-free systems. These eight separate broad categories are listed respectively in Table 9.3 through Table 9.10. There is some

TABLE 9.3

ICR Effects in Skeletal Tissues

Frequency (Hz)	B_0 (μT)	Tuning	Ratio B/B_0	Comments	Reference
100	130	Ca^{2+}	1.0	Enhanced cell (fibroblast) proliferation; B varied between 50 and 500 μT	23
75	98	Ca^{2+}	1.0	Enhanced proliferation	23
16	42	Ca^{2+}	1.0	Enhanced proliferation	23
16	20.9	Ca^{2+}	1.0	Increases in rudiment length and midshaft diameter in embryonic chick femur	24
16	12.7	Mg^{2+}	1.0	Similar results to Ca^{2+} tuning	24
16	40.9	K^{+}	1.0	Results opposite to Ca^{2+} and Mg^{2+} cases: bone growth inhibited	24
80	20	Ca^{2+}/Mg^{2+}	1.0	Both fifth Ca^{2+} to third Mg^{2+} harmonics; enhanced collar thickness and length	24
72.6–80.6	20	Ca^{2+}	1.0	Resonance in IGF-II concentration at 76.6 Hz in osteosarcoma cell line	25
76.6	20	Ca^{2+}	1.0	Fifth harmonic: enhanced proliferation in osteosarcoma and human bone cells	25
15.3	20	Ca^{2+}	1.0	Reduction in tissue growth factor (TGF) β-1 inhibition in chondrocyte culture	26
25.4	20	Mg^{2+}	1.0	Reduction of TGF β-1 inhibition in chondrocyte culture	26
76.6	20	Ca^{2+}/Mg^{2+}	1.0	Reduction of TGF β-1 inhibition in chondrocyte culture	26
15.3	20	Ca^{2+}	1.0	Enhanced protoglycans synthesis in bovine cartilage	26
76.6	20	Ca^{2+}/Mg^{2+}	1.0	Mixed third and fifth harmonics reduce bone loss related to castration in rats	27
14.3–18.3	20		1.0	Increase in $_{45}Ca$ maximized at 16.3 Hz in osteosarcoma cell line	28
14.3–18.3	20		1.0	Increase in $_{45}Ca$ maximized at 15.3 Hz in a different osteosarcoma cell line	28
15.3	20	Ca^{2+}	1.0	370% increase in stiffness in ostectomized rabbit fibula after 24 h/28 d exposure	29
25.4	20	Mg^{2+}	1.0	137% increase in stiffness in ostectomized rabbit fibula after 24 h/28 d exposure	29
15.3	20	Ca^{2+}	1.0	Enhanced DNA synthesis and IGF-II levels in osteosarcoma cell line	30
13.3–17.3	20		1.0	Resonance maximum in IGF-II receptor number and affinity at 15.3 Hz	31
16	20.9	Ca^{2+}	1.0	Enhanced chick femoral diameter and glycosaminoglycans (GAGS) content	32
16	12.7	Mg^{2+}	1.0	Large (90%) GAGS enhancement	32
16	40.7	K^{+}	1.0	Opposite effects for Ca^{2+} and Mg^{2+} tuning, replicating Smith et al. [24]	32

TABLE 9.4

ICR Effects in Cell Culture

Frequency (Hz)	B_0 (μT)	Tuning	Ratio B/B_0	Comments	Reference
14.3	21	$_{45}Ca^{2+}$	1.0	Isotopic shift in q/m resonance confirmed, $_{40}Ca$ to $_{45}Ca$	33
14.3	21	$_{45}Ca^{2+}$	1.0	Threefold incorporation of $_{45}Ca$ into human lymphocytes	33
14.3	21	$_{45}Ca^{2+}$		Effect on human lymphocytes disappears at larger AC intensity	33
14.3	20.9	$_{45}Ca^{2+}$	1.0	2.3-fold uptake in $_{45}Ca$ disappears with addition of calcium blocker nifedipine	34
38.15	50	Ca^{2+}	1.0	No effect on Ca^{2+} in four different cell lines as observed using calcium fluorochrome fura-2	35
16	20.9	Ca^{2+}	1.0	Enhanced proliferation (46%) for fibroblast culture at Ca^{2+} ICR tuning	36
?	20.9	K^+	1.0	Reduced proliferation (18%) for Raji cells exposed to K^+ ICR; frequency not provided	36
13.6	16.5	$_{45}Ca^{2+}$	1.2	ICR frequency off by 3.5 Hz; enhanced $_{45}Ca^{2+}$ levels (75–126%) in three cell lines	37
60	20	$_{45}Ca^{2+}$	1.0	Fifth harmonic for $_{45}Ca^{2+}$ uptake is enhanced by 37%	37
16	23.4	$_{45}Ca^{2+}$	1.8	Decreased Ca^{2+} influx in mitogen-activated lymphocytes but no effect on resting cells	38
16	51.1	K^+	1.0	Third harmonic: enhanced proliferation of lymphoma cells; very narrow FWHM[a]	39
16	40.9	K^+	1.0	Enhanced proliferation of human lymphoma cells	39
16	23.4	Ca^{2+}	3.8, 5.3	No change in Ca^{2+} influx at AC/DC ratio of 3.8 but enhanced influx at ratio of 5.3	40
16	20.9	Ca^{2+}	1.4	No effect on mouse lymphocytes as observed using Ca fluorochrome Quin-2	41
50	65.3	Ca^{2+}	1.4	No effect on mouse lymphocytes with and without mitogenic stimulation	41
5–100	50–60	$?Ca^{2+}$	2.3–3.0	Enhanced calcium oscillations over broad frequency range, maximized at 50 Hz	42
32	42	Ca^{2+}	2.5, 5.0	Increased micronuclei formation in human lymphocytes at Ca^{2+} ICR tuning	43
32.50	0			No change in micronuclei formation when DC field is zero	43
15.3	20	Ca^{2+}	1.0	ICR effect on fura-2 calcium activity only found for added serum in cell medium	44
76.6	20	Ca^{2+}	1.0	Fifth harmonic is also successful	44
100	130	Ca^{2+}	1.9	Another ICR fundamental successful	44
100	130	Ca^{2+}	2.8	Repeating ICR application to primary bone cell culture at higher AC intensity	44

[a]FWHM, full width at half maximum.

unavoidable overlap among these, particularly in Table 9.3 (skeletal systems), where references to bone research in cell cultures and animals are grouped together.

Although most of the reports summarized in Table 9.3 through Table 9.10 lend considerable weight to the hypothesis that ICR magnetic stimulation can affect biological systems, the effects on diatom motility (Table 9.7) are not as clear-cut, in that a number of observers [62–65] failed to find any effects whatsoever. The explanation for the poor reproducibility in this case may rest with difficulties in handling the diatom model system, one that is especially sensitive to sample preparation.

TABLE 9.5

ICR Effects on Rat Behavior

Frequency (Hz)	B_0 (μT)	Tuning	Ratio B/B_0	Comments	Reference
60	26	Ca^{2+}	1.9	Third harmonic: loss of short-term (temporal) memory in rats	45
60	26	Ca^{2+}	1.9	Third harmonic: AC threshold observed (27 μT) for above results	46
60	27	Ca^{2+}	1.9	Third harmonic: learning inhibited relative to controls	47
60	48	Mg^{2+}	1.0	Learning enhanced relative to controls	47
60	26	Ca^{2+}	1.9	Third harmonic: no effect	48
50	65	Ca^{2+}		Reduced short-term memory and aggressiveness	49
630	500	Mg^{2+}	0.5	Enhanced exploratory activity	50
380	500	Ca^{2+}	0.5	Reduced exploratory activity	50
63	50	Mg^{2+}	0.7	Enhanced locomotor and exploratory activity	51
38	50	Ca^{2+}	0.7	Reduced locomotor and exploratory activity	51
630	500	Mg^{2+}	0.7	Enhanced locomotor and exploratory activity	51
380	500	Ca^{2+}	0.7	Reduced locomotor and exploratory activity	51

TABLE 9.6

ICR Effects on Neural Cell Culture

Frequency (Hz)	B_0 (μT)	Tuning	Ratio B/B_0	Comments	Reference
16	15–40.8	? Co^{2+} or Fe^{2+}?	0.5–1.3	Enhanced proliferation over controls (60%) in neuroblastoma cell culture	52
16	15–40.8		0.5–1.3	Decreased neurite outgrowth for ?Co^{2+}/Fe^{2+} ICR stimulation; possible Na^{+} ICR effect?	52
15.3	20	Ca^{2+}	1.0	Ca^{2+} tuning increases rate of neuronal differentiation in PC-12 cells	53
45	36.6	Mg^{2+}	0.03–1.81	Changes in neurite outgrowth for Mg^{2+} ICR at different AC intensities in PC-12 cells	54
25	20.3	Mg^{2+}	0.54–1.26	Similar Mg^{2+} ICR effect on PC-12 neurite outgrowth at another frequency	54
45	2.96	H^{+}	0.14–2.0	H^{+} ICR alters PC-12 neurite outgrowth	55
30	1.97	H^{+}	0.57–1.4	Similar effects at different ICR combinations	55
45	59	Ca^{2+}	0.26–1.49	PC-12 cells at Ca^{2+} ICR exhibit changes in neurite outgrowth at different AC intensities	56
42.5–47.5	2.97	H^{+}	0.56–1.5	Bandwidth for PC-12 neurite outgrowth due to H^{+} ICR is ±10%	57
40, 50	2.97		0.56–1.5	No effect	57

TABLE 9.7

ICR Effects on Diatom Motility

Frequency (Hz)	B_0 (μT)	Tuning	Ratio B/B_0	Comments	Reference
5–32	20.9		1.0	Maximum motility occurs at 16 Hz when Ca^{2+} concentration is 0.25 nM; no effect when fields are at 90°	58
16	20.9	Ca^{2+}	0.0–3.0	Motility maximized when B/B_0 ratio is 1	58
16	20.9	Ca^{2+}	0.7	Enhanced motility	59
32	20.9	Ca^{2+}	0.7	Even harmonic: no effect	59
48	20.9	Ca^{2+}	0.7	Third harmonic: enhanced motility	59
64	20.9	Ca^{2+}	0.7	Even harmonic: no effect	59
8	10.45	Ca^{2+}	1.4	Enhanced motility	60
12–64	15.7–83.6	Ca^{2+}		Additional ICR frequencies at 12, 16, 23, 31, 32, 46, 64 Hz also enhance motility	60
24, 40, 120	10.45	Ca^{2+}	1.4	Three ICR harmonics for 10.45 μT (n = 3, 5, 15) enhance motility	60
16–136	10.45	Ca^{2+}	1.40.73	Thirteen other frequencies (n = 2, 4, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17) fail to show effect	60
8	20.45	K^+	0.73	Motility inhibited	60
16	41	K^+	0.37	Motility inhibited	60
24, 40, 120	20.45	K^+	0.37	Three ICR harmonic frequencies for B_0 = 20.45 μT (n = 3, 5, 15) also inhibit motility	60
16–136	20.45	K^+	0.37	Thirteen other frequencies (n = 2, 4, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17) fail to show effect	60
16	21	Ca^{2+}	1.0	Enhanced motility	61
16	20.9	Ca^{2+}	1.0	No effect on motility	62
30	39.2	Ca^{2+}	1.0	No effect on motility	62
60	78.4	Ca^{2+}	1.0	No effect on motility	62
16	20.9	Ca^{2+}	1.0	No effect on motility	63
16	21	Ca^{2+}	1.0	No effect on motility	64
16	20.9	Ca^{2+}	1.0	No effect on motility as viewed with real-time video system	65

9.2.1 Rat Behavior

On the other hand, some of the experimental evidence merits special emphasis because of the way the results have been positively replicated and reinforced. This is particularly true of the work on rat behavior (Table 9.5), in which four independent groups [45,47,49,51] observed significant changes in behavior for ICR exposures that were tuned to either the calcium or the magnesium ion. The end points of these experiments included changes in short-term memory [45,51], learning capacity [47], and aggressiveness [49], behavioral factors that are conceivably interconnected. Most important, these were undoubtedly resonance effects, since changes were not observed when separate runs were made for exposures to either the AC magnetic field alone or the DC magnetic field alone. Only when the AC and DC magnetic fields were jointly applied and parallel and, moreover, when the combined field characteristics conformed to Equation 9.1 were the altered behavioral responses observed.

An interesting possible explanation for the neural interaction site in these experiments has been proposed by Lovely et al. [47,92]. Using a Y-maze setup this group observed precisely opposite learning abilities for Ca^{2+} tuning and for Mg^{2+} tuning. Since the ICR combined field affects learning capacity oppositely for Ca^{2+} tuning and Mg^{2+} tuning, it may be reasonable to assume that the glutamate receptor *N*-methyl D-aspartate (NMDA) is

TABLE 9.8

ICR Effects on Complex Biological Systems

Frequency (Hz)	B_0 (μT)	Tuning	Ratio B/B_0	Comments	Reference
3–770	10–220		0064–2.8	No effect on turtle colon transepithelial current as measured in Ussing chamber	66
33.7	44	Ca^{2+}	1.41	Synthesis and release of rat pineal melatonin is reduced by Ca^{2+} ICR tuning	67
15	21	Ca^{2+}	6.7	Fluctuations in heart rate in Daphnia are maximized at Ca^{2+} ICR frequency	68
60	78.4	Ca^{2+}	0.13	Cephalic regeneration in planaria is delayed by 48 h	69
60	51.1	K^+	1.0	Regeneration rate unchanged when K^+ tuning is used instead of Ca^{2+} tuning	69
60	78.4	Ca^{2+}	0.51	Regeneration anomalies occur at Ca^{2+} tuning when larger AC intensity is used	70
16	20.9	Ca^{2+}	1.8	Enhanced rate of blastema growth during cephalic regeneration in planaria	71
16	20.9	Ca^{2+}	0.24–9.6	Evidence that ICR effect on planaria regeneration has an intensity window	71
30	39.1	Ca^{2+}	1.8	Evidence corroborating Lednev [7] prediction: ICR effects are maximized at AC/DC ratio of 1.8	72
60	78.1	Ca^{2+}	1.8	Effect of light on ICR modulation of snail opioid analgesia is independent of frequency	72
120	156.2	Ca^{2+}	3.6	Effect due to light appears to scale with DC intensity	72
60	78	Ca^{2+}	0–5.3	Ca^{2+} ICR variations with AC intensity support Lednev [7] model	73
30	76	K^+	0–2.8	K^+ ICR effects on snail opioid analgesia are reversed with K^+ channel blocker	73
35	45	Ca^{2+}	1.8	Maximum influence on bioluminescence of dinoflagellate, agreement with PRM model	74
35	45	Ca^{2+}	5.3	Influence reversed, again in agreement with PRM model	74
35	45	Ca^{2+}	3.8	No effect at ratio of 3.8, again in agreement with PRM model	74

involved. NMDA receptors act as a graded switch for memory formation, to enhance learning and memory [93], and it is well established that NMDA activity is differently sensitive to calcium and magnesium concentrations [94,95]. Similar reversals of behavioral outcome depending on which ions are tuned have been observed by Zhadin et al. [51].

This explanation also serves to reinforce the original suggestion [4] concerning the molecular explanation for ICR stimulation, namely, in terms of enhanced ionic permeability within ion channels. Further support for locating the ion channel as the site of magnetic interaction is the fact that the changes in Ca^{2+} concentration within the cell that result from ICR stimulation tuned to the Ca^{2+} ion are not observed with the addition of nifedipine [34], a well-known calcium ion channel blocker (Figure 9.3).

9.2.2 Plants

Highly consistent results have also been independently obtained in studying the effects of ICR stimulation on plant growth [75–77,96] and seed germination [20,78] (Table 9.9,

TABLE 9.9

ICR Effects on Plants

Frequency (Hz)	$B_0(\mu T)$	Tuning	Ratio B/B_0	Comments	Reference
60	78.3	Ca^{2+}	0.26	Ca^{2+} ICR field combination stimulates radish growth after delaying germination	75
60	153.3	K^+	0.13	K^+ ICR field enhances germination while reducing growth	75
60	0			No effect	75
60	78.4	Ca^{2+}	0.26	Ca^{2+} fundamental stimulates growth but slows down germination	20
60	39.2	Ca^{2+}	0.51	Ca^{2+} second harmonic: no effect	20
60	26.1	Ca^{2+}	0.77	Ca^{2+} third harmonic: same result as Ca^{2+} fundamental	20
60	153.3	K^+	0.13	K^+ fundamental results opposite to those of Ca^{2+}: growth inhibited, germination enhanced	20
60	76.6	K^+	0.26	K^+ second harmonic results weakly opposite to fundamental and third harmonics	20
60	51.1	K^+	0.39	K^+ third harmonic: effect same as K^+ fundamental	20
60	47.5	Mg^{2+}	0.42	Mg^{2+} fundamental stimulates growth	20
60	9.5	Mg^{2+}	2.11	Mg^{2+} fifth harmonic stimulates growth	20
60	0			AC only: no effect	20
60	78.3	Ca^{2+}	0.26	Replication of Smith et al.'s [75] work	76
60	78.3	Ca^{2+}	0.26	No effect on mustard plant; possible effect on barley plant	76
50	65.3	Ca^{2+}	0.61	Replication of Smith et al.'s [75] work on radish, for the 50-Hz Ca^{2+} ICR condition	77
50	39.6	Mg^{2+}	0.60	Replication of Smith et al. [75] for 50-Hz Mg^{2+} condition	77
60	76.3	Ca^{2+}	0.26	Germination weakly enhanced following Ca^{2+} ICR exposure of dry radish seeds	78
60	153.5	Mg^{2+}	0.13	No effect on germination	78
60	47.6	K^+	0.42	Significantly greater (earlier) germination of dry seeds following K^+ ICR exposure	78
35.8	46.5	Ca^{2+}	1.84	Gravitropic response in millet, flax, and clover seedlings enhanced by Ca^{2+} ICR	79
58.7	46.5	Mg^{2+}	1.84	Gravitropic response unaffected by Mg^{2+} tuning	79
54.7	46.5	K^+	1.84	Gravitropic response inhibited by K^+ ICR	79
33.8–37.8	46.5	Ca^{2+}	1.84	Frequency-dependent gravitropic response exhibits Ca^{2+} peak: FWHM[a] = 1.6 Hz	80
60	48	Mg^{2+}	1.48	CO_2 uptake significantly below control in radish, replication of Smith et al. [75]	81

[a]FWHM, full width at half maximum.

Figure 9.4). The approach in the earlier reports [75] involved direct observations of aspects of plants that are readily measurable: plant height, aboveground height, root mass, stem diameter, leaf length, and width. Remarkably, all aspects related to growth are significantly affected, suggesting that magnetic fields play some unknown role in plant physiology. As observed in other systems (see Table 9.3), Ca^{2+} and Mg^{2+} tuning tends to enhance growth while tuning to the potassium ion acts as an inhibitor. Radish (*Raphanus sativus*) was used because of its rapid growth cycle (21 d), ease of handling, and seed availability. Davies [76] observed positive results when stimulating radish with ICR

TABLE 9.10

ICR Effects in Cell-Free Systems

Frequency (Hz)	B_0 (μT)	Tuning	Ratio B/B_0	Comments	Reference
8–20	20.9		1.0	Three frequencies (13.0, 14.0, and 16.0) affect calmodulin-dependent phosphorylation	82
100	0–260		>0.45	No Ca^{2+} ICR effect on conductance in pure bilipid layer	83
50–120	0–299		>0.31	Binding of Ca^{2+} to calmodulin is not enhanced using Ca^{2+} ICR fields	84
20	50	K^+	1.4	No changes from ICR tuning in gram A channel conductance in lipid bilayer	85
760	50	H^+	15.2	No changes from ICR tuning in gram A channel conductance in lipid bilayer	85
0.1–40	25	Asn^+	0.002	Enhanced aqueous conductivity in asparagine solution at 2.9 Hz; ICR prediction 2.9 Hz	86
0.1–40	25	Arg^{2+}	0.002	Enhanced aqueous conductivity in arginine solution at 4.4 Hz; ICR prediction 4.4 Hz	86
0.1–40	25	Glu^+	0.002	Enhanced aqueous conductivity in glutamic acid solution at 2.5 Hz; ICR prediction 2.6 Hz	86
0.1–40	25	Tyr^+	0.002	Enhanced aqueous conductivity in glutamic acid solution at 1.9 Hz; ICR prediction 2.1 Hz	86
0.1–40	25		0.2	ICR effect disappears at higher ratio of AC to DC intensities	86
0.1–40	0		0.002	ICR effect disappears for very small DC fields	86
0.1–40	25		0.002	ICR effects disappear when AC magnetic field is at 90° to DC field	86
12–60	20.9		1.0	No change in Ca^{2+} transport through patch-clamped cell membrane	87
10–22	20.9		1.0	No change in Ca^{2+} transport through patch-clamped system, measured over loner times	87
1–10	20–40	Glu^+	625–1.25 (×.001)	Changes in glutamic acid conductivity in solution; good agreement with Glu^+ ICR q/m prediction	88
1–10	40		0.25–2.0 (×.001)	Confirmation of earlier work; amino acid response at AC levels of 0.02–0.04 μT	88
0–10	40	Arg^{2+}	0.001	Sharp change in conductivity observed at 7.1 Hz, the ICR tuning point for Arg^{2+}	11
20.6	48	$H_3O^+(H_2O)$	0.02	ICR fields trigger long-term increases in electrical conductivity in pure water	89
40.1	48	H_3O^+	0.02	Data in agreement with ICR effect in hydronium ion	89
530	35	H^+	0.03	Data in agreement with ICR effect in proton	89

TABLE 9.10 (continued)

ICR Effects in Cell-Free Systems

Frequency (Hz)	B_0 (μT)	Tuning	Ratio B/B_0	Comments	Reference
16	20.9	Ca^{2+}	1.0	Binding of Ca^{2+} to calmodulin is not enhanced using Ca^{2+} ICR fields	90
25.4	37	$_{45}Ca^{2+}$	0.70	$_{45}Ca^{2+}$ efflux in plasma membrane vesicles: ICR peak observed	91
24	37		0–3.2	Agreement with Blanchard and Blackman's [9] IPR model	91

magnetic fields but reported observing no similar effect in mustard plants, implying that the influence on growth may be species specific. ICR effects on radish metabolism were also reported by Yano et al. [81] using a distinctly different assay, the rate of uptake of CO_2 as a surrogate for photosynthesis activity. Still another assay [97] that responds to ICR magnetic stimulation in radish is the optical transmittivity in leaf.

The work in radish was extended [96] to four species of orchid (*Brassavola*, *Encyclium*, *Phalaenopsis*, and *Bulbophuyllum*) (Figure 9.4 and Figure 9.5), with the magnetic exposures tuned to Ca^{2+} ICR lasting months instead of days. In all treated cases, plant heights were significantly higher compared to controls.

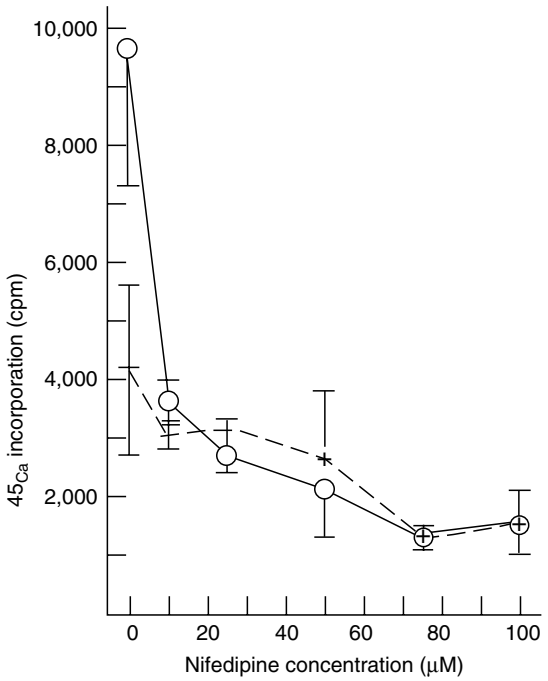

FIGURE 9.3

Incorporation of $_{45}Ca$ in human lymphocytes for unexposed cells (dashed line) and for ICR exposure tuned to the isotopic mass of $_{45}Ca$ (solid line) after 1 h. In the absence of calcium blocker nifedipine, there is a greater than twofold increase in calcium concentration over controls. The addition of nifedipine completely blocks the calcium uptake resulting from ICR stimulation, providing evidence that the ICR mechanism is related to ion channel transport. (From Rozek, R.J., Sherman, M.L., Liboff, A.R., McLeod, B.R., and Smith, S.D., Nifedipene is an antagonist to cyclotron resonance enhancement of $_{45}Ca$ incorporation in human lymphocytes, *Cell Calcium*, 8, 413, 1987.)

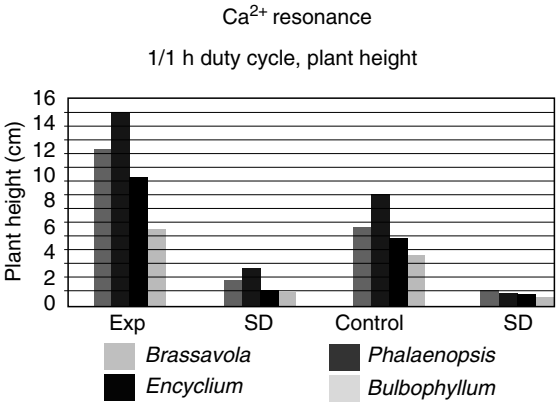

FIGURE 9.4
Comparisons of mean plant heights for four orchid varieties between unexposed controls and plants subjected to Ca^{2+} ICR stimulation. SD, standard deviation. (From Smith, S.D., Liboff, A.R., and McLeod, B.R., Calcium ICR and seedling growth in orchids (abstract), 20th Annual Meeting, Bioelectromagnetics Society, St. Petersburg Beach, FL, 1998.)

A distinctly different type of plant experiment has examined the rate of seed germination [21,78] instead of growth. In this case the assay simply involves a comparison of the time it takes for the seedling to be observed after the exposed seed is planted to the time it takes for a nonexposed seed to emerge. Unlike what is observed when examining growth rates, germination rates are significantly enhanced under K^+ stimulation and inhibited for Ca^{2+} tuning.

9.2.3 Bone

Elaborating on earlier work that used high-intensity pulsed magnetic fields [98] to treat bone disorders, ICR stimulation, operating at a much lower intensity, has proven very useful in repairing bone nonunions [29,99] and as an adjunct in enhancing spinal fusion following surgery [99]. Both these medical applications are approved by the U.S. Food and Drug Administration (FDA) and have been used to treat more than 100,000 patients in the United States [99]. There are two great advantages in these applications compared

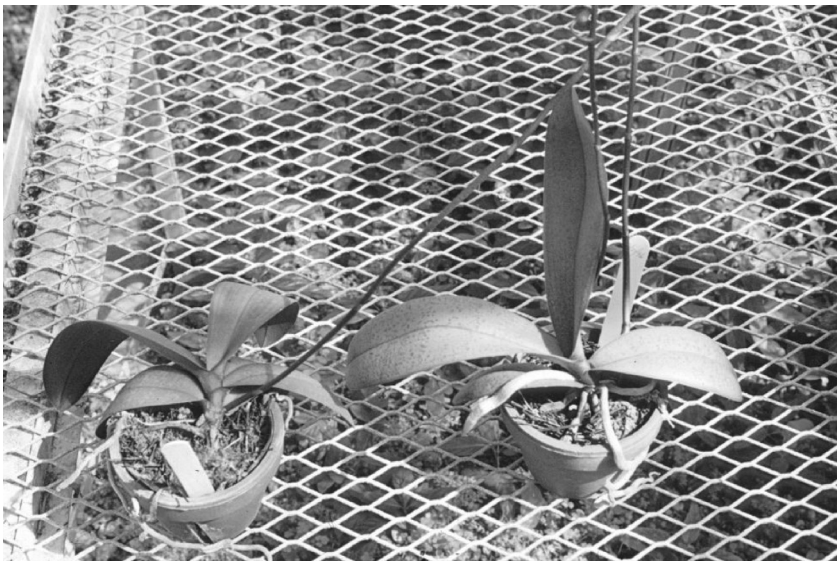

FIGURE 9.5
Typical example of difference between treated (right) and unexposed (left) orchid (*Phalaenopsis*) plants. (From Smith, S.D., Liboff, A.R., and McLeod, B.R., Calcium ICR and seedling growth in orchids (abstract), 20th Annual Meeting, Bioelectromagnetics Society, St. Petersburg Beach, FL, 1998.)

to pulsed magnetic fields therapy. Much weaker AC magnetic field intensities, less than 0.1 mT in amplitude, are employed, requiring very small power and providing the patient with greater portability. The treatment is also more efficient, requiring only 30 min/d during the therapeutic regimen.

This FDA-approved ICR device (Figure 9.6) also makes use of harmonic frequencies. The orientation of the local GMF relative to the plane of the AC coil is sensed, and the frequency of the applied sinusoidal magnetic signal generated by the coil is automatically adjusted to be in cyclotron resonance with the GMF following the relation $\omega_n = nqB/m$, where n is an integer representing either the third or the fifth ICR harmonic. Table 9.11 lists the ICR harmonics for a number of ions. In the case of bone, tuning to either Ca^{2+} or Mg^{2+} tends to stimulate bone growth [24] (Figure 9.7 and Figure 9.8). The FDA-approved device makes use of this fact by employing one resonance condition (3.80 Hz/μT) that fits both types of stimulation, namely the third harmonic for Mg^{2+} and the fifth for Ca^{2+}.

It is likely that the level of efficacy of ICR magnetic treatment in repairing bony nonunions is far from optimal. There is good evidence [9,73,82] that the ICR response may depend on the ratio of the AC to DC magnetic fields that are used in combination. As such, one can expect the search for improvements in therapeutic signals for bone repair to continue.

FIGURE 9.6
Device used to assist repair of bony nonunions. The two rectangular parallel coils are clamped over the defect, and the GMF component normal to the plane of these coils is automatically determined regardless of limb orientation. An AC magnetic field is applied parallel to the GMF field that is in ion resonance tuned to harmonics of calcium and magnesium. (Courtesy of OrthoLogic Corp., Tempe, AZ.)

TABLE 9.11

ICR Harmonics for Selected Ions

Ion	Fundamental (Hz/μT) f/B	Higher Harmonics (Hz/μT) $3f/B$	$5f/B$	Subharmonics (Hz/μT) $f/3B$	$f/5B$
Mg^{2+}	1.26	3.79	6.31	0.421	0.253
Ca^{2+}	0.77	2.30	3.83	0.255	0.153
Zn^{2+}	0.47	1.41	2.35	0.157	0.094
K^{+}	0.39	1.18	1.97	0.131	0.026

In attempting to further probe the response of skeletal tissues to resonant magnetic fields, Ryaby and colleagues [25–28,30,31] reported a number of associated metabolic changes in bone cells, most notably an increase in insulin-like growth factor-II (IGF-II) expression (Figure 9.9 and Figure 9.10) under ICR tuning for Ca^{2+}. This body of work was rather complete in that separate experiments were carried out to justify Equation 9.1. With the magnetostatic field held at one value the frequency was varied as shown in Figure 9.10. In addition, separate runs were made with a fixed frequency and different values of the DC magnetic field. Resonance peaks were observed for both arrangements in accordance with Equation 9.1.

9.2.4 Harmonics

In general, the question of which harmonics are observed in the experimental data remains unresolved. McLeod et al. [59], studying diatom motility, showed that when the DC field is kept constant, odd multiples of the ICR fundamental frequency also result in enhanced motility. The same type of frequency harmonic dependence was found for ICR stimulation of plant growth [21]. Similar experimental results were obtained by Blackman et al. [100] in determining the degree of radioactive calcium flux from chick

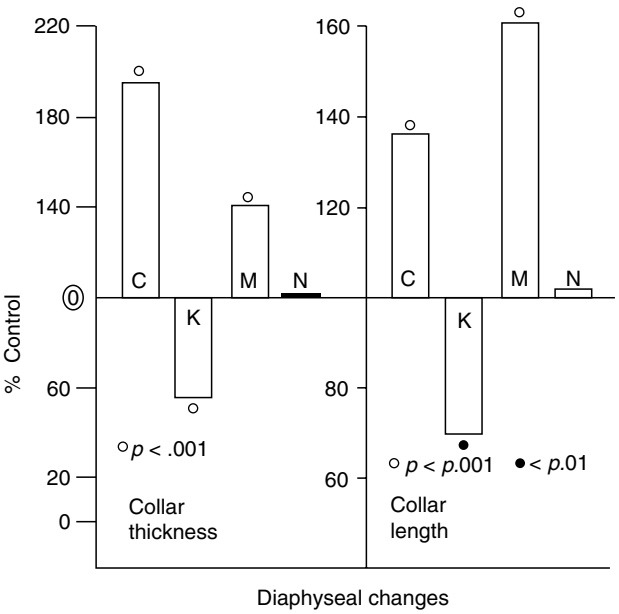

FIGURE 9.7
Ca^{2+} and Mg^{2+} ICR exposures aid bone growth. Changes in diaphysis of embryonic chick femur due to ICR stimulation are shown as percentage of controls. C and M correspond to Ca^{2+} and Mg^{2+} tuning, and K represents the effects of tuning to the q/m ratio for K^{+}. Note the reversal of effect following exposure to potassium-tuned magnetic fields. (From Smith, S.D., Liboff, A.R., and McLeod, B.R., Effects of resonant magnetic fields on chick femoral development *in vitro*, *J. Bioelectr.*, 10, 81, 1991.)

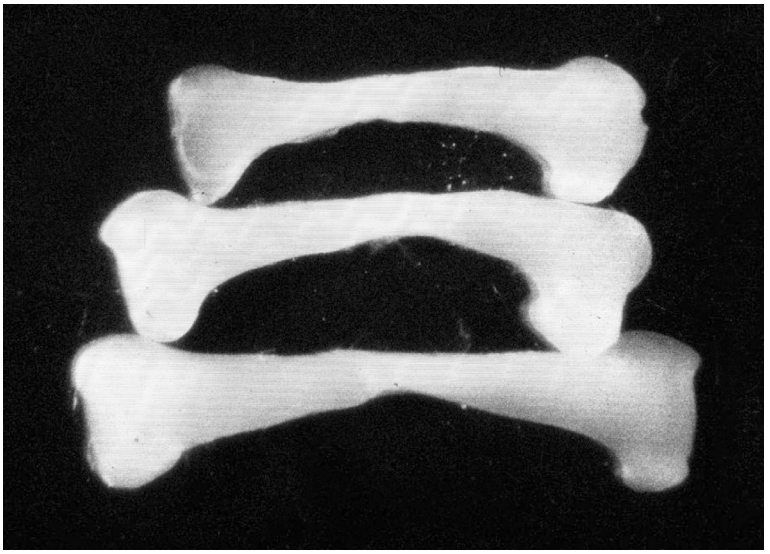

FIGURE 9.8
Typical examples of changes in embryonic chick femora with different ICR exposures. The longest femur corresponds to calcium ion stimulation, the shortest femur to potassium tuning, and the in-between size is the control. (From Smith, S.D., Liboff, A.R., and McLeod, B.R., Effects of resonant magnetic fields on chick femoral development *in vitro*, *J. Bioelectr*., 10, 81, 1991.)

brain as a function of electric-field modulation frequency. These various findings are in reasonable agreement with the predicted higher harmonic ICR signatures listed in Table 9.11.

Because subharmonics are predicted [7,101] in several theoretical models, the first two predicted odd subharmonic characteristics are also listed for convenience in Table 9.11. It

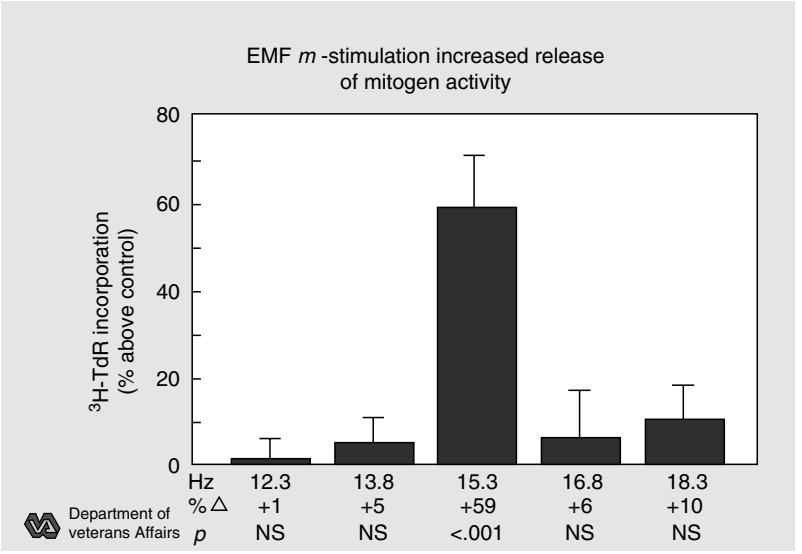

FIGURE 9.9
A sharp increase in mitogen expression in osteosarcoma cells exposed to a 20-μT DC magnetic field occurs when the AC magnetic field frequency is 15.3 Hz, corresponding to Ca^{2+} resonance. (Courtesy of Veterans Administration Hospital, Phoenix, AZ.)

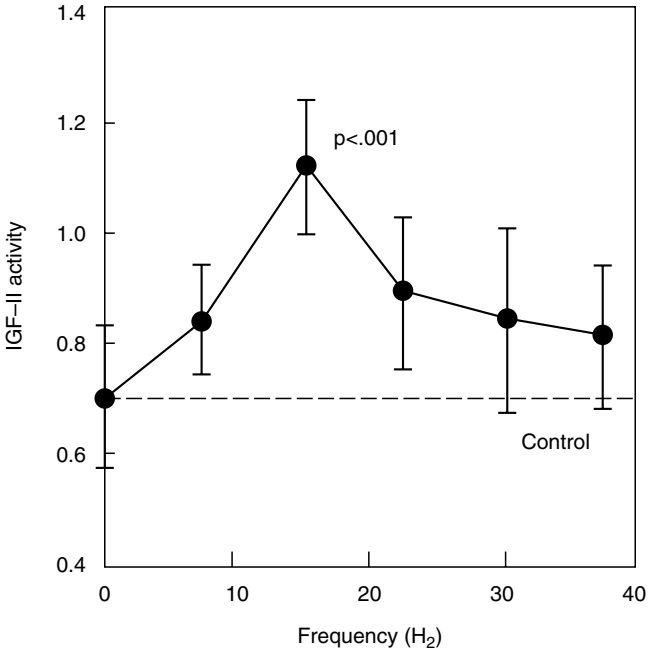

FIGURE 9.10
Peak in IGF-II expression at the fifth harmonic for Ca^{2+}. (Courtesy of J. Ryaby.) Fitzsimmons, R.J., Ryaby, J.T., Magee, F.P., and Baylink, D.J., Combined magnetic fields increase insulin-like growth factor-II in TE-85 human octeosarcoma bone cell cultures, *Endocrinology*, 136, 3100, 1995.)

is clear that a better fit between the theoretical predictions of harmonics and the nature of their experimental observations could be an important factor in further understanding of ICR phenomena in living things.

9.2.5 Physiological Reversals

There is substantial evidence [102] that changing the ICR tuning from one ionic species to another has the capacity to completely reverse physiological outcomes (Figure 9.8 and Figure 9.11). This has been reported in a number of separate fascinating observations in widely different ICR experiments. The effect is manifested by applying, at the same frequency, relatively small shifts in the local magnetic field or, equivalently, applying a changed frequency with the local magnetic field kept the same, both variations made according to Equation 9.1. Eight such sets of results are given in Table 9.12.

This type of opposite response in the data may provide an important clue in trying to understand the ICR effect at the molecular level. Such a response might be expected when looking at the effects of competitive ion concentrations on cell metabolism and signaling. One such example, mentioned above [47], is the difference in the effects of binding Ca^{2+} and Mg^{2+} to NMDA. The concentration of Ca^{2+} in the cytoplasm, itself an implicit function of other ionic concentrations, is carefully regulated through the use of calcium pumps. The production of key enzymes such as cyclic AMP is enhanced or inhibited depending on the cytoplasmic calcium ion concentration. Because of this it is reasonable to think that the action of ICR fields has its origin in membrane-bound ion channels or in those proteins involved in the cell-signaling process.

9.2.6 Water

There have been numerous puzzling reports [103–105] claiming that the physical properties of water (e.g., conductivity) can be sufficiently altered by exposure to magnetic

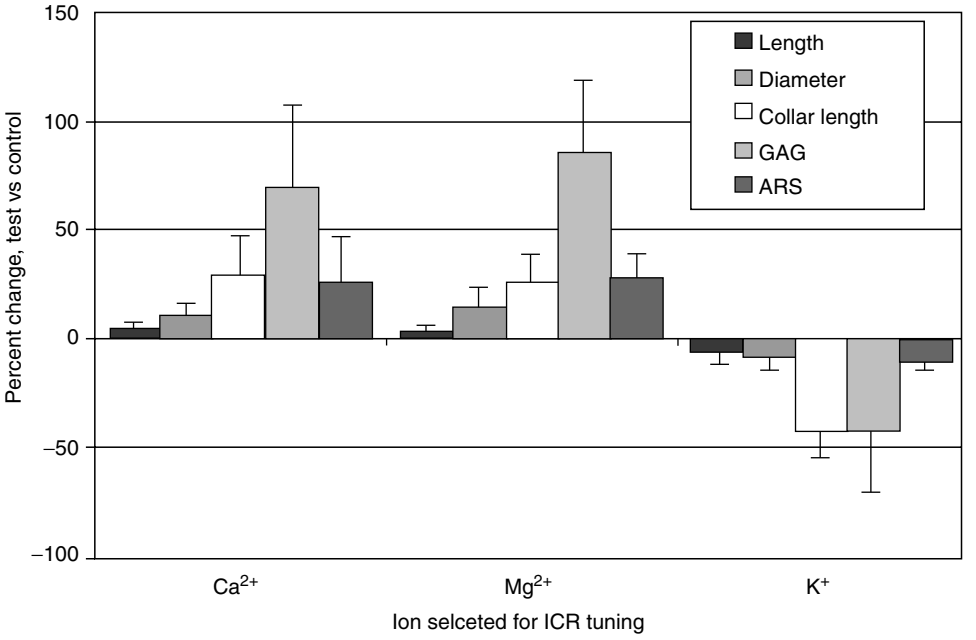

FIGURE 9.11
Independent confirmation of the results shown in Figure 9.8 for embryonic chick femur [32]. The additional assay for glycosaminoglycans (GAGS) reveals a greatly increased production of cartilage with Ca^{2+} or Mg^{2+} ICR stimulation and reduced cartilage production with K^{+} tuning.

fields to alter biological properties. Zhadin [86,88] explored this question using combined AC and DC magnetic fields, to see if there might be an ICR response. The conductivity of polar amino acids in solution (Table 9.1 and Table 9.10) was chosen as an assay. The frequency of the magnetic field was swept slowly, and a single sharp current peak was observed at the cyclotronic frequency, determined from Equation 9.1 using the naked (unhydrated) molecular mass. Originally made in glutamic acid solutions [86], these observations were subsequently extended to additional amino acids, even to the case

TABLE 9.12

Opposite Responses Resulting from Shifts in Frequency or Field

Model System	Frequency (Hz)	B_0 (μT)	Ion	Response	Reference
Diatom motility	16	20.9	Ca^{2+}	Motility ↑	58
	16	41.0	K^{+}	Motility ↓	
Embryonic bone	16	20.9	Ca^{2+}	Growth ↑	24
	16	40.7	K^{+}	Growth ↓	32
Plant growth	60	78.3	Ca^{2+}	Growth ↑	75
	60	153.3	K^{+}	Growth ↓	
Rat behavior	60	48	Mg^{2+}	Learning ↑	47
	60	27	Ca^{2+}	Learning ↓	
Rat behavior	63	50	Mg^{2+}	Activity ↑	51
	38	50	Ca^{2+}	Activity ↓	
Gravitropic response	35.8	46.5	Ca^{2+}	Response ↑	79
	54.7	46.5	K^{+}	Response ↓	
Glycosaminoglycans (GAGs) concentration	16	20.9	Ca^{2+}	GAGs ↑	32
	16	40.7	K^{+}	GAGs ↓	

where it was possible to shift the ICR peak by changing the pH of the solution, and therefore the valence of the ion. This work has been independently confirmed in two-other laboratories [11,105]. One interesting aspect of these observations is the remarkably small AC magnetic field intensity required to see this effect, on the order of 0.05 μT.

It has also been shown [89] that very short (minutes) applications of ICR-tuned magnetic fields act to trigger large (days) continuing increases in conductivity in highly purified water. The required AC intensities (1 μT) are greater than that was found necessary in the Zhadin experiments, but they are still far less than reported elsewhere as interactive. The ions that are presumably affected are hydronium (H_3O^+) and its water clusters. One intriguing aspect of this work are the long-term changes in conductivity that are observed, even after removal of the magnetic field, a phenomenon somewhat akin to that of water ''memory'' [106,107].

9.3 Theoretical Approaches

9.3.1 Physical Constraints

The conditions in living things are such that charged particles are not free but subject to damping forces. If a particle such as an ion carries charge q and mass m and is moving with velocity $\mathbf{v}$, damping is manifested in the form of a retarding force, above and beyond the Lorentz force q($\mathbf{v} \times \mathbf{B}$) and the Coulomb force $q\mathbf{E}$:

$$\mathbf{F} = q(\mathbf{v} \times \mathbf{B} + \mathbf{E}) - m\mathbf{v}/\tau \tag{9.6}$$

The last term in Equation 9.6 is the mean damping force acting on the particle expressed in terms of the collision rate τ^{-1}.

The possibility of ICR occurring in living systems is counterintuitive, mainly because of damping. Cyclotron resonance, whether involving ions [108] or electrons [109], is usually associated with motion in a vacuum, or at least a low-pressure gas. In sharp contrast, the biological milieu is generally approximated as a liquid. Electron cyclotron resonance is observed in metals [109], but only at extremely high frequencies ranging from megahertz to gigahertz, many orders of magnitude greater than the typically observed frequencies listed in Table 9.3 through Table 9.10. At very high frequencies, the periodic motion of charged particles in cyclotron resonance can take place because the periods are shorter than the collision times. At 15 Hz, however, one loop is executed in 70 ms, a time over which one might expect as many as 10^{12} collisions because of thermal scattering [110]. The problem of explaining ICR effects in living systems is indeed challenging.

A second argument against the ICR hypothesis is that ions in solution are never totally free but are surrounded by layers of water. Therefore, one would think that the values of the q/m ratio indicated in Equation 9.1 would have to be lowered to reflect the extra mass that is part of the overall ionic package.

One further criticism lies in estimates of the path radius for (free) charged particles in cyclotron resonance. This is based on equating the kinetic energy $mv^2/2$ of the charged particle to the thermal energy kT, and then arguing that the radius of the particle path must necessarily reflect the resulting velocity, because this radius is given as $\rho = v(m/qB)$. At a temperature of 37°C this results in radii that are of the order of meters, much larger than the extent of the system itself. However, it is hardly clear that one can use classical kinetics to discuss low energy charged particle interactions with

molecular structures. Further, it must be noted that the cyclotronic frequency ω_c, as given in Equation 9.1 under the condition of vanishing damping, is entirely independent of particle radius and energy.

ICR tends to somewhat mute one of the strongest arguments against the likelihood of weak extremely low-frequency (ELF) magnetic interactions with biosystems. For an electric signal to initiate a biological effect, this signal must be greater than the electric potential generated by thermal noise [111]. The mean square thermal noise voltage $(\delta V)^2$ generated is proportional to Boltzmann's constant k, the temperature T, the tissue resistance R, and the bandwidth $\Delta\nu$ as follows:

$$(\delta V)^2 = 4RKT\Delta\nu \tag{9.7}$$

The original interaction site suggested by Weaver and Astumian [111] was the plasma membrane of the cell. The lipid membrane, however, is a highly electrically insulating material, with physical properties that are not conducive to any low-frequency interaction mechanism [112] except at high voltages. When more conductive substances such as proteins are considered as weak-field interaction sites, the effective resistance R can be many orders of magnitude lower than that found in lipids. Further, experimental evidence indicates that much narrower bandwidths, $\Delta\nu$, are encountered in ICR applications [39,106] than was previously [111,113] assumed. If the product $R\Delta\nu$ is reduced in Equation 9.7 by a factor of 10^{-4}, this lowers δV by a factor of 10^{-2} below the original estimates. The ''kT'' question becomes even less of a problem if one considers electric-field ICR [114], where the frequency of oscillation in Equation 9.1 is derived from endogenous sources within the living system.

9.3.2 Ion Channels

Placing the site of the ICR interaction within the lumen of membrane-bound ion channels deals with the problems of damping and hydration layers but leaves other questions unresolved. It is clear that damping within channels is quite different from that in liquids. The very function of ion channels helps define their intrinsically small effective resistivity, often less than 0.1 Ωm [115], and therefore their vanishing damping. Channels function as shunts across the insulating cell membrane, allowing ions to percolate through, often in single file [116]. The passage of ions is determined less by collision rate, as in the solution-like regions external to channels, but is more dependent on the molecular architecture [117] of the channel proteins: the gating mechanisms that permit entry into the channel lumen and the electrical potential of the atoms lining the lumen walls.

Further, this passage of ions is unencumbered by the layers of hydration that surround all ions in solution. These waters are replaced upon entry into the channel by an equivalent fixed cage lining the lumen (Figure 9.12). Although the energetics of this water replacement is still puzzling [118], there is little question that ions can pass through ion channels in a naked fashion, with no attached waters [119]. The path of ions in a channel is clearly determined in a manner that does not permit one to apply kT arguments in trivial ways.

Although one can readily deal with the two problems associated with first, damping and second, ionic hydration layers, it is not as easy to dismiss the disparity in relaxation times when one compares the very rapid passage of ions through channels to the far slower movements associated with resonance frequencies. The ratio of these times can be well in excess of 10^{10}. To illustrate the problems raised by this disparity, consider the argument that the helicity of ionic paths occurring under ICR might be such as to match the helicity of the electric potential in the lumen [120].

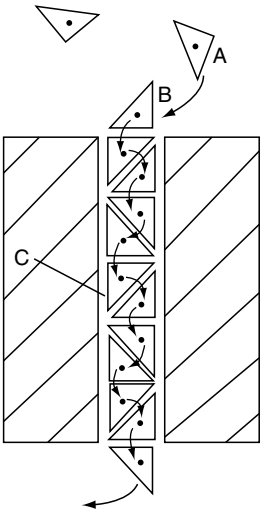

FIGURE 9.12
Hydrated ions near the mouth of an ion channel exchange their layers of water for an equivalent potential distribution within the lumen of the channel.

The electric field in Equation 9.6 can have a number of distinctly different origins. In living tissue, the electric field can be the result of endogenous sources independent of **B**. If **B** is time varying, and of sufficiently large intensity or frequency, an electric field will in addition be induced by Faraday's law. There are also experimental situations in which an electric field may be applied independently of the first two sources. When an electric field **E** is present, whatever the source, and it is at right angles to both **v** and **B**, then the circular motion becomes helical (Figure 9.13). It is then convenient to treat the velocity of the particle as composed of two components: $v_{\|}$, directed parallel to the direction of **E**, and

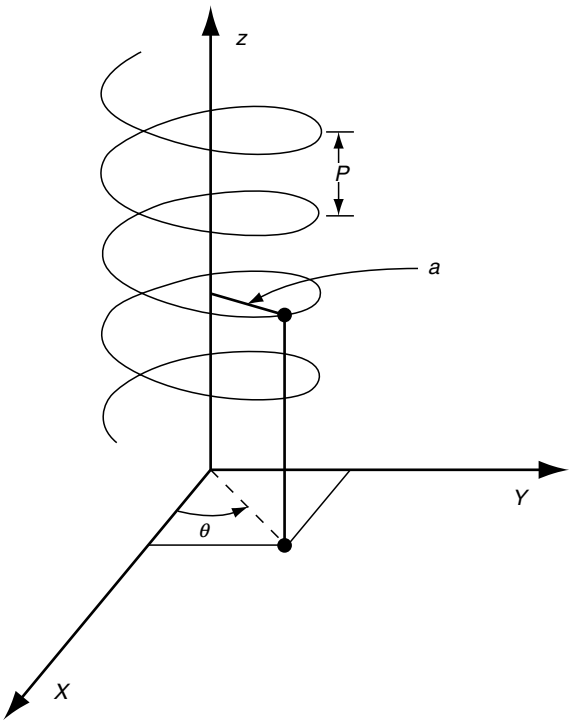

FIGURE 9.13
The Lorentz force acting on a charged particle often results in helical motion.

$v_\perp$, directed within the plane perpendicular to **E**. Then the radius of the helix is $a = mv_\perp/qB$, and its pitch is $p = 2\pi mv\|/qB$. It is not difficult to show that the total velocity v is

$$v = f_c(4\pi^2 a^2 + p^2)^{1/2} \tag{9.8}$$

The ICR frequency f_c is often only 15 Hz, and for ion channels the dimensions a and p are of the order of ångstroms (10^{-10} m). This implies a velocity of about 10^{-9} m/sec, a value that is totally inconsistent with the much greater experimentally observed speeds with which ions are transported across membranes.

Even though transit times directly through the channel lumen are very rapid, much longer relaxation times are found in other compartments of the larger channel structure. Times as long as, if not longer than, 10 ms are associated with voltage gating [121], making it conceivable that ICR could play an interactive role in channel-gating mechanisms.

9.3.3 Dependence on AC Magnetic Field

Borrowing from the theory of atomic spectroscopy [122], Lednev [7] hypothesized a functional relationship between the strength of the ICR signature and B_{AC}. When the calcium ion is bound to a calcium-binding protein such as calmodulin, the energy levels for the ion protein complex will be split, Zeeman-like, by the application of a magnetostatic field B, such that the difference in frequency between the two new levels is equal to the cyclotron resonance frequency ω_c.

Application of an AC magnetic field at this frequency then leads to a resonant condition that can alter the transition to the ground state. The ICR response itself then becomes a function of the peak value of B_{AC} expressed in terms of the probability $p(B_{AC})$ for Ca^{2+} transitions to the ground state. The field-dependent part of this probability is

$$p(B_{AC}) = (-1)^n K J_n\left(n\frac{B_{AC}}{B_0}\right) \tag{9.9}$$

where K is a constant, B_0 is the DC magnetic intensity parallel to B_{AC}, and J_n is the nth-order Bessel function having the argument nB_{AC}/B_0.

One great advantage of this expression for the probability is that one can readily design experiments that can test the predicted dependence on the AC magnetic field. Thus, the first extremum of $J_1(B_{AC}/B_0)$ occurs when the ratio B_{AC}/B_0 is equal to 1.84 (Figure 9.14). By varying this ratio while maintaining the same ICR condition, Prato et al. [72] obtained data tending to confirm this prediction. The effectiveness of this numerical ratio was also reported [74] in connection with studies on changes in calcium concentrations under ICR stimulation.

An alternative formulation to Equation 9.9 has been proposed by Blanchard and Blackman [9]. Termed ion parametric resonance (IPR) this approach considers a wider range of potential ELF interactions with metallic ions, beyond merely those processes associated with the activation of calcium-binding proteins. In the IPR formulation the probability $p(B_{AC})$ has the dependence $J_n(2nB_{AC}/B_0)$. The factor of 2 in the argument of the Bessel function has the effect of altering where the first extremum occurs, in this case at the B_{AC}/B_0 ratio of 0.92 (Figure 9.14). This ratio is close to the value of 1.0 successfully used by Smith [21,24,58,75] in all his experiments. However it is not clear in Smith's body of work whether further manipulation of the AC magnetic intensity away from this ratio of unity might have enhanced the responses that were observed. Koch et al. [91] were also able to obtain good agreement with the IPR predictions. One set of experimental results in sharp

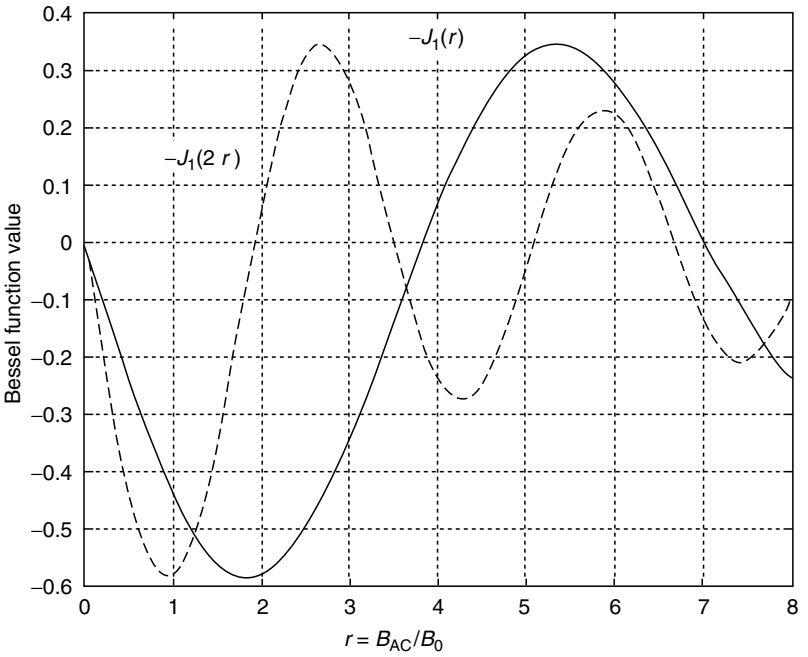

FIGURE 9.14
Comparing first-order Bessel functions with arguments B_{AC}/B_0 (solid line) and $2B_{AC}/B_0$ (dotted line). The first extremum is of experimental interest. By doubling the argument, the ratio where this extremum occurs is shifted from 1.84 to 0.92. In principle, one holds B_0 and the ICR frequency fixed and varies B_{AC} to determine where the maximum biological response occurs.

contrast with the predictions of parametric resonance are the consistent reports by Zhadin's group [86,88] and others [11], in which ICR exposures of polar amino acids in solution lead to narrow resonances, but only for B_{AC}/B_0 ratios of approximately 0.002.

The question of the dependence of the ICR interactive response on AC magnetic intensity is clouded by two additional possibilities. First, there is the problem of experimentally sorting out effects due to Faraday induction with larger AC fields [70]. Second, it is conceivable that biological responses to different AC fields may have little to do with the ICR response but rather with poorly understood physiological and energetic constraints. In any event, there is a clear record in the literature (e.g., Figure 9.15) of ICR threshold effects that do not appear to be related to functional variations such as Equation 9.9.

Adair [123,124] has criticized the parametric resonance approaches. Similar to earlier arguments [111,113] related to energetic constraints imposed by thermal noise, it was pointed out that the transition energy is only 10^{-11} of the thermal energy, kT, which would greatly suppress any meaningful effects due to Zeeman splitting. For this and other reasons [123], he concludes that application of the cyclotronic frequency ω_c cannot affect the transition rate of Ca^{2+}.

A very different approach to the problem of whether resonant magnetic fields can influence the binding of calcium has been suggested by Binhi [101]. Using Schrodinger's equation, it has been shown that ICR magnetic field combinations may redistribute the ionic probability density when one takes into account interference effects between quantum states. However, there is some question as to how much the wave function must shrink to allow ions as large as Ca^{2+} to escape.

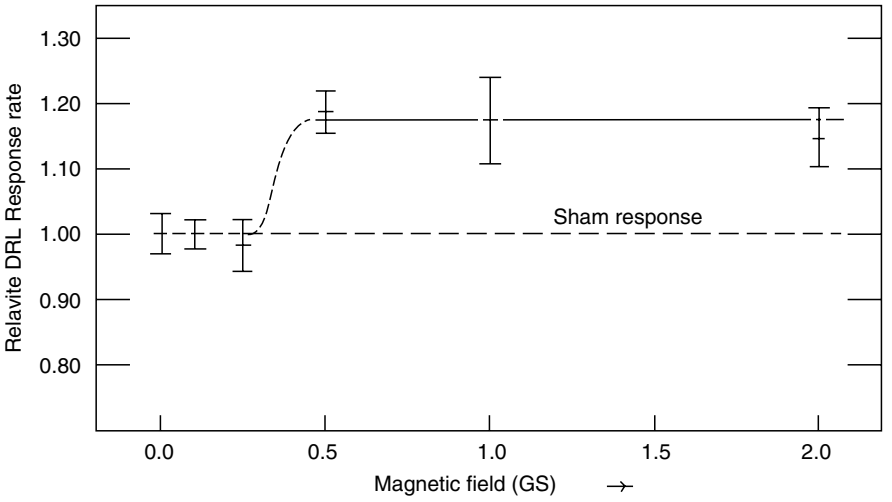

FIGURE 9.15
ICR-induced changes in rat behavior as a function of the AC magnetic field intensity. A clear threshold is evident, below which there is no effect on rat behavior. (From Liboff, A.R., Thomas, J.R., and Schrot, J., Intensity threshold for 60-Hz magnetically induced behavioral changes in rats, *Bioelectromagnetics*, 10, 111, 1989.)

9.3.4 Precessional Effects

It has been shown [8,10] that Larmor precessional effects can result from the application of weak ICR magnetic field combinations. In principle, these effects might carry physiological consequences, although no evidence along these lines has been reported. One interesting aspect of this approach [10] suggests the possibility of magnetically induced changes in the thermal energy distribution. The altered biological response in this model would not be the result of dissociative processes between ion and protein but would rather follow transfers of energy to the protein by the ion, resulting in appropriate conformational changes.

9.3.5 Coherence Domains

Del Giudice [11] has employed the principles of quantum electrodynamics (QED) in attempting to explain biological ICR, especially those results obtained in connection with the ''Zhadin Experiment'' [11,86,88]. The great advantage in this approach is that it finesses the limitations caused by Maxwell–Boltzmann statistics predictions [111,113], which require kT as a minimal threshold informational energy for electromagnetic interactions. In the QED model it is argued that in the case of electromagnetic interactions with water, coherent, highly ordered spherical domains are formed, with diameters close to 100 nm and embedded in a surrounding noncoherent water phase. An applied ICR frequency in this case couples to ions on the perimeter of the coherent spheres stimulating circulatory motion, allowing ions to escape into the noncoherent phase, where they act to enhance the measured conductivity.

One interesting aspect of this model is that because phase transitions are involved, temperature is expected to play a prominent role in the experimental outcome. The changes in amino acid conductivity under ICR conditions first reported by Novikoff and Zhadin [86] were temperature sensitive. Similar observations regarding the experimental relevance of temperature were reported in earlier [125,126] Ca-efflux studies.

9.4 Discussion

Accepting the abundant evidence that biological systems are sensitive to ICR-tuned field combinations, the question remains as to the molecular explanation. There is also the more subtle question dealing with the implications of this effect. From the physical standpoint, the seeming inability of theorists to come to grips with this phenomenon may not mean that a new physics is called for. But there is certainly good reason to believe that something is missing in the way we categorize biological function.

The fact that a low-frequency ion resonance interaction is found in an extraordinarily wide variety of organisms argues against the commonly held notion that this phenomenon merely represents one fortuitous example of the Lorentz force acting on materials that happen to occur within a biological context.

Indeed, the reports listed in Table 9.10 lend strength to another notion, that the weak-field ICR phenomenon is not limited to biological systems, but is actually a subtle physical effect that has not heretofore been recognized. For example, one can argue that this effect is particularly evident in water, which in turn results in the biological effects that are observed. In other words, because of the ubiquity of water in biological systems, any ELF-induced change in the properties of water might help explain the variety of biological effects that have been reported.

Whatever its molecular origin, it is likely that the ICR-related biophenomenon is an evolutionarily well-conserved property of the physiological armory, one that is enabled by the interaction of the ubiquitous Earth's magnetic field with the equally ubiquitous electric fields that are found throughout living things. This concept is embodied in the reasonable likelihood [114] that electric-field ICR processes were incorporated into living things over evolutionary times. Unlike the laboratory experiments involving the applications of parallel combined AC and DC magnetic fields, *E*-field resonance occurs maximally for time-varying electric and magnetostatic fields at right angles. This naturally occurring interaction therefore relates the GMF and the AC electric fields found within the biosystem. It has been hypothesized [127], for example, that this putative interaction mechanism can be used to explain the problem of bird navigation.

One can speculate that this ICR phenomenon conserved very early in living things has evolved into a number of separate biological expressions, where the physics is always the same but the physiological pathway leads to different end points. For example, two sharply different possible end points, both apparently relying on ICR, are the magnetic compasses in animals [124] and growth and repair mechanisms [24,37,75]. A third intriguing possibility is found in the ICR interactive changes in the central nervous system [45,47,49,51], an area where there are obvious effects but where the end points are still unresolved.

It is also tempting to speculate on the larger implications of the work that is detailed in Table 9.3 and Table 9.9, on bone and plants, respectively. In both cases there is evidence that ICR signals affect growth and repair responses more than they affect stasis. Drawing on possible endogenous mechanisms related to *E*-field ICR, it is conceivable that the interactive relation of the GMF to living systems is especially important as regards growth and repair during development.

Whatever be the explanation for the ICR effect, it is clear that while nothing new may be required in our understanding of physical law, new approaches are necessary in comprehending how physics has been incorporated in biology, particularly with regard to cell signaling and regulation. This is strongly implied by the remarkable data indicating reversed physiological outcomes with minor changes in electromagnetic field conditions. There are protein systems in physiology that are switch-like in their function. Two such

examples are the calcium-binding proteins and NMDA. Another example is found in synaptic transmission. The electromagnetic reversal effects observed in ICR experiments are evocative of the way such switch-like proteins function.

This begs the fascinating question as to whether the ICR stimulus merely serves as an adjunct to an existing biochemical process, perhaps acting to sharpen enhancement or inhibition, or whether it acts in a totally different manner, as a separate and distinct class of interactions, one that is completely electromagnetic in its operation. In this regard, note that the GMF preceded by far the first appearance of living things on Earth and would therefore have been part of the original physical template that determined the course of early evolution.

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10

Computational Methods for Predicting Field Intensity and Temperature Change

James C. Lin and Paolo Bernardi

CONTENTS

10.1 Introduction

Electromagnetic energy at both high and low-frequencies can be transmitted into biological materials through the use of antennas or applicators. Antennas launch the electromagnetic energy into the medium. They serve to couple the generating source of electromagnetic energy into the medium, which surrounds it. The spatial distribution of electromagnetic energy from an antenna is directional and varies with distance from the antenna. At distances sufficiently far from an antenna, so that local field distribution changes predictably and varies mostly with distance, the region is called a far field or radiation zone. In the near field or near zone close to the antenna, the electromagnetic energy distribution varies as a function of both angle and distance. Moreover, the behavior of electromagnetic fields (EMFs) and their coupling and interaction with biological systems are very different, depending on whether they are in the near or far zone. In fact, these differences constitute the major variances between radio frequency (RF) and low-frequency energy deposition into biological systems. As shown in subsequent sections, the induction of electric and magnetic fields, deposition of electromagnetic power, absorption of electromagnetic energy, and their penetration into tissue, all are functions of the source and its frequency or wavelength. In general, when considering the interaction of EMFs with biological systems, it is necessary to account for the frequency or wavelength and its relationship to the physical dimensions of the body.

In addition, the interaction of EMFs with biological systems is characterized by the electromagnetic properties of tissue media, specifically, dielectric permittivity. Biological materials have magnetic permeability values close to that of free space and are independent of frequency. In a medium such as biological tissue with a finite electrical conductivity σ, a conduction current, $\mathbf{J} = \sigma\mathbf{E}$, can be induced to flow, giving rise to energy loss by joule heating. Clearly, fields must be coupled into tissues, and energy must be deposited or absorbed in the biological systems, regardless of the mechanism that is accountable for an effect, for the system to respond in some manner. Thus, to achieve any biological response, the electric field, magnetic field, or EMF that is exerting its influence must be quantified and correlated with the observed phenomenon.

The purpose of this chapter is to present an account of electromagnetic interactions in biological media, with special emphasis on the energy coupling and distribution characteristics in models of biological structures. Such information is essential for analyzing the interrelationships among various observed biological effects, for separating known and substantiated effects from those that are speculative and unsubstantiated, for assessing

the therapeutic effectiveness of electromagnetic waves, and for extracting diagnostic information from field effects.

There exist a wide variety of methods for quantifying fields in biological bodies. The extent of computer usage varies, depending on the specific information sought and the complexity of tissue geometry. This chapter outlines a number of techniques that have been successfully employed to analyze the propagation and absorption characteristics of electromagnetic energy in tissue structures. There are two general approaches: one involves extensive use of analytical development and the other relies more heavily on numerical formulation. Analytical computations are most suited for calculation of the distribution of absorbed energy in simplified tissue geometries such as plane slabs, cylinders, and spheroids, whereas numerical methods offer the opportunity of analyzing the coupling of electromagnetic energy to animal and human bodies, which is difficult, if not impossible, to approach analytically. The advantages and limitations of various methods for field computations, along with representative results, are provided in this chapter. In some cases, for additional details, the reader is referred to previous editions of this handbook [1,2]. This chapter will begin with a brief introduction to the concepts of induced field and power deposition and the characteristics of field intensities and dosimetric quantities.

10.1.1 Induced Field Intensity and Dosimetric Quantities

The quantities of import to characterize coupling of electromagnetic energy into biological systems include the incident field, induced field, power deposition, and absorbed energy. The metrics of specific absorption rate (SAR) and specific absorption (SA) in biological systems or tissue models have been adopted as the dosimetric quantities, especially at RF frequencies. The metric SAR (in W/kg) is defined as the time derivative of the incremental energy absorbed by (or dissipated in) an incremental mass contained in a volume of a given density. SA (in J/kg) is the total amount of energy deposited or absorbed and is given by the integral of SAR over a finite interval of time. Information on SA and SAR is of interest because it may serve as an index for comparison and extrapolation of experimental results from tissue to tissue, from animal to animal, from animal to human, and from human to human exposures. It is also useful in analyzing the relationships among various observed biological effects in different experimental models and subjects. This is in clear contrast to incident field or any other external measures of exposure, which often do not provide the same field inside biological systems of different sizes, species, or constitutions.

Moreover, determination of the induced field would be preferred because it (1) relates the field to specific responses of the body, (2) facilitates understanding of biological phenomena, and (3) is independent of mechanisms of interaction. Once the induced field is known, quantities such as SAR (in W/kg) can be derived from it by a simple conversion formula. For example, from an induced electric field E (in V/m), the SAR can be derived as

$$\mathrm{SAR} = \frac{\sigma E^2}{\rho_{\mathrm{m}}} \tag{10.1}$$

where σ is the bulk electrical conductivity (S/m) and ρ_{m} is the mass density (kg/m^3) of tissue. However, at present, a small, isotropic, implantable electric field probe has yet to be developed with sufficient sensitivity for practical use. Consequently, a common practice in experimental dosimetry relies on the use of temperature elevation produced under a short-duration ($<$30 sec), high-intensity exposure condition. The short duration is not enough for

significant convective or conductive heat contribution to tissue temperature rises. In this case, the time rate of initial rises in temperature (slope of transient temperature response curve) can be related to SAR through a secondary procedure, that is,

$$\text{SAR} = \frac{c\Delta T}{\Delta t} \tag{10.2}$$

where ΔT is the temperature increment (°C), c is the specific heat capacity of tissue (J/kg °C), and Δt is the duration (sec) over which ΔT is measured. Thus, the rise in tissue temperature during the initial or a transient period of RF energy absorption is linearly proportional to the value of SAR. It is important to distinguish the use of SAR and its derivation from temperature measurement. The quantity of SAR is merely a metric for energy deposition or absorption, and it should not be construed to imply any mechanism of interaction, thermal or otherwise. However, it is a quantity that pertains to a macroscopic phenomenon by virtue of the use of bulk electrical conductivity in its derivation (Equation 10.1).

It is of particular significance to emphasize the use of bulk electrical conductivity, the specific heat capacity, and the mass density (kg/m^3) of tissue in the derivation of SAR from electric field strength or temperature elevation. Their use in the definition means that a volume of tissue mass must be selected over which SAR is determined. It is self-evident that the numerical value of SAR would be the same, regardless of what volume is chosen, if the induced field or power deposition is uniform in a tissue medium. A difficulty arises when the absorption is not uniform or when tissues with differing properties and conductivities are within the same volume. Thus, in general, a smaller averaging mass or volume would allow SAR—as a metric—to provide a closer representation of its variation inside the body or tissue medium.

10.1.2 Characterizing EMFs

The space surrounding a source antenna can be divided into near and far zones as a function of distance from the antenna [3]. The demarcating boundary occurs at a conservative distance of $R = 2D^2/\lambda$, where D is the largest dimension of the antenna. Furthermore, the near zone can be divided into two subregions: the radiative region and the reactive region. In *the radiative region*, the region closer than $2D^2/\lambda$, the radiated power varies with distance from the antenna. The vicinity of the antenna where the reactive components predominate is known as *the reactive region*. The precise extent of these regions varies for different antennas. For most antennas, the transition point between reactive and radiative regions occurs from 0.2 to $0.4D^2/\lambda$. For a short dipole antenna, the reactive component predominates to a distance of approximately $\lambda/2\pi$, where the radiative and reactive components are equal to each other. However, the outer limit is on the order of a few wavelengths or less in most cases.

A typical wavelength in free space at extremely low-frequencies (ELF between 3 Hz and 3 kHz) is ~5000 km. The $\lambda/2\pi$ distance is about 800 km for the induction and radiation fields to have equal amplitudes. Therefore, for most purposes, ELF transmission line fields are not radiative but are inductive and quasi-static in nature. This fact governs the coupling and induced field characteristics of ELF and other low-frequency electric and magnetic fields in biological tissue. In particular, (1) the electric field is enhanced at the surface of the biological body and is nearly perpendicular to the surface of the body, (2) electric and magnetic fields are decoupled inside a biological body, (3) the electric field applied through air is weakened by a large dielectric permittivity (by about 10^{-6}) upon penetration into biological tissues, (4) the magnetically induced electric field encircles the

magnetic field and produces an eddy current whose magnitude increases with distance from the center of the body, and (5) an eddy current appears in each region inside the body with a different conductivity and behaves as a unit with its own body center and radius or an equivalent radius. These observations apply to all frequencies where the wavelength is high or the largest dimension of the body is small compared with the wavelength [2]

In contrast, the $2D^2/\lambda$ distance is approximately 6 cm for a 10-cm RF antenna operating at 900 MHz in free space. Clearly, both near-zone reactive and far-zone radiative interactions are encountered in the vicinity of wireless RF telecommunication systems. In the near zone, the coupling of RF energy into the human head is substantial. As much as 40% to 50% of the radiated RF power is transferred back and forth between the radiating antenna and the head. SAR will vary with specific antenna configuration and its placement next to the head. The bulk of power deposition is on the side of the head nearest to the radiating structure of the cellular mobile telephone and follows an exponential trend away from the antenna side. The anatomy of the head and tissue inhomogeneity can influence the maximum value and distribution of SAR in the head of a mobile telephone user. However, the integrated SAR in the head is similar for a homogenous or inhomogenous model. Some of the major features of near-zone field are that (1) RF electric and magnetic fields are decoupled and are not uniform, (2) wave impedance varies from point to point, (3) beam width from the antenna is divergent and is small compared with the head or human body, (4) electric field ffect is weaker since dielectric permittivity of tissue is relatively high, and (5) inductive coupling of antenna-current-generated magnetic field dominates power deposition.

In the far field, coupling is characterized by plane wave RF field interaction and is independent of source configurations. Electric and magnetic fields are uniquely defined through the intrinsic impedance of the medium. Thus, determination of the electric field behavior is sufficient to characterize the interaction. The coupling of RF power from air into planar tissue ranges from 20% to 60% at wireless communication frequencies. However, enhanced coupling can occur at a greater depth in bodies with curved surfaces. In fact, RF energy is resonantly absorbed by the head at 400 to 1500 MHz, and SAR peaks or hot spots may occur near the center of the head. The interaction of RF energy with biological systems depends on electric field polarization for elongated bodies whose height-to-width ratio is large. It is significant to observe that the integrated SAR or total absorption in the biological body is similar for a homogenous and inhomogenous model.

10.2 Planar Tissue Models

When the radius of curvature of the body surface is large compared to the wavelength and beam width of the impinging radiation, planar tissue models may be used to estimate the absorbed energy and its distribution inside the body. As a first-order approximation, the plane wave configuration is often used for its simplicity to assess EMF interaction with planar biological tissues. This section presents a summary of specific results that have been obtained, using analytical approaches, for thick or semi-infinite layers and for multilayered planar models of biological tissue structures.

10.2.1 Thick or Semi-Infinite Layers

The reflection and transmission of a plane wave at a planar tissue interface depend on the frequency, polarization, and angle of incidence of the wave and on the dielectric constant and conductivity of the tissue. For a linearly polarized plane wave impinging normally on

a boundary separating two semi-infinite media, the reflection and transmission coefficients are given by

$$\Gamma = \frac{\eta_2 - \eta_1}{\eta_2 + \eta_1} \tag{10.3}$$

and

$$T = \frac{2\eta_2}{\eta_2 + \eta_1} \tag{10.4}$$

respectively, where η_1 and η_2 are the intrinsic impedances ($= \sqrt{(\mu/\varepsilon)}$) of media 1 and 2. If intrinsic impedances of the two media are approximately equal or if the dielectric permittivities are comparable, most of the energy is transmitted into the second medium, and the reflected field is relatively small. Conversely, if intrinsic impedances differ greatly, or if the dielectric permittivities are very different, the transmitted field is small, and the quantity of reflected energy is large.

Table 10.1 summarizes the magnitude of the reflection coefficient at the boundary separating various tissues. The fraction of normally incident power reflected by the

TABLE 10.1

Reflection Coefficient (Magnitude in %) between Biological Tissues at 37°C

	Frequency (MHz)	Air	Fat (Bone)	Lung	Muscle (Skin)	Blood	Saline
Air	433	0	46	76	82	81	83
	915	0	43	73	78	79	80
	2,450	0	41	71	76	77	79
	5,800	0	39	70	75	76	78
	10,000	0	37	70	74	76	78
Fat (bone)	433		0	46	56	56	60
	915		0	43	52	54	57
	2,450		0	42	50	53	57
	5,800		0	42	50	53	56
	10,000		0	45	52	54	58
Lung	433			0	14	13	19
	915			0	12	14	18
	2,450			0	10	15	19
	5,800			0	10	14	19
	10,000			0	10	13	18
Muscle (skin)	433				0	4	6
	915				0	4	7
	2,450				0	5	10
	5,800				0	4	9
	10,000				0	3	9
Blood	433					0	6
	915					0	4
	2,450					0	5
	5,800					0	5
	10,000					0	6
Saline	433						0
	915						0
	2,450						0
	5,800						0
	10,000						0

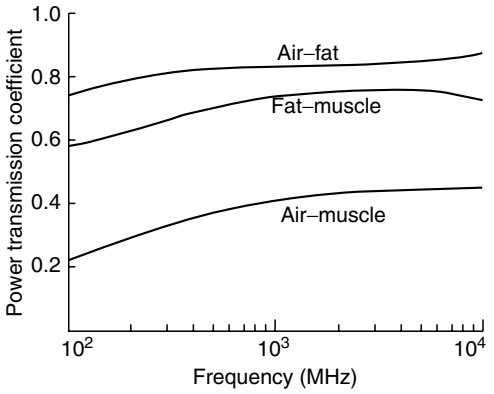


FIGURE 10.1
Power transmission coefficients at three tissue interfaces as functions of frequency.

discontinuity is given by Γ^2. Clearly, about one half of the incident power is reflected at these boundaries. Further, the reflection coefficient for tissue–tissue interfaces generally is smaller than for air–tissue interfaces. The percent reflected power for tissue–tissue interfaces ranges from a low of 5 for muscle–blood to a high of 50 for bone–biological fluid interfaces. This suggests that the closer are the dielectric properties on both sides of the interface, the smaller is the power reflection.

The fraction of power transmitted is related to the power transmission coefficient, T^2. It is readily apparent from Table 10.1 that the power transmitted at air–tissue interfaces is quite substantial at RF and microwave frequencies. Moreover, Figure 10.1 shows that the power transmission coefficient is highly frequency dependent, especially at lower frequencies.

As the transmitted wave propagates in the tissue medium, energy is extracted from the wave and absorbed by the medium. This absorption will result in a progressive reduction of the power density of the wave as it advances in the tissue. This reduction is quantified by the depth of penetration, which is the distance in which the power density decreases by a factor of e^{-2}. Table 10.2 presents the calculated depth of penetration in selected tissues using typical dielectric constants and conductivities. A graphical representation of penetration depth vs. frequency for blood, muscle, and fat is given in Figure 10.2. It is seen that the penetration depth is frequency dependent and takes on different values for different tissues. In particular, the penetration depth for fat and bone is nearly five times greater than for higher-water-content tissues.

TABLE 10.2

Depth of Penetration of an EMF in Biological Tissues as a Function of Frequency

	Tissue				
Frequency (MHz)	**Saline**	**Blood**	**Muscle (Skin)**	**Lung**	**Fat (Bone)**
Depth of Penetration (cm)					
433	2.8	3.7	3.0	4.7	16.3
915	2.5	3.0	2.5	4.5	12.8
2,450	1.3	1.9	1.7	2.3	7.9
5,800	0.7	0.7	0.8	0.7	4.7
10,000	0.2	0.3	0.3	0.3	2.5

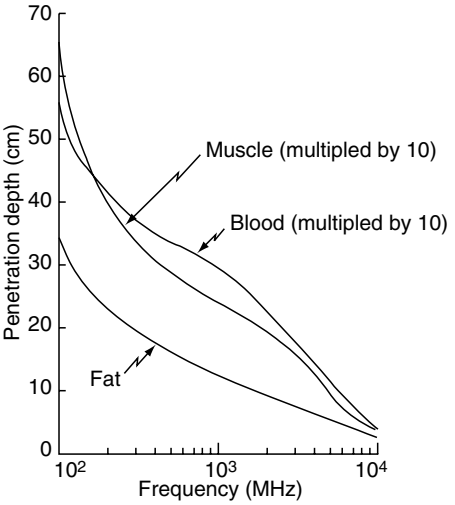


FIGURE 10.2
Depth of penetration for blood, muscle, and fat as functions of frequency.

A wave of general polarization usually is decomposed into its orthogonal linearly polarized components whose electric or magnetic field parallels the interface. These components can be treated separately and combined afterward. Figure 10.3 and Figure 10.4 illustrate the magnitude and phase of the reflection coefficients of representative tissue interfaces at a temperature of 37°C for irradiation at 2450 MHz. The figures clearly show the difference between *E* and *H* polarization. *E* polarization, also called perpendicular polarization, and *H* polarization, also referred to as parallel polarization, are defined in Chapter 1. For *E* polarization, there is only a slight variation in magnitude and phase of the reflection coefficient with incidence angle. For *H* polarization, however, there is a

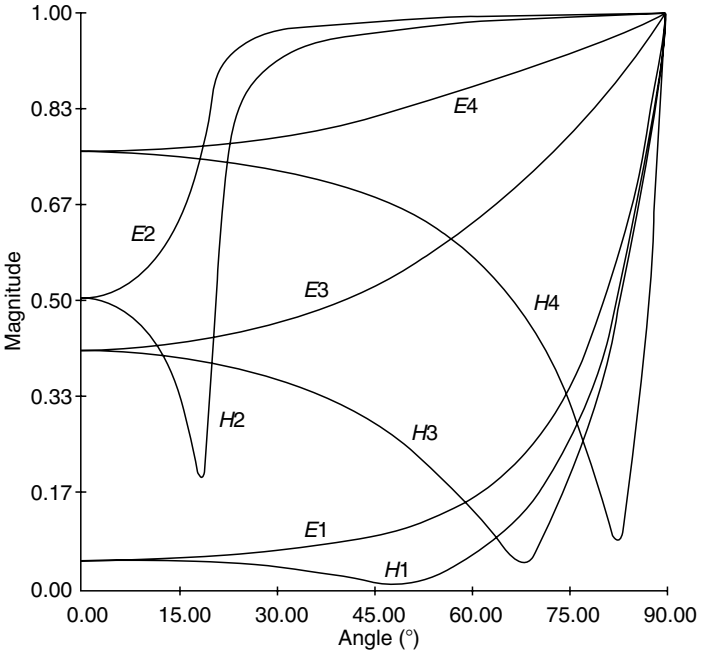


FIGURE 10.3
Magnitudes of reflection coefficients for *E*- and *H*-polarized plane waves at 2450 MHz.

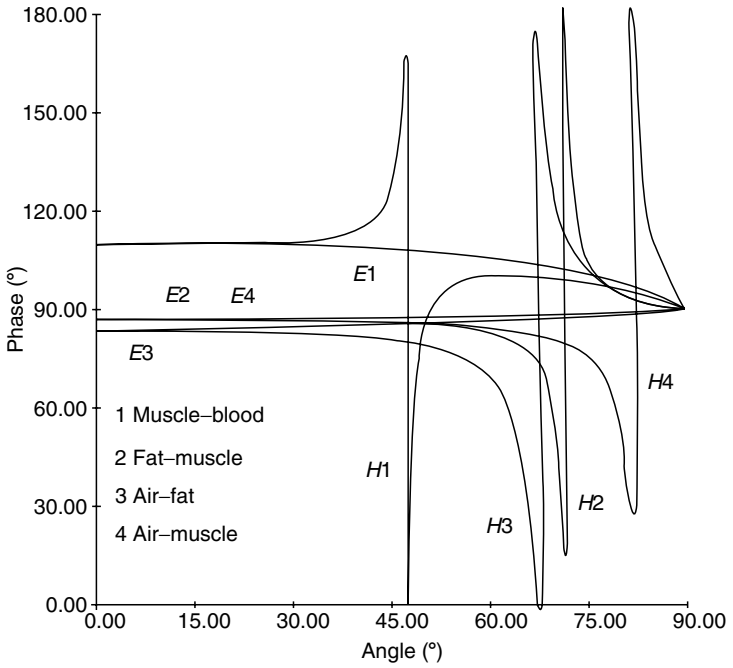


FIGURE 10.4
Phase of reflection coefficients for *E*- and *H*-polarized 2450 MHz plane waves.

pronounced dependence on incidence angle. The reflection coefficient reaches a minimum magnitude and has a phase angle of 90° at Brewster's angle. Thus, the *H* polarized wave is totally transmitted into the muscle medium at Brewster's angle.

10.2.2 Multiple Layers

When there are several layers of different tissues, the reflection and transmission characteristics become more complicated. Multiple reflections can occur between the skin and subcutaneous tissue boundaries, with a resulting modification of the reflection and transmission coefficients [4–7]. In general, the transmitted wave will combine with the reflected wave to form standing waves in each layer. This phenomenon becomes especially pronounced if the thickness of each layer is less than the penetration depth for that tissue. Plane waves impinging on the human body, considered as consisting of parallel layers of subcutaneous fat and more deeply lying muscle, have been studied in detail by Schwan and Li [5,6].

For the tissue model depicted in Figure 10.5, the electric field strength in the fat layer is given by

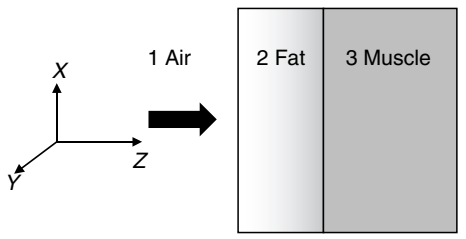


FIGURE 10.5
Plane wave impinging on a composite fat–muscle layer.

$$E_f = F_1 E_0 \left[e^{-(\alpha_2 + j\beta_2)z} + \Gamma_{32} e^{(\alpha_2 + j\beta_2)z} \right] \tag{10.5}$$

and the electric field in the underlying muscular tissue is given by

$$E_m = F_t E_0 e^{-(\alpha_3 + j\beta_3)z} \tag{10.6}$$

where α_2, β_2 and α_3, β_3 are the attenuation and propagation coefficients in fat and muscle, respectively. The layer function F_1 and the transmission function F_t are given by

$$F_1 = \frac{T_{12}}{e^{(\alpha_2 + j\beta_2)l} + \Gamma_{21}\Gamma_{32} e^{-(\alpha_2 + j\beta_2)l}} \tag{10.7}$$

$$F_t = \frac{T_{12}T_{23}}{e^{(\alpha_2 + j\beta_2)l} + \Gamma_{21}\Gamma_{32} e^{-(\alpha_2 + j\beta_2)l}} \tag{10.8}$$

where T_{12} and T_{23} are the transmission coefficients at the air–fat and fat–muscle boundaries, respectively. Γ_{21} and Γ_{32} denote the reflection coefficients at these boundaries, respectively; l is the thickness of the fat layer. The power deposition in a given layer can be obtained from Equation 10.1.

Figure 10.6 shows the results of SAR distribution obtained using the dielectric data given in part 1. The values are normalized to the SAR in muscle at the fat–muscle boundary. Note that the absorbed energy is much lower in fat than in muscle. The standing-wave maximum becomes bigger in fat, and the penetration into muscle becomes less as the frequency increases.

The electromagnetic energy absorbed in models composed of planar layers of skin, fat, and muscle can be analyzed in a similar manner [5–8], except that the distribution of

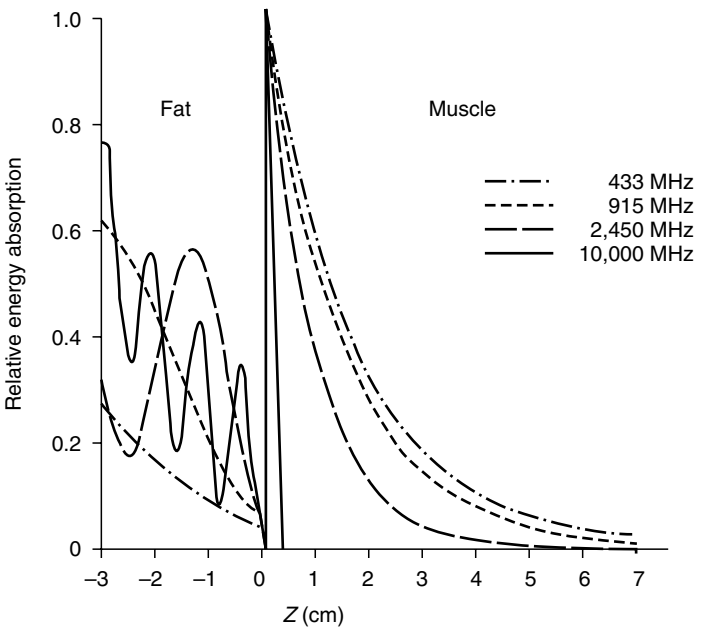


FIGURE 10.6
SAR (absorbed power density) in plane fat–muscle layers.

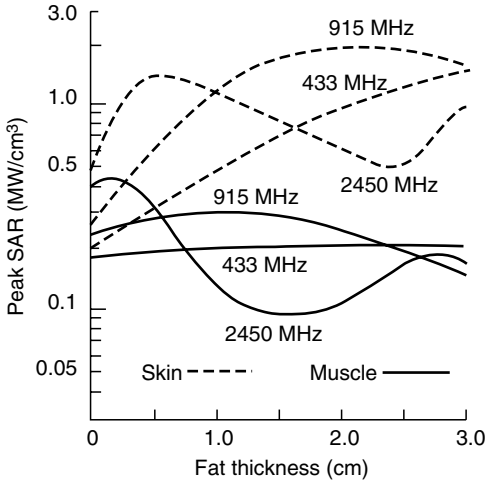


FIGURE 10.7
Peak SAR (absorbed power density) in models composed of fat–skin–muscle layers.

absorbed energy becomes more complex. Figure 10.7 shows that in addition to frequency dependence, the peak SAR exhibits considerable fluctuation with thickness of the subcutaneous fatty layer. The incident power density is, in this case, $10\,W/m^2$, and the skin layer is 0.2 cm thick. Note that the peak SAR is always higher in the skin layer for planar models at microwave frequencies. The depth of penetration for 10 GHz radiation in skin is less than 0.5 mm—the transmitted energy is almost completely absorbed in the skin, and the SAR is rather unaffected by changing fatty layer thickness. The fact that SAR is highest in the skin is significant, since skin is populated with thermosensitive free nerve endings, which may be excited along with cutaneous pain receptors when the absorbed energy exceeds the normal range that can be handled by thermoregulation.

Figure 10.8 shows the distribution of induced electric field strength in a layer of muscle beneath layers of fat, muscle, and bone for two frequencies [5–8]. It is seen that in addition

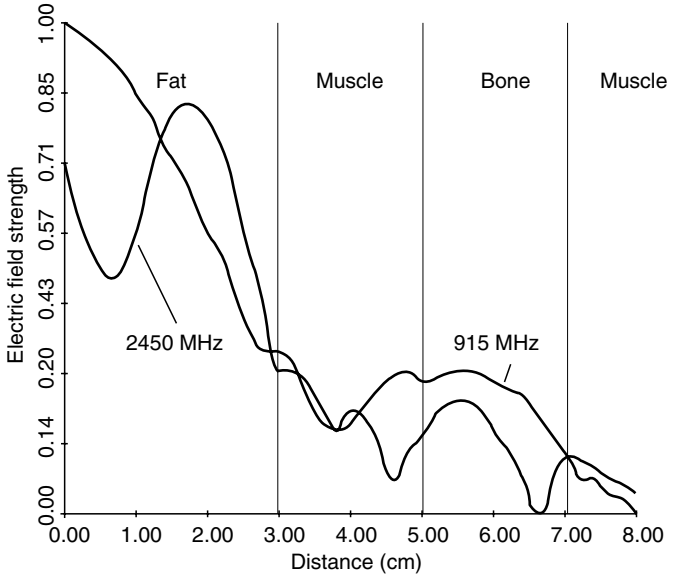


FIGURE 10.8
Distribution of electric field strength in planar layer of fat–muscle–bone–muscle tissue model.

to frequency dependence, the electric fields exhibit considerable fluctuation within each tissue layer. While the standing-wave oscillations are larger at 2450 than at 915 MHz, microwave energy at both frequencies penetrates to deeper tissues. This result, together with Figure 10.6 and Figure 10.7, implies that at frequencies between 300 and 3000 MHz, sufficient energy may be transmitted and reflected to allow examination of organs within the body. Furthermore, at these frequencies, electromagnetic energy can penetrate into more deeply situated tissues, making it especially desirable for therapeutic applications. They also call for special attention for safety considerations since electromagnetic energy in this frequency range can produce higher SAR at greater depth compared to superficial tissues.

10.3 Bodies of Revolution

Although depth of penetration and reflection and transmission characteristics in planar tissue provide considerable physical insight into the coupling and distribution of electromagnetic energy, biological structures generally are more complex in form and exhibit substantial curvature that can modify electromagnetic energy transmission and reflection. For bodies with complex shapes, the propagation characteristics depend critically on polarization and on orientation of the incident wave with respect to the body, as well as on the ratio of body size to wavelength. These complications place severe limitations on calculations of reflected and transmitted energy for bodies of arbitrary shape and complex permittivity. This section presents a summary of results for homogenous and multilayered models based on bodies of revolution that approximate certain mammalian tissue structures.

10.3.1 Spherical Models

Some representative calculations of the SAR are shown in Figure 10.9 for four different-sized models at 918 and 2450 MHz [7,8]. The 6-cm diameter sphere approximates a cat or rhesus monkey brain, and the 10-cm diameter sphere approximates the head of a child, while the 14- and 18-cm diameter spheres are more typical of human adult heads. The figures illustrate the SAR distributions along the three perpendicular axes whose origin coincides with the center of the sphere. An incident plane wave power density of $10\,\mathrm{W/m^2}$ is assumed. The plane wave is propagating in the positive z direction and is polarized along the x axis. It is seen that for 918 MHz, maximum absorption occurs near the center or inside of all the brain spheres. When the frequency is increased to 2450 MHz, the location of peak SAR for the cat-size brain sphere remains near the center, whereas that for a human-size brain sphere is moved to an anterior location.

In general, standing-wave patterns with many oscillations are observed. Note that while peak and average SARs in the cat brain are larger by a factor of 2 than in the human brain at 918 MHz, at 2450 MHz the peak absorption is four times and the average absorption is three times greater in the cat brain than in the human brain. Other studies [9–12] indicate that the peak absorption may be as much as five times greater than the average, and the enhanced absorptions near the center of these brain models may be two to three orders of magnitude greater than that expected from the planar tissue models. The increased absorptions are due to a combination of high dielectric constant and curvature of the model, which produces a strong focusing of energy toward the interior of the sphere that more than compensates for the transmission losses through the tissue.

The peak absorption per unit volume, average absorption per unit volume, and average absorption per unit surface area as functions of frequency and radius of the spherical brain model are illustrated in Figure 10.10. It can be seen that the absorbed energy varies widely with sphere size and frequency. In general, the absorption increases rapidly with increasing radius and is then followed by some resonant behavior. The peaks of these resonant oscillations are related to the maxima, or hot spots, in the distribution of absorbed energy inside the head model, as shown in Figure 10.9. Therefore, for $(2\pi a/\lambda_0) < 0.4$, where a is the sphere radius and λ_0 is the wavelength in vacuum, hot spots do not occur inside the sphere. However, for some combinations of irradiation frequency and radius, hot spots will occur, for example, in spheres with radii between 2 and 8 cm at 918 MHz and between 0.9 and 5 cm at 2450 MHz. For spheres whose radii exceed the size ranges mentioned above, the maximum absorption appears at the anterior portion (exposed surface) of the sphere, and the penetration depth at the surface becomes a dominating factor for exposures at frequencies in this range. The planar model discussed previously may be applied to obtain a theoretical estimation of the absorbed energy in this case.

The frequency dependence of energy absorption is illustrated in the upper graphs in Figure 10.10 for the head of a small animal, such as a cat or rhesus monkey, and a sphere the

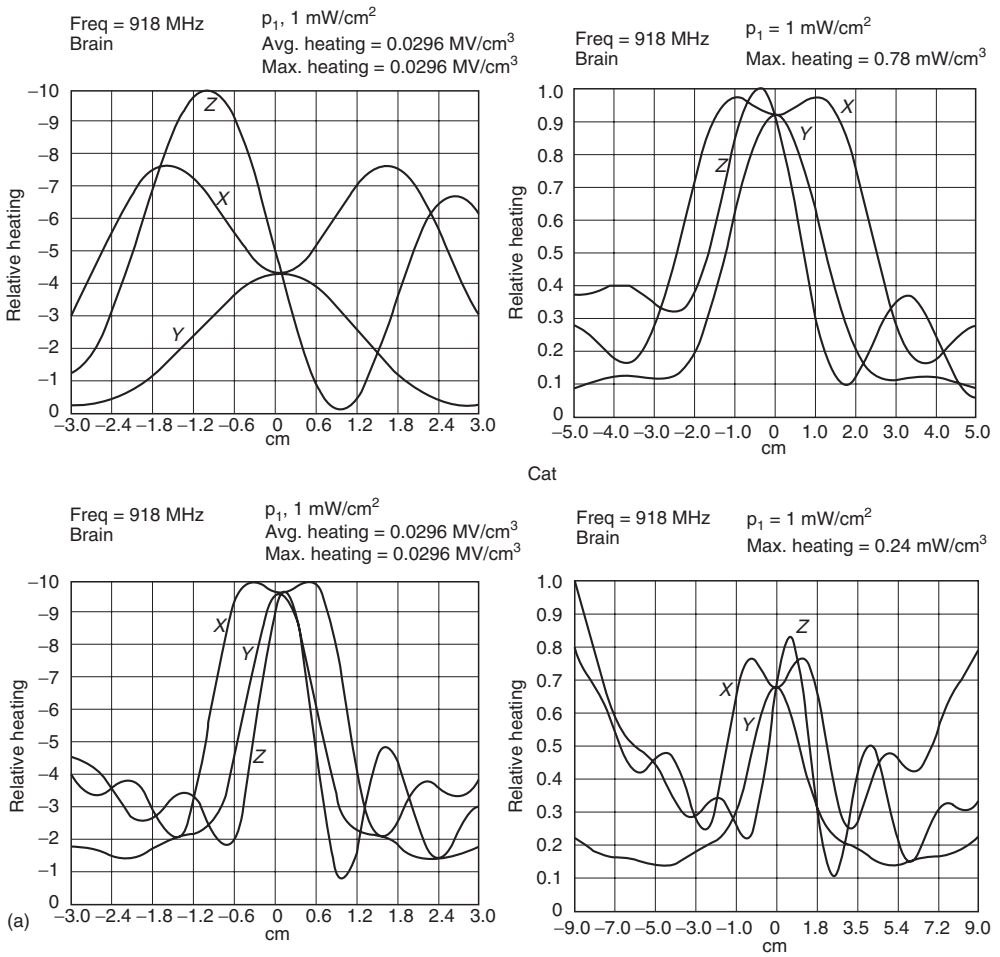


FIGURE 10.9
(a) Predicted SAR distribution (heating pattern) along the three rectangular axes of spherical models of brain exposed to 918-MHz uniform plane waves.

continued

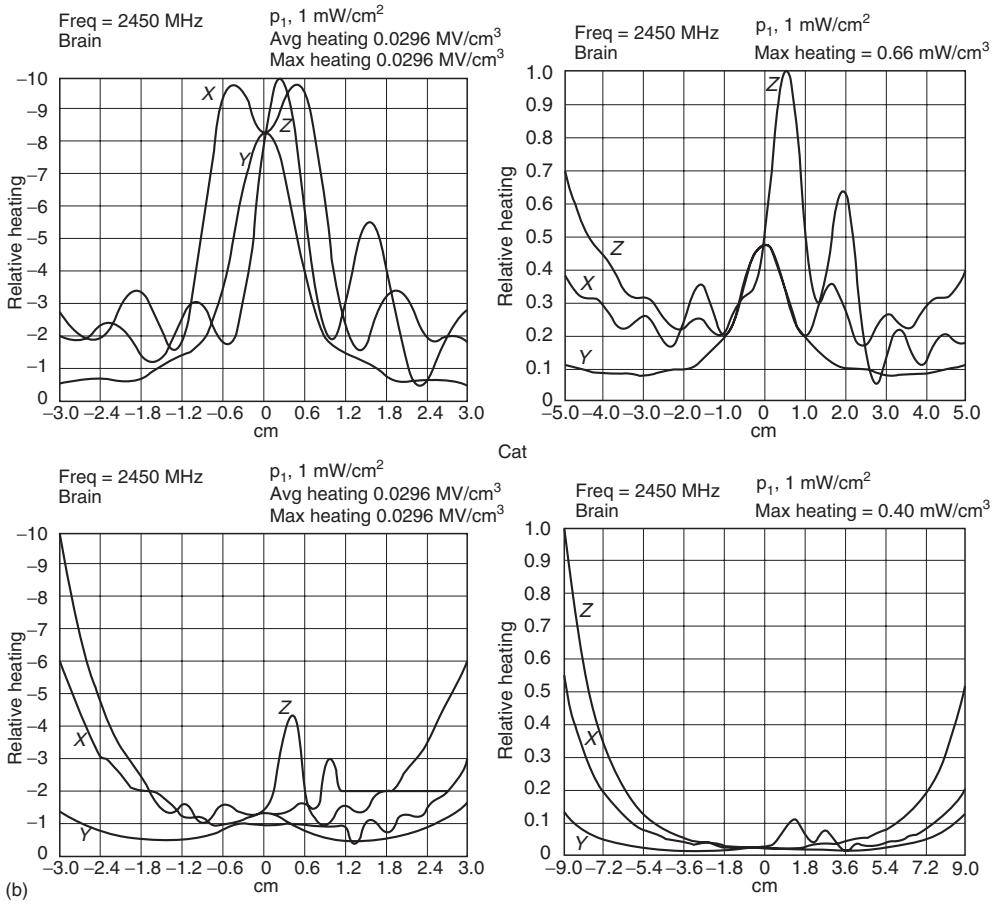


FIGURE 10.9 (continued)
(b) Predicted SAR distribution (heating pattern) along the three rectangular axes of spherical models of brain exposed to 2450-MHz uniform plane waves.

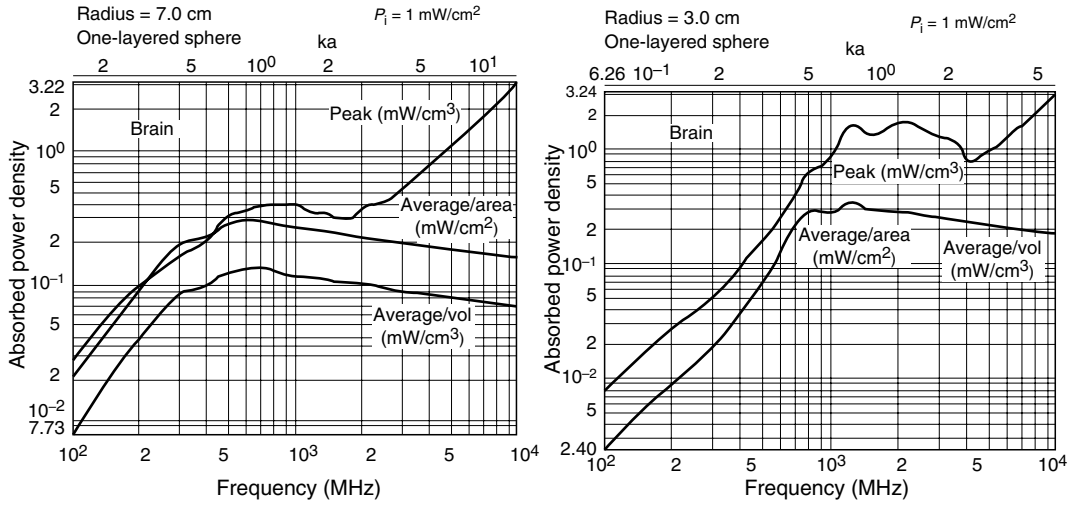


FIGURE 10.10
Electromagnetic energy absorption characteristics for spherical models of brain.

size of a human head. Besides the occurrence of resonant peaks, with increasing frequency, energy is absorbed in a decreasing volume as a result of shortened penetration depth.

The effects of skin, fat, bone, dura, and cerebrospinal fluid on the absorption of RF radiation by the brain have been investigated in several laboratories [9,13–15], using more complex spherical structures where the spherical core of brain is surrounded by five concentric shells of tissues. It is interesting to note that if brain sizes remain unchanged, but the overall sphere diameter is increased to account for the outer tissue layers, absorption in brain tissues may be increased by 25% for human- and cat-size heads at 918 MHz or decreased by 70% or more in the case of 2450 MHz. Moreover, surface absorption is greatly increased in the case of layered models, while fat and bone always absorb the least amount of energy.

If the outer diameter of the sphere remains the same, while the tissue layers are allowed to be either layered or homogenous, the peak and average SARs show very little change except when the radius of the spherical head is between 0.1 and 1.0 times the wavelength in air. The peak and average SARs for layered models may be several times greater than for homogenous models. Enhancement is apparently the result of resonant coupling of energy into the sphere by the outer tissue layers.

A study also has been made of the interaction of circularly polarized plane electromagnetic waves with six-layered spherical models of the mammalian head [15]. The approach is a classic one; Mie equations were modified to account for the two polarizations that are orthogonal in space. For example, calculations at 918 and 2450 MHz for a 7-cm diameter sphere representing a cat or monkey head and a 20-cm diameter sphere typical of a human adult head indicated that the maximum absorption for 918 MHz occurs near the center of a cat-size head, whereas the maximum absorption for a human-size head is at the surface, as in the case of linearly polarized plane waves. However, at 2450 MHz the location of maximum absorption for both the smaller and the larger spheres shifts to the leading surface. The distribution of absorbed energy for circularly polarized waves is more uniform compared with the linearly polarized case. In fact, the absorbed energy distribution in the planes transverse to the direction of propagation is rotationally symmetric, that is, it is independent of angular variation. Note also that the maximum energy absorbed in the spherical head models varies only slightly between these two frequencies. However, a greater quantity of energy is deposited in the inner sphere (representing the brain of a human head) for 918- than for 2450-MHz radiation.

Spherical models of muscle [16,17] have been used as a first-order approximation for the extrapolation to human beings of results obtained from laboratory animals and as an index of whole-body absorption of electromagnetic energy as a function of frequency. The spherical model is attractive since exact solutions for absorbed energy can be obtained for all frequencies and body sizes. While in this case the peak absorption is of very limited utility, the average absorption per unit surface area is related to the time and power required to overload the thermoregulatory capacity of an exposed subject. The absorptions for homogenous muscle spheres, whose volumes correspond to small animals, such as a rat, and standard man, computed as functions of frequency, showed that the average absorption for the rat model is at least ten times higher than for a muscle sphere representing a human body at frequencies greater than 500 MHz. The absorption increases rapidly with frequency until the free space wavelength of the impinging radiation approaches the diameter of the sphere. A number of resonant oscillations appear that tend to increase the amount and nonuniformity of absorbed energy. Above this range the absorption falls off slowly, indicating that details of body surface curvature are of little significance.

We have, thus far, dealt mainly with situations where the diameter of the sphere is comparable to or larger than the wavelength in air. It is interesting to note that when the sphere is small compared with the wavelength, the absorbed energy distribution varies

almost as the square of the radius or distance from the axis parallel to the direction of the magnetic field vector. If the sphere is extremely small compared with the wavelength, the absorbed energy distribution becomes nearly uniform in the transverse directions but decreases continuously with distance from the exposed surface. This behavior can be explained by a quasi-static field theory [16]. The electric component of the incident field couples to the object in the same fashion as an electrostatic field. This gives rise to a constant induced electric field inside the sphere that has the same direction but is reduced by $3/\varepsilon$ from the applied electric field for biological materials and is independent of sphere size. Similarly, the magnetically induced electric field inside the body is identical to the quasi-static solution whose magnitude is given by $E = \pi f \mu r H$, where f is the frequency, μ is the permeability, r is the radius, and H is the magnetic field component. Thus, the magnetic component of the incident field produces an internal electric field that varies directly with distance from the axis and in proportion to the frequency. This magnetically induced electric field encircles the magnetic axis and gives rise to an eddy current whose magnitude increases with distance from the y axis. It indicates that while the H-induced energy absorption in a mouse or larger animal is much greater than the E-induced component, electrically and magnetically induced absorption may be equally significant in smaller animals at lower frequencies (below 30 to 40 MHz). Moreover, for a small insect or pupae the electric field will be the predominant factor.

The variation of average and maximum energy absorption with frequency for a human-size sphere is illustrated in Figure 10.11. In the frequency range from 1 to 20 MHz, the maximum absorption rate is only 10^{-6} to 10^{-3} (W/kg)/(W/m^2) of incident power. Inspection of the maximum absorption rate induced by a plane wave, a quasi-static electric field, and a quasi-static magnetic field shows that absorption at frequencies below 20 MHz is primarily due to the magnetically induced eddy current and is characterized by a square-of-frequency dependence. The approximate frequency dependence of average or total energy absorption throughout the frequency range from 1 MHz to 10 GHz is indicated by the dashed line. For frequencies below 20 MHz the average absorption varies as the square of the frequency. In the frequency range of 20 to 200 MHz, the average absorption increases directly in proportion to frequency and attains a maximum of about 2×10^{-3} (W/kg)/(W/m^2) of incident power at 200 MHz. The average absorption rate remains fairly constant with increasing frequency. (Its slow variation is inversely proportional to frequency for higher frequencies.) There is thus little doubt that electromagnetic energy absorption varies both with frequency and with body size, and in a predictable manner.

10.3.2 Prolate Spheroidal Models

Since the bodies of humans and experimental animals are seldom spherical in shape, a better geometric model is needed to analytically and numerically describe the induced fields and absorbed energy inside experimental subjects. A prolate spheroid emulates more closely the shape of mammalian bodies, but most analyses have been restricted to homogenous models for humans and experimental animals [18–22]. As in the case of spherical models, for frequencies below resonance, long-wavelength formulations [19,20] and quasi-static approximations [22] have been used to obtain absorption information. Geometric optics approximations also have been developed for computation of absorption characteristics of prolate spheroidal models of humans at frequencies whose wavelengths are short compared with body size [21].

Three orientations of the impinging plane wave with respect to the body must be distinguished: E-polarization, in which the electric field is parallel to the major axis of

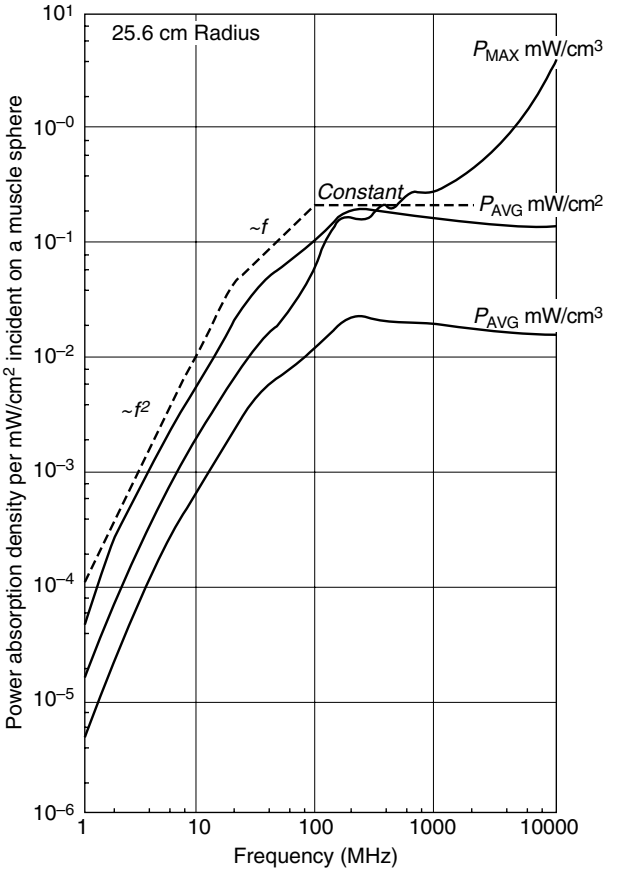


FIGURE 10.11
Frequency dependence of absorption in a spherical model of the human body.

the spheroid; *H*-polarization, in which the magnetic field vector is parallel to the major axis; and *K*-polarization, in which both electric and magnetic field vectors are perpendicular to the major axis of the spheroid. In general, *E*-polarization produces the highest energy absorption for frequencies up to and slightly beyond the resonance region.

For a plane wave with long wavelength, that is, $\lambda > a$, where a is the semimajor axis of the prolate spheroid, the induced fields within the spheroid are uniform and independent of size when the external field is uniform. For $\varepsilon_r > 1$, the field inside the spheroid is weaker than the applied field. Moreover, the whole-body energy absorption depends not only on the strength of impressed fields but also on the orientation of the field with respect to the major axis of the body. As in the case of spherical models, the absorption is produced by an electrically induced current in the direction of the applied *E*-field vector, combined with a circulating eddy current induced by the incident magnetic field [16]. One would therefore expect the electrically induced absorption to be uniform, whereas the absorption due to the circulating eddy current would be zero at the center of the body and increase as the square of the distance from the center.

Note that for a given incident field orientation, the average SAR for humans may be either higher or lower than for rats, depending on the frequency. For example, at 70 MHz, the average SAR is the highest for humans, having a value of 0.25 W/kg for an incident power density of 10 W/m^2; the average SAR for a rat is only 0.0125 W/kg. In contrast, the average SAR of 0.8 W/kg at 700 MHz is the highest for rats; the corresponding value for humans is less than 1/25. It is thus extremely important to take into account the body size

and operating frequency to draw any relationship between the biological effects that arise in the laboratory and the corresponding effects that might occur in humans at a given incident power density [1,2].

The frequency for maximal absorption (resonance frequency) depends on the subject and its orientation with respect to the incident field. In general, the shorter the subject, the higher the resonance frequency and vice versa. Further, the frequency dependence of whole-body or average absorption may be partitioned into three regions. This may be illustrated using the orientation that is most efficient in energy coupling, *E*-polarization. For frequencies well below resonance such that the ratio of the longest body dimension (L) to free space wavelength (λ) is less than 0.2, the average SAR is characterized by an f^2 dependence. The average absorption goes through a resonance in the region where $0.2 < L/\lambda < 1.0$. In this case, the average SAR rapidly increases to a maximum near $L/\lambda = 0.4$ and then falls off as $1/f$. At frequencies for which $L/\lambda > 1.0$, the whole-body absorption decreases slightly but approaches asymptotically the geometrical optics limit of about one half of the incident power (1 − power reflection coefficient).

It should be noted that the resonant absorption length of 0.4λ is in good agreement with results from antenna analysis. In addition, whole-body absorptions for *H*- and *K*-polarizations are totally different. The resonances are not nearly as well-defined as for *E*-polarization. In fact, the whole-body absorption curve for *H*-polarization gradually reaches a plateau and stays at that plateau for higher frequencies.

At 10 MHz, the size of the spheroidal model approximating an average human body—height equals 1.75 m with a major-to-minor axis ratio of 6.34 and a 70-kg mass—is small compared with the wavelength. The distribution of absorbed energy in the spheroidal model is qualitatively similar to that for spherical models. But quantitatively, the difference could be as much as one order of magnitude. As expected, the absorbed energy is highest for *E*-polarization. There is a strong coupling of the applied electric field into the interior of the prolate spheroid, and a relatively weak eddy current contribution due to a smaller cross section for intercepting the magnetic flux. The current distribution along the direction of incident field indicates that the electrically and magnetically induced field components are nearly equal. The electric polarization field and the circulating eddy current add at the front side and subtract on the back side of the spheroid to render an absorption pattern that peaks at the front surface and is reduced to almost zero deeper inside the spheroid.

For *H*-polarization, the electrically induced current flows along the x axial direction of incident **E** field, and the eddy current field encircles the z axial direction of incident **H** field. The relatively low power on the z axis comes solely from the incident electric field. The combination of *E*- and *H*-induced components generates a displaced parabolic energy absorption pattern along both the x and the y axes. Clearly, the magnetically induced eddy current predominates in this case, and the absorption is highest along the transverse circumference at the middle of the prolate spheroid. For *K*-polarization, both the electric and the magnetic components of the incident field are along the minor axes of the spheroid: the electrically induced current flows along one axis, and the incident magnetic field induces an eddy current electric field that encircles another axis. The absorption is lowest at the center. Whereas in both *E*- and *H*-polarization cases, the peak absorption occurs at the front surface of the spheroid irradiated by the incident field, this is not the case for *K*-polarization. Maximum absorption appears at the surface of the narrow cross section, and the absorbed energy varies parabolically. This is the result of the large quantity of magnetic flux intercepted by the broad cross section (and the resulting concentration of eddy current). It should be noted that the results match very well with experimental measurements [23]. Moreover, the peak absorptions may be two orders of magnitude higher than those for dielectric spheres of equal mass.

10.4 Anatomically Based Models

We have summarized above some of the computational approaches to quantify the absorbed energy in simple models of biological objects. It should be recognized that while spheres and spheroids are good models of some animal bodies and certain body parts, they may not always be adequate for humans and experimental animals under a variety of exposure situations. More realistic models, such as models of human bodies formed from small-sized, computational-cell volumes have been developed to account for the irregular shapes [24–28]. These models, based on numerical techniques have been a great asset in efforts to accurately predict energy absorption and its distribution in biological objects exposed to EMFs and RF radiation. In what follows we shall summarize a number of computer techniques that have been applied with some success in solving electromagnetic energy absorption and SAR distribution problems. We shall also describe some results obtained using these methods.

10.4.1 Brief Survey of Numerical Methods

The numerical methods used to predict induced fields in biological bodies of realistic shape and composition include the quasi-static impedance method, the method of moments (MoM), the finite element method (FEM), and the finite difference time domain (FDTD) method. Note that the quasi-static impedance method is restricted to lower frequencies (<30 to 40 MHz for the human body), but the MoM, the FEM, and the FDTD method may be used for any frequency of interest. In addition, both the finite element and the FDTD methods involve solving Maxwell's equations in the differential form for the computation of induced fields.

10.4.1.1 Quasi-Static Impedance Method

For low-frequency situations, where the dimensions of the biological body are small compared to the wavelength, the impedance method has been found to be highly efficient as a numerical procedure for calculating internal current densities and induced electric fields [29–33]. In this method, the biological body or the exposed part thereof is represented by a three-dimensional (3-D) network of impedances whose individual values are obtained from the complex conductivities $\sigma + j\omega\varepsilon$ for the various locations of the body. The impedances for various directions for the 3-D network can be written as

$$Z_m^{i,j,k} = \frac{\delta_m}{\delta_n \delta_p (\sigma_m^{i,j,k} + j\omega\varepsilon_m^{i,j,k})} \tag{10.9}$$

where i, j, k indicate the cell index; m is the direction in x, y, or z for which the impedance is calculated; and σ_m and $j\omega\varepsilon_m$ are the conductivities and the dielectric permittivities for the cell (i,j,k). δ_m is the thickness of the cell in the mth direction, and δ_n and δ_p are the widths of the cell in directions at right angles to the mth direction.

In the impedance method formulation, it can be seen that the cells need not be identical so that fairly thin features of the body can be modeled as well as the interfaces between the various tissues and organs. Also, the conductivity for a given cell can be directionally dependent. This feature will be useful in allowing for the highly anisotropic conductivities of the tissues that have been reported for low-frequencies including the power-line frequencies [34,35].

Employing anatomically based models of the human body, the impedance method has been used for the following applications:

1. Calculation of SAR distributions for operator exposure to spatially variable fields of induction heaters [31]
2. SAR distributions for linearly or circularly polarized RF magnetic fields representative of magnetic resonance imagers [32]
3. SAR distributions due to capacitive-type electrodes used for hyperthermia [33]
4. SAR distributions for interstitial RF needle applicators for hyperthermia [36]

Some calculations using the impedance method are listed below:

1. Internal electric fields and current densities induced in the human body by exposure to magnetic fields of high-voltage power transmission lines [37]
2. Electric fields and current densities induced in the human head by magnetic fields of a hair dryer [38]
3. Current densities induced in the arm and the body by magnetic fields of an electric hand drill [39]
4. Currents induced in the anatomically based model of the human body by the electric and magnetic fields of electric blankets [40].

In the section that follows, the use of the impedance method is described for calculating currents in models of the human body exposed to electric and magnetic fields of both the conventional (pre-1990) electric blanket and the new low-magnetic-field electric blanket.

10.4.1.2 Volume Integral Equation MoM

The MoM [41] is used in conjunction with either the volume integral equation method or the surface integral equation method for finding solutions to the unknown fields inside the body. The approaches differ, however, in specifics, in that the surface integral equation MoM (SMoM) finds the unknown currents on the body surface and calculates the interior fields from the surface currents, the reciprocity theorem, and a ''measurement matrix.'' In contrast, the volume integral equation MoM (VMoM) requires determination of unknown fields throughout the volume of the body using the volume equivalence principle and the MoM.

The numerical technique that has been adopted for most of the early field intensity computations is the VMoM, employing the volume equivalence principle [26,27,42,43]. The MoM is used to transform the integral equation into a matrix equation by subdividing the body into N simply shaped cells. This is accomplished with the aid of an appropriate set of expansion functions, chosen to satisfy the boundary conditions, and a set of weighting (testing) functions to reduce the matrix fill-in time. The total electric field in each of the N cells is given by matrix inversion. A more detailed description of the volume integral equation method is included in the next section.

However, it should be noted that a fundamental limitation of this method is the use of full or nearly full matrices and, therefore, the requirement of extensive computer storage and long running time. Even with the availability of larger and faster computers, this difficulty is not completely resolved. The need for excessively large numbers of mathematical cells to render a more accurate representation of the body will give rise to an equally large and full matrix. The inversion of large, full matrices often leads to numerical instabilities in the solution. Nevertheless, the method does allow the use of inhomogenous models

with up to 1000 cells. In fact, this method has been employed, successfully, to calculate whole-body averaged absorption and to obtain regional distribution of absorbed RF energy using inhomogenous block models composed of rectangular cells [29–28,44]. This method also has been used to study the interaction of the near-zone field of an antenna with biological bodies [45,46].

10.4.1.3 SMoM

Another approach for predicting the distribution of absorbed electromagnetic energy is the SMoM [47–50]. This method makes use of two coupled integral equations, that is, the electric field and magnetic field integral equations for the tangential components of the field on the surface separating the biological body from air. The unknown surface currents are found by Fourier decomposition and the moment method. The fields inside the biological body are calculated using the previously computed surface currents, the reciprocity theorem, and the concept of measurement matrix [48,51–53].

The method begins with the matrix representation of the coupled integral equations. If the body is assumed to be rotationally symmetric, the incident wave and the induced current could then be expanded in a Fourier series expansion in the angle of rotation. This reduces the problem to that of solving a system of orthogonal modes. The method further expands the surface components in terms of triangular expansion or basis functions and allows the testing functions to be the complex conjugate of the basis functions taking advantage of the orthogonality property. Thus, the major advantage of introducing the Fourier series is to enable each mode to be treated completely independently of all other modes. This results in a much smaller-size, manageable matrix equation to be evaluated for the unknown expansion coefficients that determine the surface currents. It should be noted that for biological bodies, triangular expansion and testing functions are preferred over flat pulse expansion functions [47,48]. In fact, an expansion function with a continuous first derivation may constitute an even better choice for the expansion basis function. In any event, once the surface currents are obtained, the fields everywhere, or SAR at each point inside the body, can be calculated using the reciprocity theorem [52,53]. The total absorption can be found by integrating the surface Poynting vector.

The validity of SMoM has been substantiated by using a dielectric sphere [47]. Calculations for a human torso modeled by a homogenous muscle body of revolution with a height of 1.78 m at 30, 80, and 300 MHz showed enhanced absorption in the neck region for all three frequencies and both vertical and horizontal polarizations [48]. Note that the vertical direction is aligned with the long dimension of the torso and serves as the axis of symmetry. The strongest absorption in the torso model was found to occur with vertical polarization and near the first resonance frequency of the torso (80 MHz). In general, the surface integral equation method is applicable to any arbitrarily shaped homogenous body of revolution. The method can be used not only with incident plane waves but also with a wide variety of other field exposure conditions, including direct contact situations and near-zone sources.

Since both the surface and volume integral equation methods for field intensity prediction rely on the MoM for implementation, it is instructive to compare the relative advantages of these two techniques. For simplicity, consider a homogenous cube with N samples on each side: the computer storage requirements are N^2 and N^3 for the surface and volume integral methods, respectively [48]. For sufficient sampling to ensure accurate description of field variations, N is usually a large number. Thus, the surface integral equation method requires significantly fewer unknowns for homogenous models. Moreover, in cases where permittivity and conductivity values are large, such as in biological bodies, the wavelength becomes contracted inside the body, and a much larger number of cells than that indicated above may actually be needed. If the model is inhomogenous,

then the volume integral equation would prove to be more suitable. It is possible, however, to generalize the surface integral equation technique to account for inhomogeneities by employing the invariant imbedding procedure [54].

10.4.1.4 FEM

The FEM has been a preferred numerical algorithm in many fields of application. However, its use and popularity in predicting field intensities in biological systems have been modest until recent progress in mesh generation, boundary conditioning, and large matrix solvers. The FEM method is a near-neighbor, volume method for solving Maxwell's differential equations and is associated with a sparse system of equations [55,56]. Aside from the low memory requirement (on the order of N), an inherent attraction of FEM is its adaptability in modeling inhomogeneities and complex geometries. The feature of conforming and the variable-sized cell elements of the computational volume are extremely important in bioelectromagnetics.

The basic approach of the FEM method for predicting EMF distributions inside biological bodies starts by subdividing the physical space and biological body of interest into meshes of small volumes or cells of tetrahedral elements. This step is very important since the manner in which the volume is subdivided will dictate the computational resources required and the speed of the computation and accuracy of the results. Each cell element and node location will have to be systematically numbered and described. Once the volume has been subdivided, labeled, and the appropriate property values ascribed, the unknown field within each element is then approximated using linear extrapolation. A major step in FEM is the formulation of the system of linear equations using either the Ritz or the Galerkin algorithm with proper boundary conditions. There are two approaches to solve the system of linear algebraic equations: the direct method of Gaussian elimination or the iterative method that starts with an initial guess. In practice, either method can produce an approximate solution to the unknown field intensity with a prescribed accuracy.

It should be noted that a large region exterior to the biological body is often encountered in bioelectromagnetic situations, where the biological body, or portion of it, is part of a region into which electromagnetic energy is radiated and scattered. The region of space exterior to the biological body and applicator must be truncated with an artificial boundary to limit the volume elements and the number of unknowns. Consequently, an appropriate boundary condition needs to be established at this artificial boundary for a unique finite element determination of the induced fields inside the body. The most common boundary conditions selected for this purpose are the absorbing boundary conditions that minimize the nonphysical reflections from the artificial boundaries by making boundaries transparent to the scattered field.

Fairly large-scale calculations, on the order of 200,000 elements, have been conducted effectively in the workstation-computing environment. Specifically, detailed power deposition patterns have been simulated in full and partial models of the human body undergoing electromagnetic hyperthermia treatment for cancer [57]. In this case, the cell elements were generated from computerized tomographic data obtained on human patients.

10.4.1.5 FDTD Method

The FDTD approach is an attempt to solve Maxwell's curl equations by directly modeling propagation of waves into a volume of space containing the biological body. By repeatedly implementing a finite difference representation of the curl equations at each cell of

the corresponding space lattice, the incident wave is tracked as it first propagates to the body and then interacts with it through surface current excitation, transmission, and diffraction. This wave tracking process is completed when the steady-state behavior is observed at each lattice cell. Considerable simplification is achieved by analyzing the interaction of the wavefront with a part of the body surface at a time, rather than attempting a simultaneous solution of the entire problem.

The FDTD method has become one of the most successful methods for SAR calculations. The method was first proposed by Yee [58] and later developed by Taflove [59–61], Holland [62], and Kunz and Lee [63]. Several books [64–66] are devoted to the FDTD method and some of its applications. For bioelectromagnetic applications the FDTD method has been found to be extremely versatile and has been used for whole-body or partial-body exposures due to spatially uniform or nonuniform fields (far or near fields), sinusoidally varying EMFs, and transient fields such as ultra-wide-band (UWB) and electromagnetic pulses (EMPs) [67–71]. Accordingly, some details of FDTD are included in this section.

10.4.1.5.1 The Traditional FDTD Method

In this method, the time-dependent Maxwell's curl equations

$$\nabla \times \mathbf{E} = -\mu \frac{\partial \mathbf{H}}{\partial t} \tag{10.10}$$

and

$$\nabla \times \mathbf{H} = \sigma \mathbf{E} + \varepsilon \frac{\partial \mathbf{E}}{\partial t} \tag{10.11}$$

are implemented for a lattice of subvolumes or Yee ''cells'' that may be cubical or parallelepiped with different dimensions, δ_x, δ_y, and δ_z in the x-, y-, or z-directions, respectively. The components of **E** and **H** are positioned about each of the cells as shown in Figure 10.12 and calculated alternately with half-time steps where the time

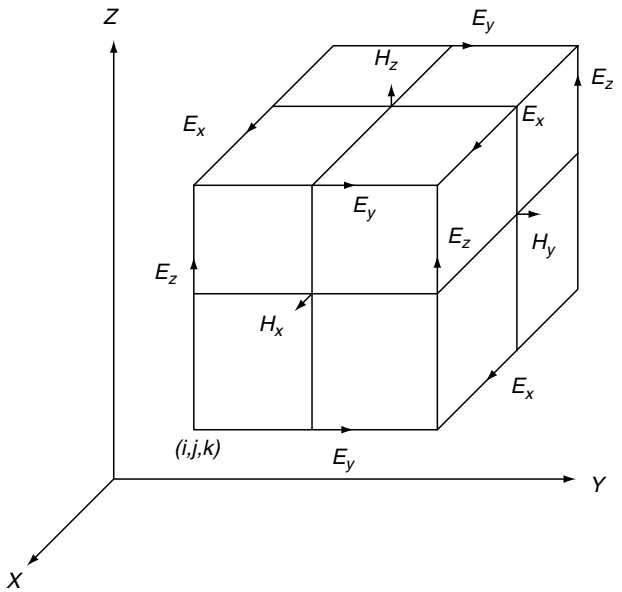


FIGURE 10.12
Unit cell of Yee lattice indicating positions for various field components.

step $\delta t = \delta/2c$. Here δ is the smallest of the dimensions used for any of the cells, and c is the maximum phase velocity of the fields in the modeled space. Since some of the modeled volume is air, c corresponds to the velocity of EM waves in air.

In the FDTD method, it is necessary to represent not only the scatterer or absorber, such as the human body or a part thereof, but also the EM sources, including their shapes, excitations, etc., if these sources are in the near-field region [70,71]. The far-field sources, on the other hand, are described by means of incident plane wave fields prescribed for a ''source'' plane [68,69], typically six to ten cells away from the exposed body. The source–body interaction volume is subdivided into Yee cells of the type shown in Figure 10.12. The interaction space consisting of several hundred thousand to a few million cells is truncated by means of absorbing boundaries. The prescribed incident fields are tracked in time for all cells of the interaction space. The solution is considered completed when either the fields have died off or, for sinusoidal excitation, when a sinusoidal steady-state behavior for **E** and **H** is observed for the interaction space.

The body of interest is mapped into the lattice space by first choosing the lattice increment and then assigning values of permittivity and conductivity to each cell. The boundary conditions at media interfaces are naturally generated by the curl equations. Thus, once a computer program is developed, the basic routines need not be changed for different model geometries. In fact, inhomogeneities and fine structural details could be modeled with a maximum resolution of one unit cell.

Time stepping for the FDTD method is accomplished by an explicit finite difference procedure [58,64]. For a cubic-cell lattice space, this procedure involves positioning the electric and magnetic field components about a unit cell of the lattice and then evaluating the components at alternate half-time steps. In this manner, centered difference expression can be used for both the space and the time increments without solving simultaneous equations to compute the fields at the latest time step.

The explicit formulation of the FDTD method is particularly suited for execution with minimum computer storage and run time using current array-processing computers. The required computer storage and run time increase only linearly with N, the number of cells. In fact, it has been shown that the FDTD method is capable of solving for more than 1 million unknown field components within a few minutes on an array-processing computer. Field intensities have been predicted to within 2.5% accuracy relative to known analytical and experimental bench marks. Recently, this FDTD technique has been improved to allow solutions for field penetration and absorption in large, complex, inhomogenous, and irregularly shaped biological bodies in three dimensions, with millimeter range spatial resolution. With the exception of a few early attempts with lossy biological objects [59,67], a majority of early efforts have been directed toward application of the FDTD method to electromagnetic interaction in time-varying inhomogenous media [60], and with metallic bodies of revolution [61]. However, during the last decade, the FDTD method has become the most extensively used numerical procedure for bioelectromagnetic computations.

10.4.1.5.2 Frequency-Dependent FDTD Formulation

For short pulses where wider bandwidths are generally involved, a frequency-dependent FDTD or $(FD)^2TD$ method is needed. Two general approaches have been used for the $(FD)^2TD$ method. One approach is to convert the complex permittivity from the frequency domain to the time domain and convolve this with the time domain electric fields to obtain time domain fields for the dispersive material. This discrete time domain method may be updated recursively for some rational forms of complex permittivity, which removes the need to store the time history of the fields and makes the method feasible. This method has

been applied to materials such as water, for which the permittivity may be described by a first-order Debye relaxation equation [72–74] or more complex materials with dielectric properties given by a second-order Lorentz equation with multiple poles [75].

A second approach is to add a differential equation relating the electric flux density **D** to the electric field **E** and solve this new equation simultaneously with the standard FDTD equations. This method has been applied to 1-D and 2-D examples with materials described by a first-order Debye equation or second-order single-pole Lorentz equation [76], and to a 3-D sphere and homogenous two-thirds muscle-equivalent man model with properties described by a second-order Debye equation [77,78]. In the following we describe this differential equation approach, which has now been used for induced current and SAR calculations for a heterogenous model of the human body [79].

The time-dependent Maxwell's curl equations used for the FDTD method have already been given as Equation 10.10 and Equation 10.11. The curl ***H*** can also be written as follows:

$$\nabla \times \mathbf{H} = \frac{\partial \mathbf{D}}{\partial t} \tag{10.12}$$

where the flux density vector **D** is related to the electric field through the complex permittivity $\varepsilon^*(\omega)$ of the local tissue by the following equation:

$$\mathbf{D} = \varepsilon^*(\omega)\mathbf{E} \tag{10.13}$$

Since Equation 10.10 and Equation 10.12 are to be solved iteratively in the time domain, Equation 10.13 must also be expressed in the time domain. This may be done by choosing a rational function for $\varepsilon^*(\omega)$, such as the Debye equation with two relaxation constants (see Chapter 1):

$$\varepsilon^*(\omega) = \varepsilon_0 \left[\varepsilon_\infty + \frac{\varepsilon_{s1} - \varepsilon_\infty}{1 + j\omega\tau_1} + \frac{\varepsilon_{s2} - \varepsilon_\infty}{1 + j\omega\tau_2} \right] \tag{10.14}$$

Rearranging Equation 10.14 and substituting in Equation 10.13 gives

$$\mathbf{D}(\omega) = \varepsilon^*(\omega)\mathbf{E}(\omega) = \varepsilon_0 \frac{\varepsilon_s + j\omega(\varepsilon_{s1}\tau_2 + \varepsilon_{s2}\tau_1) - \omega^2\tau_1\tau_2\varepsilon_\infty}{1 + j\omega(\tau_1 + \tau_2) - \omega^2\tau_1\tau_2}\mathbf{E}(\omega) \tag{10.15}$$

where the static (zero frequency) dielectric constant is given by

$$\varepsilon_s = \varepsilon_{s1} + \varepsilon_{s2} - \varepsilon_\infty \tag{10.16}$$

Assuming $e^{j\omega t}$ time dependence, Equation 10.15 can be written as a differential equation in the time domain:

$$\tau_1\tau_2 \frac{\partial^2 \mathbf{D}}{\partial t^2} + (\tau_1 + \tau_2)\frac{\partial \mathbf{D}}{\partial t} + \mathbf{D} = \varepsilon_0 \left[\varepsilon_s \mathbf{E} + (\varepsilon_{s1}\tau_2 + \varepsilon_{s2}\tau_1)\frac{\partial \mathbf{E}}{\partial t} + \varepsilon_\infty \tau_1\tau_2 \frac{\partial^2 \mathbf{E}}{\partial t^2} \right] \tag{10.17}$$

For the $(FD)^2TD$ method, Equation 10.10 and Equation 10.12 need to be solved subject to Equation 10.17. These equations can be written in the difference form [77,78] and solved to find **E**, **H**, and **D** at each cell location. The $\mathbf{E} \rightarrow \mathbf{H} \rightarrow \mathbf{D}$ loop is then repeated until the pulse has died off.

10.4.2 Human Bodies Exposed to EMFs

Computational algorithms based on numerical techniques described in the previous section have been applied to predict field intensities and SAR distributions in anatomically realistic models of human bodies. However, the use of a given numerical method and the number of computational cells involved in the models typically dictate the applicability of the techniques, how real the model is, the degree of accuracy attainable, and its domain of applicability. In the following sections, a few of the models will be described, and they will be followed by some representative results obtained using the models.

10.4.2.1 Realistic Models of the Human Body

Models proposed as better representations of the complex geometry and composition of the human body include constructions using small-volume cubic cells or cell meshes and anatomically based models generated from computerized tomographic and magnetic resonance image data.

10.4.2.1.1 Cubic-Cell Models

Models of the human body consisting of 200 to 1000 cubic cells that account more realistically for the gross anatomic and biometric characteristics of human bodies have been used by several investigators [24–28]. The models are 1.75 m tall and can be made either homogenous or inhomogenous by choosing an equivalent or a volume-weighted complex permittivity for each cell. The cubic-cell model has been employed successfully to calculate whole-body averaged absorption. It is important to note that for subdivision with less than three cells per wavelength, the magnitude and phase resolutions would be such that even with convergence the reliability of the MoM-computed SAR would be questionable. Therefore, if the interest is primarily in whole-body SAR, this model may provide quite adequate results for frequencies lower than 30 MHz. To achieve more accurate structural representation of the human body, anatomically based models have been offered in recent years.

10.4.2.1.2 Millimeter-Resolution Model Based on Magnetic Resonance Imaging Scans of the Human Body

A new millimeter-resolution model of the human body has been developed from the magnetic resonance imaging (MRI) scans of a male volunteer of 176.4-cm height and 64-kg weight [80,81]. The MRI scans were taken with a resolution of 3 mm along the height of the body and 1.875 mm for the orthogonal axes in the cross-sectional planes. Even though the height of the volunteer was quite appropriate for an average adult male, the weight was somewhat lower than an average of 71 kg, which is generally assumed for an average male. This problem can, to some extent, be ameliorated by assuming that the cell dimensions for the cross sections are larger than 1.875 mm by the ratio of $(71/64)^{1/2} = 1.053$. By taking the larger cell dimensions of $1.053 \times 1.875 = 1.974$ mm for the cross-sectional axes, the volume of the model can be increased by $(1.053)^2 = 1.109$, that is, by about 10.9%, which results in an increase of its weight by approximately the same percentage, that is, to a new weight of approximately 71 kg. The MRI sections were converted into images involving 29 tissue types whose electrical properties can then be prescribed at the exposure frequency. The tissue types are fat, muscle, bone, cartilage, skin, brain, nerve, cerebrospinal fluid (CSF), intestine, spleen, pancreas, heart, blood, eye, eye humor, eye sclera, eye lens, ear, liver, kidney, lung, bladder, stomach, ligament, compact bone, testicle, spermatic cord, prostate gland, and erectile tissue. As described above, this

model has been used to calculate the electromagnetic absorption in the human head, neck, and shoulders for cellular telephones operating at frequencies of 800 to 900 MHz. Because of the localized nature of EMFs, it was possible to use the model corresponding to the top 42 cm of the body for SAR calculations.

10.4.2.1.3 The ''Visible Human'' Model

The Visible Human (VH) Project, developed by the National Library of Medicine, is a 3-D digital image library representing an adult human male and female [82]. The dataset for both male and female includes photographic images obtained through cryosectioning of human cadavers and digital images obtained by computer tomography and MRI of the same cadavers. In particular, the photographic images represent a highly accurate and realistic counterpart of the anatomical cross sections contained in human anatomy atlases. The male dataset, the first to be constructed, consists of 1871 digital axial images obtained at 1.0-mm intervals, with a pixel resolution of 1 mm, while the female one contains 5189 digital axial images, obtained with a finer spatial step of 0.33 mm. While these digital datasets represent a unique tool to explore human anatomy, their direct use for computational electromagnetic dosimetry is limited by the fact that images cannot be directly used as an input for a numerical electromagnetic tool but must be converted to a so-called ''segmented'' version. A segmented model is a model where every pixel, usually called in such models ''voxel,'' does not contain information about the color (like in digital images) but rather a label that is uniquely associated to a given tissue. In such a way, it is possible to know which tissue fills each of the model voxels and hence assign the correct complex permittivity values to be used in numerical simulations.

Segmentation of the original image sets is a complex and time-consuming activity, which is difficult to carry out making exclusive use of automatic procedures, such as contour recognition algorithms, but inevitably requires intervention by experts in human anatomy. The segmentation procedure has been carried out for the male model by researchers at the Air Force Research Laboratory, Brooks Air Force Base, TX [83]. The final segmented model, made freely available to the scientific community, comprises $586 \times 340 \times 1878$ voxels with a resolution of $1 \times 1 \times 1$ mm, and is segmented in about 40 different tissue types [84]. The model has been widely used to study both whole-body and localized human exposure to EMFs radiated by different types of sources and is now being included in many commercially available electromagnetic simulation tools with capabilities for dosimetric evaluation.

10.4.2.2 Currents Induced in the Human Body by Low-Frequency EMFs

This section reports the results obtained for low-frequency EMF. Specifically, it includes the use of the impedance method to calculate currents induced in the human body by the EMFs of electric blankets. It also includes the use of the FDTD method for calculations of internal **E** and **H** fields and induced current densities for exposure to electric, magnetic, or combined electric and magnetic fields at power-line frequencies. The results given below were obtained using a 1.31-cm resolution, anatomically based model of the human body. Since the term $j\omega\varepsilon$ can be neglected as compared to σ for the various tissues at ELF including electric power frequencies (50/60 Hz), the impedances for the various cells of the model given by Equation 10.9 can be replaced by resistances. It is recognized that the conductivities of various tissues, for example, skeletal muscle, heart, and bone, are anisotropic for power-line frequencies [34,35,85]. This has been neglected in this case, however, and average values of conductivities given in Table 10.3 have been taken for the various tissues for the calculations.

TABLE 10.3

Tissue Conductivities Used for Calculations at the Power-Line Frequency of 60 Hz

Tissue Type	σ (S/m)
Air	0
Muscle	0.52 or 0.11
Fat, bone	0.04
Blood	0.6
Intestine	0.11
Cartilage	0.04
Liver	0.13
Kidney	0.16
Pancreas	0.11
Spleen	0.18
Lung[a]	0.04
Heart	0.11
Nerve, brain	0.12
Skin	0.11
Eye	0.11

[a]The dielectric properties of the lung consist of 33% lung tissue and 67% air.

10.4.2.2.1 Electric Blankets

To illustrate the use of the impedance method, currents induced in the human body by the EMFs of two types of electric blankets have been calculated [1,2]. The two models used for the blanket are (a) a low-magnetic-field blanket and (b) a conventional (pre-1990) electric blanket. The low-magnetic-field blanket uses two parallel leads carrying equal and opposite currents to reduce the net magnetic field around the conductors. The two leads are separated typically by 1.5 mm and are embedded in a positive temperature coefficient (PTC) conductive polymer and insulated by polyvinyl chloride (PVC). The PTC conductive polymer surrounding the two leads may be represented by a set of distributed resistors, which would result in linearly decreasing equal but opposite currents flowing through the two leads over the length of the wiring used for the blanket. By comparison, the conventional electric blanket uses a resistive alloy wire wrapped on a nylon cord and insulated with PVC. Because of the distributed resistance of the wire, this blanket would therefore have a linearly diminishing voltage and identical magnitude of current over the length of the wiring used for the blanket.

The validity of the calculated results has been established by comparing the results obtained using the impedance algorithm and those reported by others. The calculated fields are in excellent agreement with the data given by Florig et al. [86] and Hayashi et al. [87].

Currents are induced in the body by the following sources:

1. Time- and spatially varying magnetic fields of the blanket induced voltages in the various resistance loops of the body.
2. Currents launched into different subareas at the body surface by means of the capacitively coupled currents from the various conductors of the blanket.

The spatial variations of the magnetic fields were calculated from Biot-Savart's law for a short current-carrying conductor [2]. By integrating it over the entire length of the

current-carrying conductors, one can obtain the vector magnetic fields at the centers of the cells representing the model of the human body or any of the other points in space. From the vector magnetic fields thus calculated for each of the cell centers for the impedance model of the human body, the induced voltages for each of the faces of the cells can be written [32]. This information is then used to calculate the induced currents for the various impedances, that is, resistances. The average current densities J_x, J_y, and J_z for each of the cell centers can be obtained by taking the average of the currents through the resistances representing each of the four edges of the cell in the respective directions and dividing the same by the cross-sectional area δ^2 ($= 1.31 \times 1.31$ cm).

To calculate the electric field distribution in air, a 3-D impedance model consisting of capacitors representing the space between the various faces of the cells was used. For cubic cells of dimension $\delta = 1.31$ cm, the capacitances used are $\varepsilon_0 \delta^2/\delta = 0.116$ pF.

For currents induced in the human body due to electric fields, it should be recognized that the energized conductors of the blanket are capacitively coupled to the body. The capacitance between a given conductor and the highly conducting human body can be obtained by using an expression similar to that for a conductor at a distance S from the ground plane. Capacitance per unit length C of a wire of diameter d parallel to but separated at a distance S from the ground plane is given by

$$C = (2.73\varepsilon_{\text{eff}})/[\log_{10}(4S/d)], \quad \text{pF/m} \tag{10.18}$$

For a spacing $S = 5$ mm and a wire diameter $d = 0.8$ mm, and for $\varepsilon_{\text{eff}} = 2.5\varepsilon_0$, which is a value intermediate between the permittivity ε_0 for air and $4\varepsilon_0$ for the material of the blanket, we can calculate $C = 43.1$ pF/m. For a cell length $d = 1.31 \times 10^{-2}$ m, the coupling capacitance C_c between the wire and the cell can be calculated to be 0.565 pF. Since the interconductor spacing of 1.5 mm for a PTC blanket is fairly small as compared to the cell size, a proportionately smaller resistance is taken for the tissue-equivalent cells immediately underneath the conductors for the direction parallel to the interconductor spacing. Capacitances of 0.565 pF are taken from each of the conductors of the PTC blanket to the appropriate points on the impedance model of the human body. In the presence of an electrical grounding surface, the space underneath the model is represented by a 3-D network of capacitors, each of value 0.116 pF, representing the air space between the various faces of the cubic cells of dimension $d = 1.31$ cm for each of the sides.

For the PTC low-magnetic-field blanket, a constant voltage of 110 V AC is taken between the conductors of the twin-lead wiring for calculation of currents induced or injected into the human body as a result of electric fields. For calculating the magnetic fields, an input current of 1 A is taken. On account of the conductive polymer surrounding the parallel wires, this current diminishes linearly to zero at the end of the PTC wiring. This assumes a blanket input power of 110 W under normal operating conditions. If magnetic fields or induced current densities due to higher input powers are desired, the numbers calculated for 1 A input current may then be multiplied by the appropriate factor.

The conventional blanket, on the other hand, uses a resistive conductor for which the voltage diminishes linearly from 110 to 0 V over the length of the wiring. For this blanket the current throughout the length of the wiring is the same as at the input, that is, 1 A, which is assumed for the calculation of magnetic fields.

The magnetically induced, section-averaged magnitudes of the total current densities from head to feet for the two types of blankets are shown in Figure 10.13a and b, respectively. For these calculations, the wiring of the blanket was taken to be 0.5 cm from the surface of the body. Nearly identical current densities were also obtained for a grounding plate underneath the body at distances of 0.25, 0.5, and 1.0 m. It is interesting to

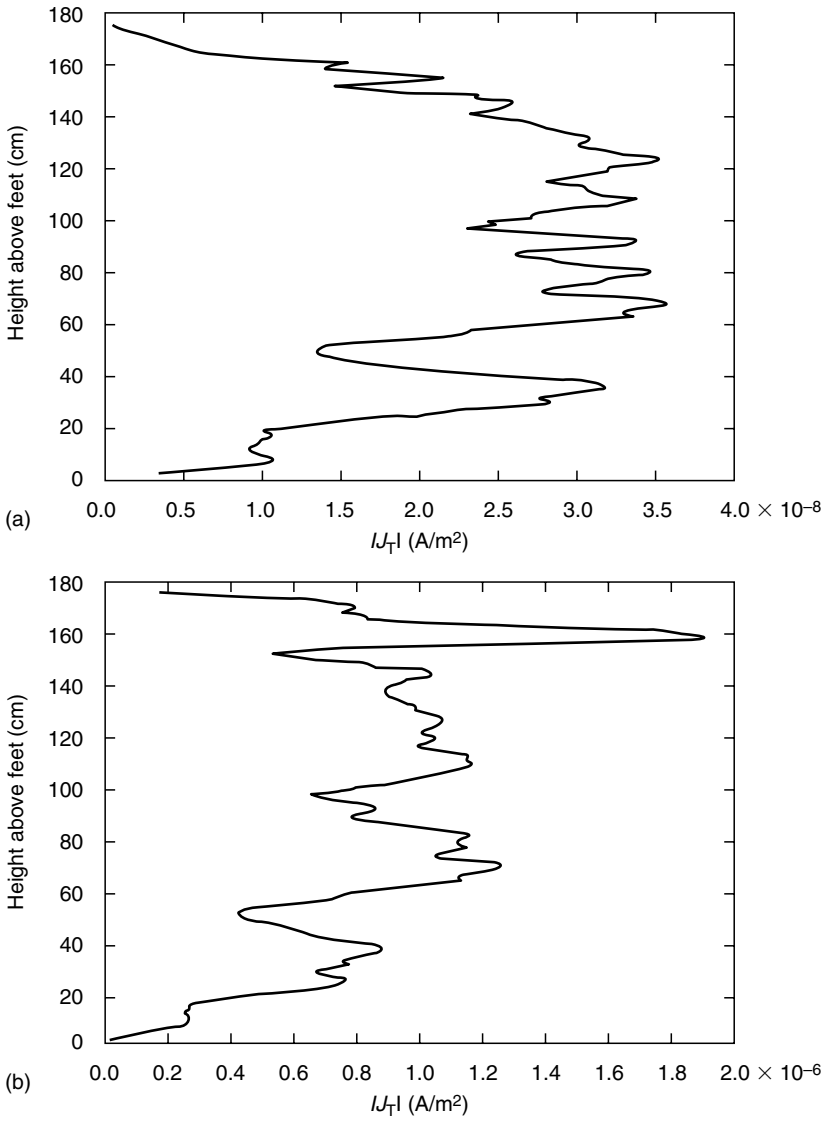


FIGURE 10.13
Section-averaged magnitudes of total current densities for the various sections of the body for magnetic fields of the blankets. Nearly identical current densities were obtained also for a grounding plate at distances of 0.25, 0.5, and 1.0 m underneath the body. Input current = 1 A.

note that the induced current densities are larger by a factor of about 500 for the conventional blanket vis-a-vis those for the low-magnetic-field blanket.

The calculated section-averaged magnitudes of the total current densities due to electric fields of both the blankets in the absence of a grounded plane are shown in Figure 10.14a and b, respectively. It should be noted that while the current densities induced by the electric fields of a low-magnetic-field blanket (Figure 10.14a) are considerably higher than those due to magnetic fields (Figure 10.25a), the converse is true for a conventional blanket. For this blanket, the current densities induced by the magnetic fields (Figure 10.13b) are higher than those due to electric fields (Figure 10.14b). In fact, while the current densities due to magnetic fields are fairly small for a low-magnetic-field blanket

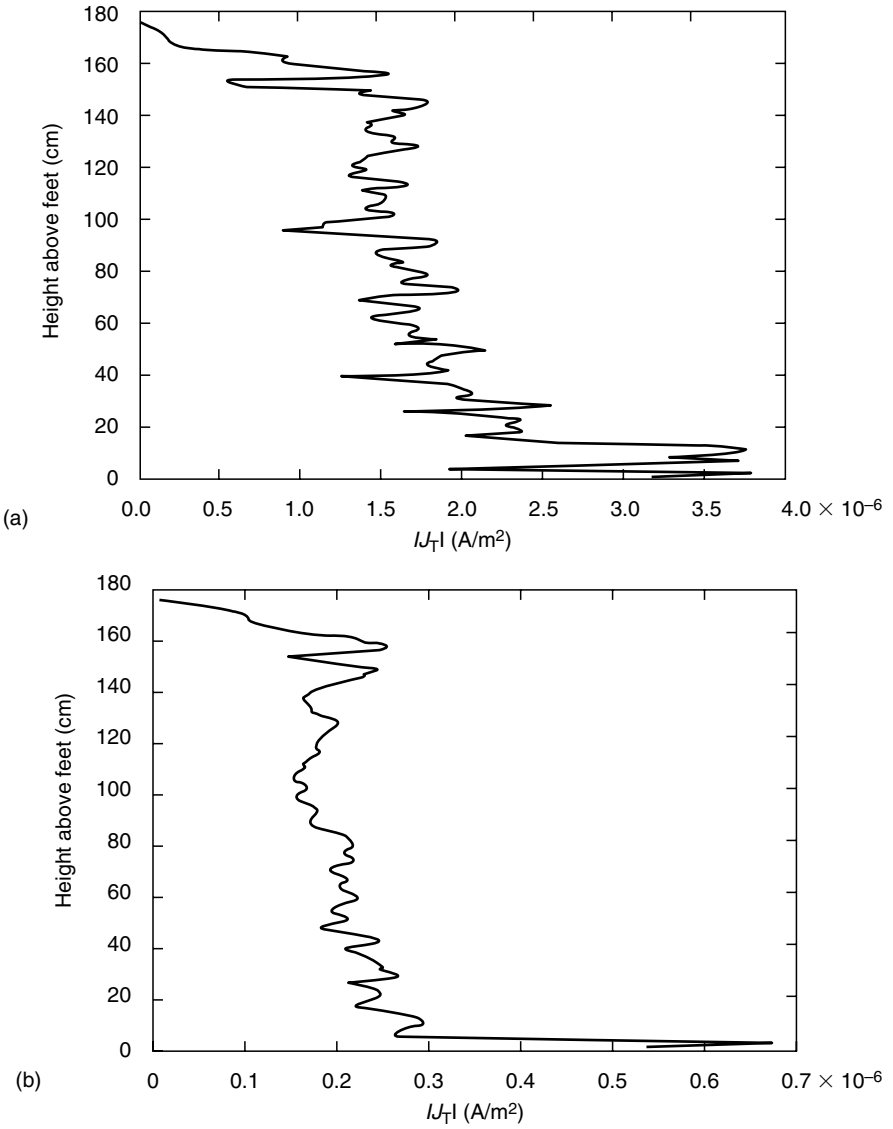


FIGURE 10.14
Section-averaged magnitudes of total current densities for the various sections of the body for electric fields of the blankets. No ground plane underneath the body.

as compared to those for a conventional blanket, the current densities due to electric fields of a low-magnetic-field blanket are even higher than those for a conventional blanket (see Figure 10.14a and b). The reasons for these observations can be seen from the values of magnetic and electric fields given in Table 10.4 for the two types of blankets, respectively. While fairly small magnetic fields are calculated for the low-magnetic-field blanket as compared to those for the conventional blanket, the converse is true for the electric fields created by these blankets. As seen in Table 10.5, somewhat higher electric fields are created by the low-magnetic-field blanket as compared to those for the conventional blanket. This is likely due to the higher potential difference between the twin-lead conductors that are used for the low-magnetic-field blankets.

TABLE 10.4

Comparison of the Calculated and Measured Magnetic Field (μT) and Electric Field (V/m) Close to a Flat Blanket [2]

	Grid Size (cm)	Calculated	Measured
Low-magnetic-field blanket[a]			
Magnetic field			
Average	1.31 × 1.31	0.056	—
	10.5 × 10.5	0.072	0.09
Peak	—	0.20	0.26
Electric field			
Average	1.31 × 1.31	103.7	—
	10.5 × 10.5	144.6	111.2
Peak	—	159.7	176.0
Conventional electric blanket[b]			
Magnetic field			
Average	1.31 × 1.31	2.16	—
	10.5 × 10.5	2.45	2.18
Peak	—	3.52	3.94
Electric field			
Average	1.31 × 1.31	57.3	—
	10.5 × 10.5	70.1	95.4
Peak	—	176.1	167.2

[a]For this blanket, the magnetic-field results are normalized for a blanket input current of 1.227 A, that is, a power input of 135 W.
[b]For this blanket, an input current of 1 A is assumed.

10.4.2.2.2 Power Transmission Lines

The FDTD method has been used for calculations of internal **E** and **H** fields and induced current densities for exposure to electric, magnetic, or combined electric and magnetic fields at power-line frequencies [37]. While recognizing that the conductivities of many biological tissues (skeletal muscle, bone, etc.) are highly anisotropic for power-line frequencies, however, the effect of anisotropy is neglected for the sake of simplicity. They could be included in more complex models by separately identifying these tissues.

Both sinusoidal and prescribed time-varying incident fields can be used with the FDTD procedure—hence the method is well suited also for transient exposures that are often of interest at power-line-related frequencies. For sinusoidally varying fields, the solution is completed when a sinusoidal steady-state behavior for **E** and **H** fields is observed for each of the cells. For lossy biological bodies this typically takes a time step on the order of three to four time periods of oscillation. Since Δt is fixed for a given cell size, a larger number of iterations are therefore needed at lower frequencies. Because of the large number of iterations, the FDTD procedure would be clearly inapplicable for calculations at power-line frequencies were it not for the quasi-static nature of the coupling at low-frequencies [16,88,89]. Thus, the field outside the body does not depend on the internal tissue properties, but it depends only on the shape of the body so long as the quasi-static approximation holds, that is, the size of the body is a factor of 10 or more smaller than the wavelength, and $| \sigma + j\omega\varepsilon | \gg \varepsilon_0$, where σ and ε are the conductivity and the permittivity of the tissues, respectively; $\omega = 2\pi f$ is the radian frequency; and ε_0 is the permittivity of the free space outside the body. Under these conditions, the electric fields in air are normal to the body surface, and the internal tissue electric fields can be obtained from the boundary conditions in terms of fields outside:

TABLE 10.5

Reported SAR Values, Averaged over the Whole Body (SAR_{WB}), for Plane Wave Exposures

	SAR (W/kg)					
Frequency (MHz)	Grounded Shoes [98]	Grounded [102]	Isolated [102]	Isolated (resolution 3 mm) [103]	Isolated (resolution 5 mm) [103]	Grounded [105]
10	0.027	0.045				
20	0.102	0.182	0.021			
30	0.180	0.313	0.054			
40	0.291	0.348	0.114			
50	0.230	0.293	0.199			
60	0.177	0.231	0.288			
70	0.152	0.188	0.302	0.270	0.290	
80	0.130	0.162	0.251			
90	0.107		0.195			
100	0.092	0.118	0.155			0.123[a]
200	0.062	0.081	0.080	0.048	0.051	0.078[b]
300	0.054					
400	0.060	0.063	0.063	0.064	0.060	
500	0.058					0.060
600	0.057		0.063	0.067	0.066	
700	0.059					
800	0.061			0.064	0.063	
900	0.061	0.062	0.064			
1000				0.063	0.061	0.057
1400			0.063			
1800		0.057	0.058	0.056	0.060	
2000				0.055	0.060	

[a]The frequency considered is 120 MHz.
[b]The frequency considered is 210 MHz.

$$j\omega\varepsilon_0 E_0 = (\sigma + j\omega\varepsilon)E_{\text{tissue}} \tag{10.19}$$

A higher quasi-static frequency f', at 5 to 20 MHz, may therefore be used for irradiation of the E model, and the internal fields E thus calculated may be scaled back to frequency f of interest, for example, 60 Hz. Since in the FDTD method, one needs to calculate in the time domain until convergence is obtained, this frequency scaling to 5 to 20 MHz for f reduces the required number of iterations by over five orders of magnitude. From Equation 10.19 we can write

$$\omega'(\sigma + j\omega\varepsilon)E_{\text{tissue}}(f) = \omega(\sigma' + j\omega\varepsilon')E'_{\text{tissue}}(f') \tag{10.20}$$

or

$$E_{\text{tissue}}(f) = (f\sigma'/f'\sigma)E'_{\text{tissue}}(f') \tag{10.21}$$

assuming that $\sigma + j\omega\varepsilon \sim \sigma'$ at both f' and f [2,90]. To validate the use of a higher frequency f to obtain induced E fields at ELF frequencies, test cases involving homogenous and layered spheres have been used. Excellent agreement between the numerical and analytical results lends support to the validity of the FDTD method for calculating internal E fields and current densities at power-line-related frequencies. It should be noted that incident E and H fields of any orientation and relative magnitudes can be prescribed in the FDTD method, allowing the possibility of calculations for realistic

exposure conditions. Also, the choice of a considerably higher frequency such as 5 to 20 MHz reduces the number of iterations needed to obtain converged results by five to six orders of magnitude as compared to those that would be needed at ELF frequencies of 10 Hz to 1 kHz.

Some calculated results using a 16-tissue, 1.31-cm resolution, anatomically based model of the human body are given in Figure 10.15. A frequency f' of 5 to 10 MHz was used to reduce the computation time. At the higher irradiation frequency f', $\sigma' = \sigma$ was assumed, that is, conductivities of the various tissues at 60 Hz. Furthermore, the incident **E** field, $\mathbf{E}_i(f') = 60\mathbf{E}_i(f)/f'$, was used to obtain $\mathbf{E}_{\text{tissue}}(f)$ at, say, $\mathbf{E}_i(f) = 10\,\text{kV/m}$. The incident magnetic field $\mathbf{H}_i(f')$ has similarly been taken to be considerably lower ($= 60\mathbf{H}_i(f)/f'$) to account for the fact that the induced current densities and internal electric fields are proportional to the frequency of the incident fields and would therefore be higher at the assumed frequency f'. Recognizing the anisotropy in the conductivity of skeletal muscles, two different values of muscle conductivities are taken for curves (1) and (2). For these curves a higher conductivity of 0.52 S/m is taken for the skeletal muscle, and an average value of 0.11 S/m is taken for the muscle in the interior of the body. For curves (3) and (4), however, a lower conductivity of 0.11 S/m is taken for all of the muscle, interior or skeletal. The results shown in Figure 10.15, curves (1), (3), and (4) are for $E_{\text{inc}} = 10\,\text{kV/m}$ (vertical) and $H_{\text{inc}} = 26.5\,\text{A/m}$ ($B_{\text{inc}} = 33.3\,\mu\text{T}$) from side to side of the model. To point out the preponderance of the induced currents due to incident electric field, $H_{\text{inc}} = 0$ is assumed for the calculations shown in curve (2). It is interesting to note that the layer currents due to *E*-field exposure alone are almost 98% to 99% of the currents calculated for the combined electric and magnetic fields. It is also interesting to note that the calculated foot currents of 155 to 160 μA are in excellent agreement with 165 μA that would be projected from the measurements of Deno [91] for the human body. The variations of the induced currents calculated along the height of the body have been checked against the results by DiPlacido et al. [92]. The agreement with the results of these two authors who had

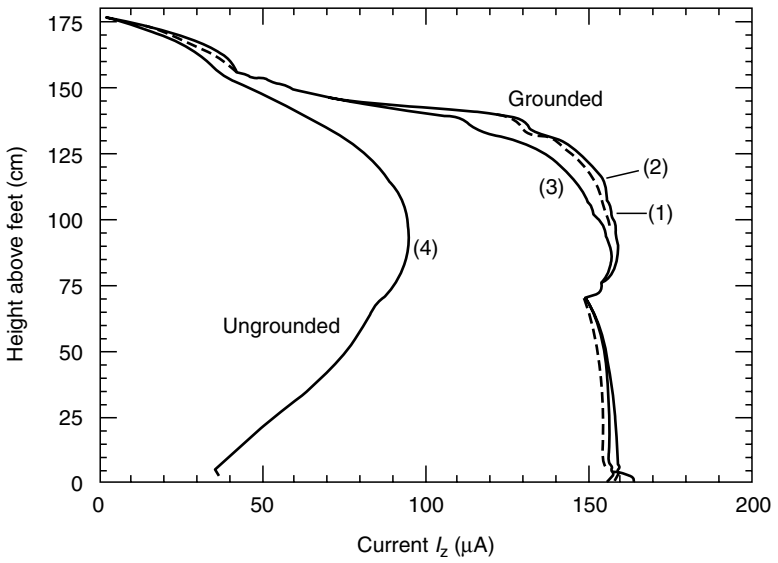


FIGURE 10.15
Calculated layer currents for anatomically based grounded and ungrounded models exposed to EMFs at 60 Hz. For curves (1) and (2), $s = 0.52\,\text{S/m}$ for skeletal muscle, and $s = 0.11\,\text{S/m}$ for the interior muscle. For curves (3) and (4), $s = 0.11\,\text{S/m}$ for all of the muscle. $E = 10\,\text{kV/m}$ (vertical), $H = 26.5\,\text{A/m}$ from side to side for all of the curves except for curve (2), for which only **E**-field exposure is assumed.

used a vertical electric field such as that under a high-voltage power line was found to be very good [37].

10.4.2.3 Absorption in Human Bodies Exposed to Far Field of RF Sources

As noted, the configuration and frequency of the electromagnetic source and the geometry and composition of the biological body will influence the induced field and power absorption and distribution inside the body. Moreover, the field emitted from a source is dictated by the frequency, size, and configuration of the source. Near an antenna, the radiated energy is in the form of a spherical wave in which the wave fronts are concentric shells. The spheroidal wave front expands as the wave propagates outward from the source. At distances far from the source, the radius of curvature of the spherical shells becomes so large that the wave front would essentially appear as a plane. They are therefore referred to as plane waves. Plane waves are important since their behavior is well quantified; the fields are uniform in planes normal to the direction of propagation, and the power density varies only in the direction of propagation. In this case, both electric and magnetic fields of the propagating wave are orthogonal in space and lie in the plane of the wave front, and are related through the intrinsic impedance of the medium. In other words, in the far or radiation zone, the electric and magnetic fields have only transverse components.

In this section, we shall briefly summarize some of the efforts devoted to field computation using various models of the human body, which consists of large quantities of numerical cells, and present some results obtained for plane wave exposures. Note that some, especially the simpler, models are of interest primarily for whole-body SAR and can provide quite adequate results for frequencies lower than 30 MHz. To achieve more accurate structural representation of the human body, anatomically based models are needed.

10.4.2.3.1 SAR Induced in Cubic-Cell Models

The VMoM for field computation has been used for models of the human body consisting of 200 to 1000 cubic cells. These models account for the gross anatomic and biometric characteristics of human bodies and have been used by several investigators [24–28]. The models are 1.75 m tall and can be made either homogenous or inhomogenous by choosing an equivalent or a volume-weighted complex permittivity for each cell. The cubic-cell model has been employed, successfully, to calculate whole-body averaged absorption. It is important to note that for subdivision with less than three cells per wavelength, the magnitude and phase resolutions would be such that even with convergence the reliability of the MoM computed SAR would be questionable.

According to the MoM, the body may be partitioned into N cubic subvolumes or cells that are sufficiently small for the electric field and dielectric permittivity to be constant within each cell. The integral equation is then transformed into a system of $3N$ simultaneous linear equations for the three orthogonal components of the electric field at the center of each cell. The simultaneous equations may be written in matrix form as

$$[G][E] = -[E^i] \tag{10.22}$$

where $[G]$ is a $3N \times 3N$ matrix and $[E^i]$ and $[E]$ are column matrices representing incident and induced electric fields at the center of each cell. The elements of $[G]$ can be evaluated as shown in Liversy and Chen [24]. In particular, the diagonal elements of the $[G]$ matrix may be evaluated exactly by approximating each subvolume with a sphere of equal volume centered at the position of an interior point. If the actual shape of the cell differs

appreciably from that of a sphere, this approximation may lead to unsatisfactory numerical results [36]. In such cases, a small cylindrical volume may be created around an interior point. It may also be necessary to evaluate these terms by numerical integration throughout the cubic subvolume for increased accuracy. The evaluation of off-diagonal elements of the [G] matrix is considerably simplified since it does not involve principal value operations. Therefore, for a given applied field configuration, the induced electric fields inside the body are obtained by matrix inversion. That is,

$$[E] - [G]^{-1}[E^i] \tag{10.23}$$

Factors that influence the computational accuracy include frequency, body size, cell dimensions, and computer memory. It has been found that reliable numerical results can be obtained if the linear dimensions of the cell do not exceed a quarter free-space wavelength [24]. For a computer with sufficient capacity to invert a 120 $\times$ 120 matrix, the maximum number of cells is limited to 40. If we assume, for simplicity, symmetries between the right and the left half and the front and the back of a 1.7-m-tall adult human body, this computer would handle approximately a cell size around 10^{-5} m^3. Once the 10^{-5}-m^3 cell size is adopted, 750 MHz would be the highest frequency that can be considered for field intensity calculation without violating the criterion that the linear dimension of the cell not exceed a quarter free-space wavelength.

The computational resources necessary to obtain even a regional SAR using this MoM approach are quite extensive. A relatively full complex matrix, $3N \times 3N$ in dimensions, is required for a model with N cells. The computation time required for a noniterative solution of the matrix equation is therefore proportional to a value between N^2 and N^3, which increases rapidly as N increases. The faithfulness with which a cubic-cell model approximates the detailed structure of a biological body and the maximum usable frequency increases with the number of cells. In fact, substantial errors will occur if

$$N \leq (2\pi L)/(\lambda' 6^{1/2}) \tag{10.24}$$

where L/λ' is the ratio between the linear dimension of the body and the wavelength in the body.

The accuracy of the numerical method can be verified by comparison with known results from exact analytic solutions based on well-characterized geometric bodies, such as spheres. It should be noted that perfect agreement between the exact solution, based on Mie theory, and the numerical method, based on the volume integral equation, is not expected unless a large number of cubic cells are used to simulate the sphere. Figure 10.16 shows one eighth of a sphere approximated by one eighth of a ''cubic model of a sphere,'' which is constructed from 73 cubic cells. Clearly, a better approximation can be achieved by a larger number of smaller cubic cells. Nevertheless, for a brain sphere constructed from 40 cubic cells at a frequency of 918 MHz, the computed maximum field intensity deviated from the exact solution by less than 9% [93].

A model of a human body consisting of 180 cubic cells that accounts for the anatomic and biometric characteristics of human beings is shown in Figure 10.17. The model is 1.75 m tall and can be made either homogenous or inhomogenous by using an equivalent or a volume-weighted complex permittivity for each cell [94]. The average absorption or whole-body SAR for the model of the human body shown in Figure 10.17 as a function of frequency is illustrated in Figure 10.18. The electric field vector is along the height of the body, and the plane wave propagates from front to back of the model with an incident power density of 10 W/m^2. A homogenous complex permittivity approximately two thirds of that for muscle is used in the calculations. Note that the whole-body SAR

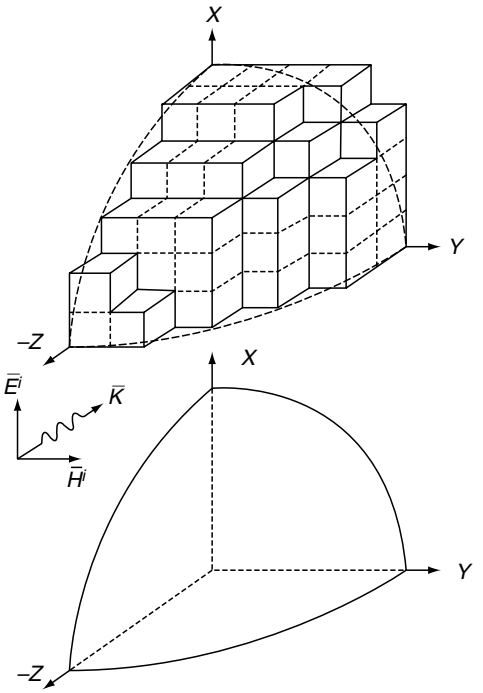


FIGURE 10.16
Approximation of one eighth of a sphere by an equivalent cubic-cell-formed structure.

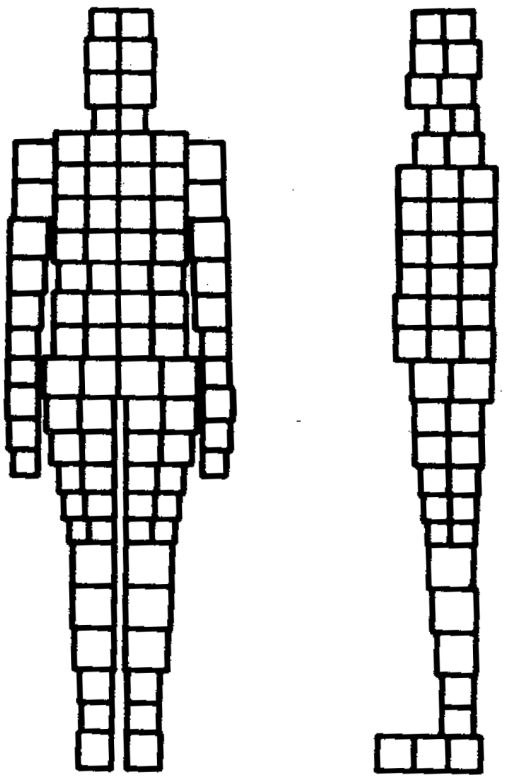


FIGURE 10.17
A cubic-cell representation of the human body.

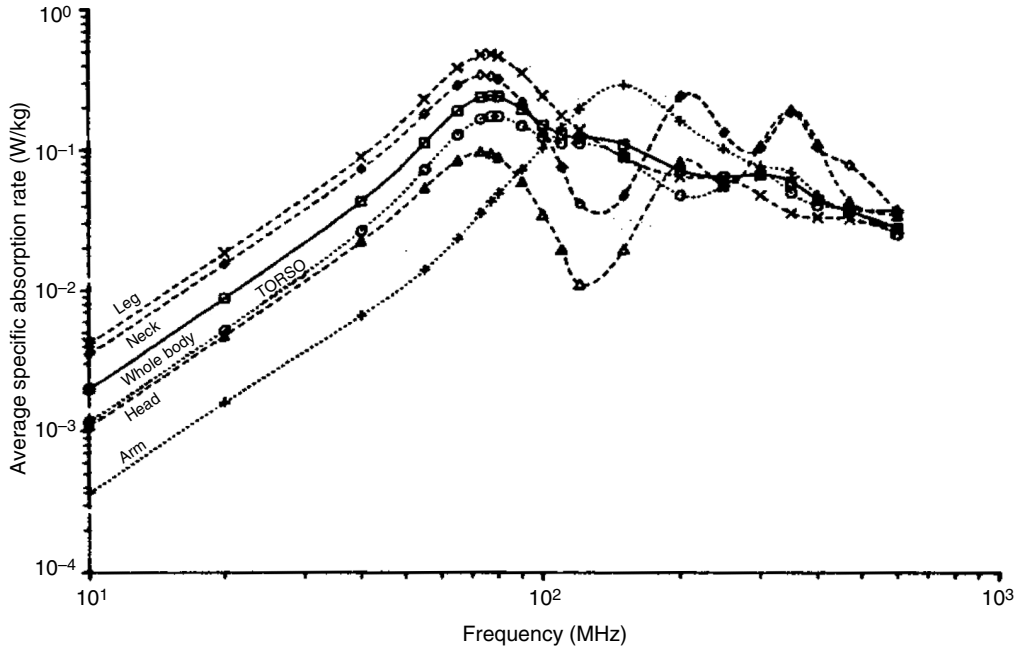


FIGURE 10.18
Average SARs for a homogenous 180-cell model of the human body exposed to a vertically polarized, 80-MHz plane wave. The incident power density is 10 W/m^2.

increases with frequency until it reaches a maximum of about 0.23 W/kg at 77 MHz (resonance frequency), and it then decreases as 1/frequency. The experimental data shown in Figure 10.19 are obtained from a saline-filled scale model of the human body. It can be seen that the calculated absorption is in good agreement with that found experimentally [27,95], except for the resonant frequency, which is somewhat lower (70 MHz) in the experimental case. It should be mentioned that whole-body SAR, given in Figure 10.18, is typically within 10% of that estimated from prolate spheroidal models of the same height and dielectric property. Further, when inhomogenous complex permittivities are used with the model, the whole-body SAR changes less than 2% from that depicted in Figure 10.18. Thus, if one is primarily concerned with average absorption over the body, a homogenous prolate spheroidal model may be quite adequate.

While the MoM based on the volume integral equation has been a useful numerical procedure for computation of average SAR and SAR distribution in complex tissue geometries, the requirement of a full $3N \times 3N$ matrix presents severe limitations. The computation times required to provide even regional SAR distribution of sufficient resolution to delineate the resonant frequency for the head region are enormous. A minimum of 340 cells was needed, increasing the computation time by a factor of 4 over the 180-cell models [95,96].

Matrix inversion operations consume the largest block of time in moment method solutions for the cubic-cell models. The computer time required is proportional to the cube of the number of cells. However, the matrix generated is usually diagonally dominant and well-conditioned. For a human-size body, iterative procedures for matrix inversion are practical at frequencies below about 60 MHz. The convergence rate decreases with increasing frequency and fails above 90 MHz. This is most likely caused by the decrease in the degree of diagonal dominance with increasing frequency. A number of approaches have been investigated to alleviate this difficulty. A semi-iterative procedure

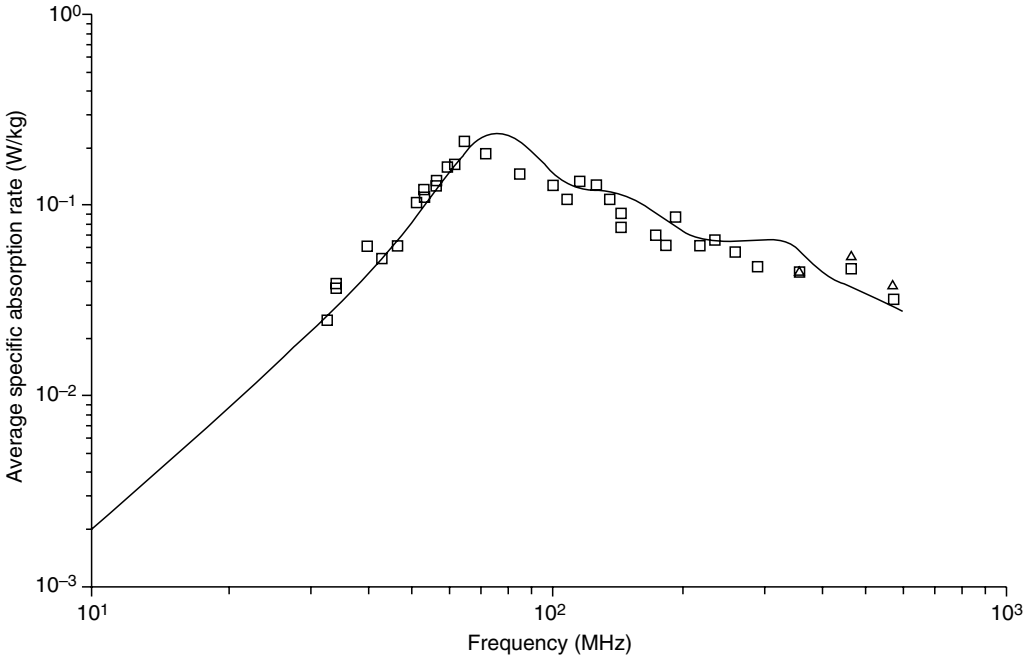


FIGURE 10.19
Whole-body averaged absorption for a homogenous cubic-cell model of humans exposed to vertically polarized plane in free space. The incident power density is 10 W/m^2.

called band approximation method appears to be an efficient algorithm that can be profitably used to invert large matrices generated by the number of cells for human models at arbitrarily high frequencies, and converges significantly faster than standard iterative algorithms [96].

10.4.2.3.2 SAR Induced in Fine Resolution Anatomical Models

To accurately evaluate the SAR induced in the human body, the FDTD method was introduced during the late 1980s, when the limitations of the MoM due to its memory requirements were reached. The capability of FDTD to take into account heterogeneities in models of the human body was first demonstrated using a model of the isolated human torso [69]. Later, a complete model of the human body was considered [97], and results for an isolated homogenous man model standing in free space were compared with results for an inhomogenous man model, under both isolated and grounded conditions [97]. The incident field was a plane wave propagating parallel to the ground plane and with the electric field vertically polarized (parallel to the long axis of the human body), at frequencies of 100 and 350 MHz. The human body model was obtained from cross-sectional diagrams and had a resolution of 2.62 cm at 100 MHz. The total occupied volume was $23 \times 12 \times 68$ cubic cells. At 350 MHz, the resolution was 1.31 cm for a total volume of $45 \times 24 \times 135$ cubic cells. The result, depicted as layer-averaged SAR or organ-averaged SAR, demonstrated the importance of considering inhomogenous models of the human body. For example, the homogenous model was not able to predict the peak SAR obtained in the eyes at 350 MHz, or the difference in absorption among the different organs.

Since these first works on power absorption, several papers have been published using anatomical models of the human body with finer resolutions.

The VH body model has been used to evaluate power absorption and temperature increase as a function of frequency of the incident plane wave, by considering a grounded male, either barefoot or with shoes [98]. The model had a resolution of 5 mm, a total height of 180 cm, and weight of about 103 kg. The large mass was due to the use of the VH model, which is far from the so-called ''reference man,'' as defined by International Commission on Radiological Protection (ICRP). The reference man weighs 73 kg and has a height of 176 cm [99]. In the referenced paper [98], for the frequency range between 10 and 900 MHz, SARs averaged over the whole body (SAR_{WB}) and locally, that is, averaged over 1.0 g (SAR_{1g}) and 10 g (SAR_{10g}), were evaluated. In particular, it has been found [98] that when the incident power density is equal to the reference levels set in the exposure standards, the basic restrictions on SAR_{WB} and on local SARs are never exceeded. Moreover, it has been shown [98] that the ratio, SAR_{10g}/SAR_{WB} was about the same (either 25 or 50 according to the body part considered) as the value used in the safety guidelines to convert basic restrictions on SAR_{WB} to basic restriction on local peak SAR [100]. On the other hand, the SAR_{1g}/SAR_{WB} ratio was found to be always higher than the value of 20 adopted in the safety guideline [101].

Figure 10.20 gives the SAR_{WB} as a function of frequency in a grounded male for an incident plane wave with a power density of 10 W/m^2 for two different human body models [98,102]. The SARs are slightly different because the two body models were different in height, weight, and tissue composition. The influence of the human body model on electromagnetic power absorption is further illustrated in Figure 10.21, where a comparison among the SAR_{WB} values obtained with the heterogenous VH model and a homogenous VH model consisting either of muscle or fat is reported. The frequencies considered are from 10 to 200 MHz to highlight the differences in power absorption at resonance.

It can be seen from the figures that a higher peak appeared at resonance in the homogenous muscle model, and lower absorptions were obtained in the homogenous fat model. Moreover, data from a lighter model (65.8 kg) obtained by reducing the cell dimension on the horizontal plane suggested that the lighter body absorbed more elec-

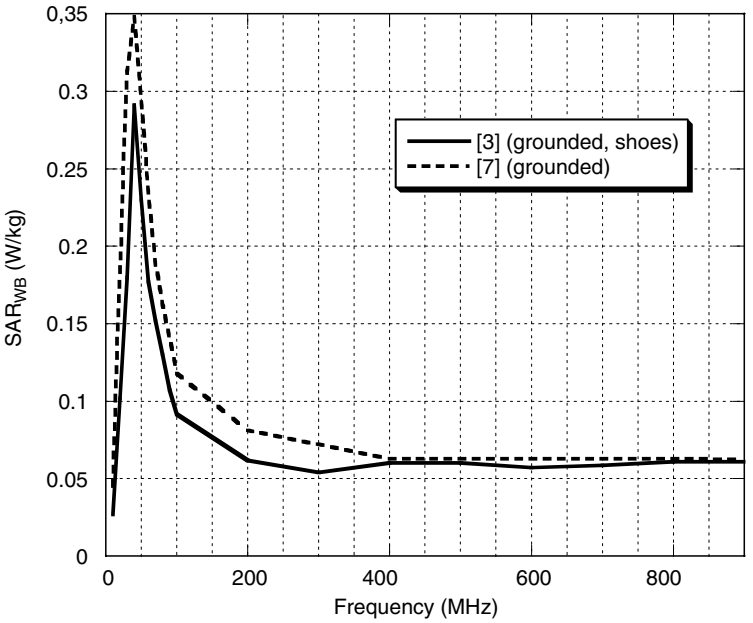


FIGURE 10.20
SAR as averaged over the whole body as a function of the frequency.

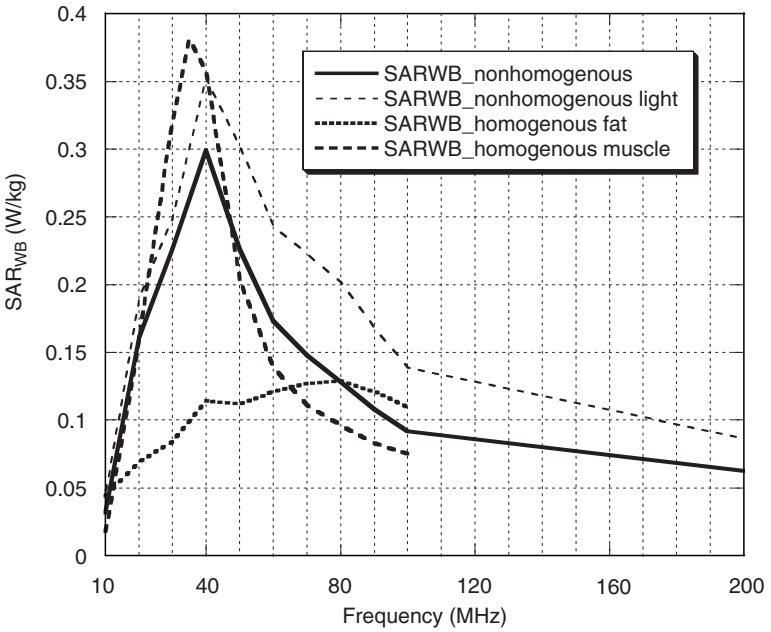


FIGURE 10.21
SAR as averaged over the whole body as a function of the frequency for different VH body models: nonhomogenous, nonhomogenous with a lighter weight (65.8 vs. 103 kg), homogenous fat, and homogenous muscle.

tromagnetic power than the heavier one. The frequency dependence of power absorption is clearly evidenced by Figure 10.20 and Figure 10.21. Indeed, this frequency dependence was the basis of the different limits imposed on the reference levels for different frequencies in the safety guidelines [100,101].

In Table 10.5 some literature data are summarized for the SAR_{WB} as a function of frequency (10 MHz to 2 GHz) for a grounded and isolated man model exposed to an incident power density of 1.0 mW/cm^2.

The first two columns refer to data in Figure 10.20, while the successive columns report data from published literature. Note the resonant frequencies of 40 vs. 70 MHz for grounded or isolated bodies. Moreover, the data in Table 10.5 show nonsignificant differences in SAR averaged over the whole body by changing the model resolution from 3 to 5 mm [103]. For the same reason the cubic-cell model described in the previous section had been employed, successfully, to calculate whole-body averaged absorption. The SAR_{WB} has a weak dependence on model resolution.

Likewise, a study on the SAR dependence on permittivity values [104] showed that uncertainty in permittivity values does not substantially affect the SAR as averaged over the whole body, while the same uncertainties have a greater effect on local SAR. In particular, considerations of different frequencies and orientations of the incident plane wave, or higher or lower permittivity values, showed that the maximum difference in SAR_{WB} was within $\pm 20\%$ [103]. Larger differences were found in local SAR, particularly when the permittivity of muscle, representing about 42% of the whole-body mass, was changed [103].

The data in the last column of Table 10.5 were obtained from a human body model [105] that was developed by using a new, semiautomatic procedure to construct numerically a frequency-dependent, dielectric anatomy model, starting from MRI images. The main difference between this human body model and the models usually considered in FDTD calculations is that in this model permittivity and conductivity can vary, even for the

same tissue, thus reflecting the realistic spatial inhomogeneity of such parameters. The semiautomatic procedure requires a short time to construct the model; thus, it could be used for dosimetry studies based on the model of specific persons.

A high-resolution human body model ($1.974 \times 1.974 \times 3.0$ mm) and a coarser one ($5.922 \times 5.922 \times 6.0$ mm), both for isolated and grounded conditions, were employed to determine the power absorption in the head and neck region and to evaluate the frequencies at which the absorption may be maximized [106]. It was observed that under isolated conditions two resonant frequencies occurred for the head and neck, one associated with the whole-body resonance and the other with a local resonance of the head and neck. Under grounded conditions, three resonances were observed; the additional resonance was attributed to a torso resonance.

Some studies were conducted to evaluate power absorption in models of women and children. Specifically, a 10-year-old child and a 5-year-old child were considered by scaling the adult human body model [106]. It should be noted that simply scaling the adult human body model to the children's dimensions does not produce an accurate model since the different organs scale differently; however, the general features in terms of height and weight are fulfilled, thus allowing for the determination of general properties of electromagnetic power absorption. In this way, resonant frequencies of 104 MHz for the isolated model and 65 MHz for the grounded 10-year-old child were obtained, while for the 5-year-old model, they were 126 and 73 MHz, respectively.

In a different study, power absorption in scaled versions of the adult human body model representing 10-, 5-, and 1-year-old children was evaluated for both grounded and isolated conditions [102]. Figure 10.22 gives the SAR_{WB} obtained for the three child models under isolated conditions and an incident power density of $1\,mW/cm^2$. A shift in the resonant frequency with the height of the model—the taller the model, the lower

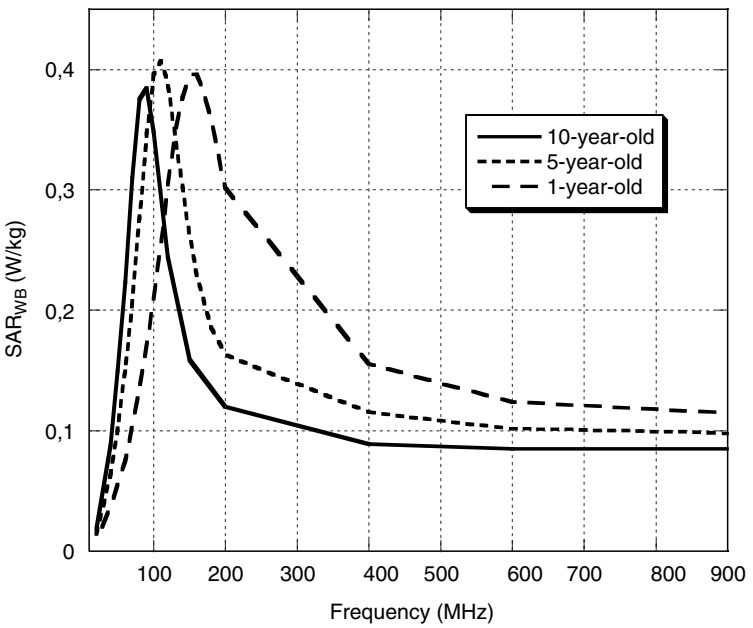


FIGURE 10.22
SAR as averaged over the whole body as a function of the frequency for different child body models: 10, 5, and 1 year old. Incident power: $1\,mW/cm^2$. (Data from Dimbylow, P.J., *Phys. Med. Biol.*, 47, 2835, 2002.)

the resonance frequency—can be observed from the figure; note also the higher absorption in the smaller child body model [102].

The potential differences between SAR induced in man and woman have been explored using slightly different models [107,108]. In one study, 2-mm resolution models were developed for evaluating power absorption in Japanese males and females. Note that the use of the 2-mm resolution body models had led to an overestimation of the skin weight by 50% or more than the average value for the Japanese reference body [107]. The computed results showed that the difference in SAR_{WB} between male and female models was small, within 1.1 dB. The authors concluded that gender does not affect SAR_{WB}. Similarly, they obtained no significant differences between the male and female models with regard to local SARs. However, the overestimation of skin weight, and perhaps other tissues, in the 2-mm resolution body models could have influenced their results and conclusions.

In contrast, a clear difference in power absorption was reported [108] between Caucasian male and female models. The two Caucasian body models were developed using the semiautomated procedure previously cited [105]. In particular, considerably greater SAR_{WB} was obtained in the female model than in the male one (about 40% higher in the frequency range between 500 MHz and 2.0 GHz and 25% higher in the frequency range between 2.0 and 4.0 GHz). The difference in local SARs (both SAR_{1g} and SAR_{10g}) were insignificant between genders for up to 3.0 GHz, while above this frequency, say up to 4 GHz, the SAR_{1g} and SAR_{10g} in the female model became larger than those in the male model. The authors observed that this result could be explained by the difference in subcutaneous fat between man and woman. It was noted that a better identification and modeling of the skin layer could influence the results. Clearly, further studies are needed to assess the similarities and differences in power absorption between male and female body models exposed to EMFs of radiating sources.

In summary, available data on electromagnetic power absorption in human body models exposed to plane wave fields show that the choice of the human body model affects the results obtained. The observed differences among the published data are usually more pronounced in local SARs than in SARs averaged over the whole body. The body height, mass, tissue distribution and composition, including fat and muscle, are important factors in power absorption and can explain some differences among the published data. Another fundamental aspect is the value assigned to the dielectric properties of different tissues or organs identified in the body model. In the case of children, the variation in tissue dielectric properties with age also may influence the computed results. It is noteworthy that the above publications have used dielectric properties from the same sources [109,110].

10.4.2.4 Human Exposure to the Field Radiated by Transceiver Base-Station Antennas

The enormous growth in the number of subscribers of mobile telecommunication systems during the past few years has pushed upward the system's capacity. As a result, more and more base stations have been installed on the rooftop of existing buildings in densely populated areas, and many more are expected to be set up as the next-generation mobile networks (UMTS, IMT2000, etc.) are deployed. These installations are giving rise to widespread concerns among the population about possible deleterious effects on human health from exposure to the EMFs radiated by the base-station antennas. Recently, increasing attention has been paid to the topic of numerical exposure and compliance assessment for base-station installations.

A great deal of work has been done in the area of field intensity prediction in the vicinity of base-station antennas to determine the so-called free-space compliance boundary. The studies were aimed toward a direct comparison with reference levels suggested

by international exposure guidelines [100,101]. They generally have neglected both the influence of the environment in which the antennas operate and the dosimetric problem of SAR evaluation inside an exposed subject. In particular, considerable efforts have been spent on determining simplified and efficient analytical [111,112] and numerical [113,114] models to evaluate field levels near base-station antennas. Starting from the theory of collinear dipole arrays, typically employed in base transceiver station (BTS) antennas, practical analytical formulas have been derived to predict average power density falloff as a function of distance from the antenna. The space surrounding the antenna is often divided into a cylindrical-wave region, closest to the antenna, and a spherical-wave region, further away [111]. A complementary formulation also has been proposed, on the basis of an exact asymptotic solution for the radiated field, to derive approximate analytical formulas that allow a conservative prediction of equivalent peak power density as a function of the distance from the antenna [112].

Besides the aforementioned practical analytical formulations, simplified numerical models are often used, by subdividing the antenna into elementary radiators [113,114]. Under the hypothesis of weak coupling between the subelements, the near field can be quickly computed through a superposition of the fields independently radiated by the different elements. Once the radiation pattern of the subelements is known, the field is derived using the antenna gain-based formula [113,114]. For better accuracies in the vicinity of the antenna, an MoM simulation of the subelement can be invoked [114]. These simplified approaches represent extremely fast tools for field intensity prediction, but they are limited by a minimum distance from the antenna where they can be applied in order to maintain an acceptable computational accuracy. On the other hand, when field computations within a distance of a few wavelengths from the antenna have to be done, full-wave numerical techniques, such as FDTD, must be adopted. The accuracy of FDTD models for evaluating the near field of base-station antennas has been investigated and validated through a comparison with measurements carried out in a fully anechoic chamber [115].

Full-wave approaches require knowledge of the internal structure of the antenna, which is not always available. Cylindrical- and spherical-wave expansion techniques have been proposed to evaluate the near field, starting from measurements performed on a surface enclosing the antenna [116–118]. The basic approach consists of performing field measurements on a spherical surface surrounding the antenna and describing the measured field as a superposition of spherical modes [115]. Once the spherical-wave expansion coefficients have been determined, the near field can be extrapolated for all points lying outside the minimum sphere enclosing the antenna. This technique also has been improved to allow extrapolation of the field inside the minimum sphere [117]. To this end, the spherical-wave expansion coefficients are derived for each of the antenna subelements. This approach extends the range of applicability of the formulation to all points outside the minimum sphere of a single subelement, which is much closer to the antenna than the minimum sphere of the overall array. Recently, an alternative solution to extend field extrapolation close to the antenna was proposed, which consists of spherical-wave expansion outside the minimum sphere of the antenna and cylindrical-wave expansion for the region close to the antenna, with an appropriate matching of the two expansions [118].

The effect of the surrounding environment must be taken into account to some extent in dealing with the problem of evaluating induced SAR in a subject exposed to the field radiated by BTS antennas, since the antenna is not operating in a free-space condition. A very interesting approach, applicable to on-site evaluations, consists of using mixed experimental and numerical procedures [119–121]. One procedure is based on on-site measurement of the amplitude and phase of the exposure field distribution over a surface

surrounding the antenna. The measurement is then used to numerically evaluate induced SAR distributions inside a phantom. The measured fields are used to excite the FDTD domain via the equivalence principle [119]. A much faster and efficient procedure uses previously stored FDTD-computed **E**-field distributions inside a phantom exposed to spatially impulsive electric fields, the equivalent spatial impulsive responses of the phantom or Green's functions. The on-site measurement of amplitude and phase of the exposure field is made over an equally spaced grid of points placed on an appropriately chosen surface [120]. The procedure has recently been enhanced and made faster by substituting the spatial impulse response with responses to spatial harmonic components [121]. In this way, good accuracy is achieved using only six to ten spatial harmonic components, as opposed to the 54 spatial impulse responses needed previously.

The aforementioned hybrid experimental–numerical procedures have the great advantage of allowing easy characterization of environmental perturbations to the exposure field by directly including them in the measured field. On the other hand, they require the antenna to be already installed and operating at the time of measurement. The last point makes such procedures not suitable for *a priori* compliance assessment evaluations during the planning stage of a cellular network. For such evaluations, a thorough numerical dosimetric analysis is required. Once again, a possible approach, when the environment can be neglected and the antenna can be supposed to operate under free-space conditions, consists of performing full-wave FDTD simulations and modeling both the BTS antenna and a numerical phantom of the exposed subject. The applicability of such an approach has also been demonstrated, through a comparison with SAR measurements, for exposure locations in close proximity to the antenna [122]. The main drawback of full-wave FDTD analysis is the large amount of memory required to discretize the simulation space for phantom locations not in the close proximity of the antenna. This problem can be faced by exploiting parallel computer architectures with parallelized versions of the FDTD code [123]. Parallel FDTD also has the potential to allow SAR computations for large antenna–phantom distances.

More efficient techniques have been developed that combine two different techniques, one to model BTS antenna and propagation in free space and the other, SAR inside the phantom [124,125]. In particular, if the antenna–phantom distance is such that mutual coupling can be neglected, a hybrid ray-tracing (RT)–FDTD approach can be used [124]. RT is used to model field propagation from the BTS antenna to an equivalent surface surrounding the phantom, and FDTD is employed to study absorption inside the phantom, using RT-derived exposure fields for excitation. For closer antenna–phantom distances, where the mutual coupling cannot be neglected, a hybrid FEM–MoM technique has been proposed [125]. In this case, MoM is used to model the BTS antenna, while FEM is used to study absorption inside the phantom. The MoM and FEM formulations are coupled together and are solved iteratively. These hybrid approaches allow very efficient SAR computation for different antenna–phantom distances and are well suited for evaluating free-space compliance distances, on the basis of SAR restrictions. They do not require the use of derived exposure field reference levels. For example, the RT–FDTD technique has been applied to a common 14-dBi-gain GSM900 antenna using the VH phantom. It was shown that for a total radiated power of 30 W, typical for urban area installations, SAR basic restrictions for the general population may be exceeded at distances of 2 m or less. Note that, at these distances, only occupational personnel are allowed [124].

The RT–FDTD hybrid technique also has been successfully employed to study human exposure to the field radiated by a BTS antenna in an urban scenario, including the effect of environmental perturbations to the exposure field [126]. In this case, image sources have been introduced to represent corner-reflector-like urban scenarios. Three different exposure conditions have been considered for a rooftop-mounted 14-dBi-gain BTS

TABLE 10.6

Spatial Maximum (E_{iMAX}) and Spatial Average (E_{iAVE}) of the Incident Field (rms Value); Maximum SAR Values Averaged over 1 g (SAR_{1g}) and over 10 g (SAR_{10g}), and SAR Value Averaged over the Whole Body (SAR_{WB}) for Three Exposure Conditions

	E_{iMAX} (V/m)	E_{iAVE} (V/m)	SAR_{1g} (mW/kg)	SAR_{10g} (mW/kg)	SAR_{WB} (mW/kg)
Rooftop	4.2	2.8	5.3	3.0	0.12
Balcony	8.1	5.5	13.2	8.5	0.46
Street	1.3	1.1	0.26	0.17	0.01

antenna, radiating 30 W in the GSM900 frequency band: (1) a subject standing on the rooftop, near the antenna mast; (2) a subject standing on a balcony of a building facing the antenna at a distance of 30 m, within the antenna main beam; and (3) a subject standing in the street below the 30-m tall building on which the BTS antenna was mounted. The computed results for the incident electric field and SARs, under these exposure conditions, are given in Table 10.6.

From Table 10.6, because of the high directivity over the vertical plane of base-station antennas, it appears that the highest field levels are not obtained on the rooftop of the building where the antenna is located. Instead, they are on the nearby building, in the direction of the maximum antenna radiation. As expected, the lowest field levels are experienced by a subject standing in the street, as a result of the large distance from the antenna and the off-axis position with respect to the antenna pointing direction. In all cases, the computed SARs are at least two orders of magnitude lower than the basic restrictions, confirming the expected low exposure levels for people living near a BTS installation in urban areas.

More recently, some hybrid techniques have been developed, with enhanced capabilities in modeling complex urban environments, by taking into account diffraction phenomena [127–129]. One such technique uses FEM to model the BTS antenna, the uniform theory of diffraction (UTD) to model the effects of the environment on field propagation, and FDTD to study power absorption in the exposed subject [127]. The technique has been employed to study exposure of a subject standing inside a room with a microcell BTS antenna mounted on the external wall. Another possible hybrid solution exploits time domain physical optics, instead of UTD, to model field scattering from the environment and FDTD to study absorption inside the exposed subject [128].

Finally, a hybrid UTD–FDTD technique has been developed to highlight some key points related to compliance assessment procedures for cellular base-station antennas, in a realistic urban environment [129]. The scenario analyzed consists of a room in one building where the field, radiated by a GSM900 or a UMTS BTS antenna installed on a facing building, penetrates through the room's external wall and window. The relation between SAR in an exposed subject and ambient field in the absence of the subject has been investigated for the complex scenario. As expected, the ambient field showed a highly nonuniform distribution resulting from the many reflections and diffractions that took place. The results showed that whole-body averaged SARs (SAR_{WB}) are closely correlated with the exposure field value averaged over the volume that would be occupied by the exposed subject. In particular, it has been estimated that assessing SAR_{WB} on the basis of volume-averaged field values yields an average error of approximately 6%. Peak 1-g and 10-g averaged SARs, instead, show a rather complex and difficult-to-predict relation with reference to the exposure field. Analysis of the results has revealed that the use of the volume-averaged exposure field value, in the absence of the subject, can lead to

an underestimation of the peak local SARs, up to 36%. On the contrary, using the maximum volumetric value yields an overestimation of peak local SAR (up to approximately four times). The conclusion was that peak local SAR showed a good correlation (15% average error) with the maximum average exposure field value obtained by varying the position of a vertical averaging plane, having a surface equivalent to the projected human body area, inside the volume occupied by the subject.

10.4.2.4.1 *Human Exposure to the Fields Produced by Coexisting Wireless Communication Systems*

The discussions thus far have dealt with the problem of human exposure to fields radiated by a single base-station antenna from the cellular mobile communication systems (i.e., GSM, UMTS, etc.). However, as the development of communication systems making use of wireless technology expands, new exposure scenarios are encountered in everyday life. Following the enormous growth in the number of base stations in densely populated areas, one of the most promising systems in the near future may be the so-called Wi-Fi system, namely, wireless LAN adopting the IEEE 802.11b communication standard. Wi-Fi is characterized by completely different coverage ranges. Unlike base-station antennas of cellular systems, which are installed almost entirely in outdoor locations, access points (APs) of Wi-Fi systems would operate essentially inside buildings. Nonetheless, the EMFs radiated by the two systems will coexist in indoor environments, particularly if buildings located in front of a rooftop-mounted base-station antenna are considered. This poses new questions about human exposure in such environments. It becomes important to assess typical exposure levels attributable to each system.

The problem has been recently addressed by considering exposure of a subject standing inside a room with a Wi-Fi AP and facing a dual-band GSM900/GSM1800 BTS antenna mounted on the rooftop of a nearby building [130]. The AP radiates a power of 100 mW at 2.44 GHz, while the GSM BTS employs an antenna with a 18-dBi gain, radiating a total power of 30 and 20 W in the GSM900 and GSM1800 frequency bands, respectively. The computed results for exposure field values and SAR levels are summarized in Table 10.7 and Table 10.8. Specifically, the first two columns of Table 10.7 show the peak ($E_{\text{vol peak}}$) and average ($E_{\text{vol ave}}$) root mean square (rms) exposure field values over the entire parallelepiped volume where the subject will be placed, while the third column reports the average ($E_{\text{sup ave}}$) rms exposure field values over vertical sections of the parallelepiped volume. In particular, the minimum and maximum field values are given because the averages depend on where exactly the surface is placed. Table 10.8 presents whole-body, peak 1-g and 10-g averaged SARs inside the exposed subject.

It can be seen from Table 10.7 that the highest contribution to the total field level inside the room is not due to the indoor source but to the outdoor one. In particular, the average **E**-field

TABLE 10.7

Exposure Field (rms Values) for the Indoor Scenario (Coexisting Outdoor GSM BTS and Indoor Wi-Fi AP)

	$E_{\text{vol peak}}$ (V/m)	$E_{\text{vol ave}}$ (V/m)	$E_{\text{sup ave}}$, min.–max. (V/m)
GSM900	5.57	3.13	2.73–3.44
GSM1800	3.61	1.70	1.62–1.91
Total GSM	6.18	3.56	3.19–3.93
Wi-Fi	2.51	1.13	1.05–1.19
Total	6.30	3.74	3.40–4.09

TABLE 10.8
SAR Values for the Indoor Scenario (Coexisting Outdoor GSM BTS and Indoor Wi-Fi AP)

	SAR_{WB} (mW/kg)	SAR_{1g} (mW/kg)	SAR_{10g} (mW/kg)
GSM900	0.109	2.41	1.08
GSM1800	0.027	1.31	0.58
Total GSM	0.136	3.07	1.46
Wi-Fi	0.014	0.79	0.35
Total	0.150	3.66	1.60

value attributable to the Wi-Fi system is as low as 1 V/m. The computed data also demonstrate that coexistence of the two systems (GSM and Wi-Fi) is possible without exceeding the reference levels for the exposure field, as averaged over the volume occupied by the body or over an equivalent surface, even if the particularly stringent limits issued by some national regulations (e.g., 6 V/m) are considered. Finally, the SARs presented in Table 10.8 suggest that a typical exposure scenario results in RF absorption that is two orders of magnitude below the basic restrictions, both for whole-body and for locally averaged SAR.

10.4. 2.5 Coupling of Transien t EM Pulses into the Hum an Body

Electromagnetic transient radiations are widely used for studying the susceptibility of test objects to broadband EMPs, and increasingly, pulsed fields are being explored for telecommunication purposes. The main characteristics of these pulse fields are waveforms that include high peak powers, fast rise times, and a narrow pulse width. Earlier investigations on their interaction with biological systems relied on mathematical analyses of canonical shapes of dielectric equivalent bodies, such models as planar tissue layers and bodies of revolution [131–134]. The well-known effect of microwave hearing from pulse-induced thermoelastic pressure in the human head have been investigated both analytically [135–140] and numerically [141–143]. More recently, major strides have been made in the development of UWB systems for wireless telecommunications [144,145]. It promises a powerful combination of low power, high throughput, greater range, and better inherent security, using nanosecond pulses. This section presents predictions of fields and power depositions, which have been obtained from the frequency-dependent FDTD formulations described in Section 10.4.1.5, for models of the biological body.

10.4.2.5.1 Modeling of Tissue Properties with the Debye Equation

For UWB calculations using the $(FD)^2TD$ method, the measured properties for the various tissues may be fitted to the Debye equation (Equation 10.14) with two relaxation constants [77–79]. For the results shown here, the measured properties of biological tissues (muscle, fat, bone, blood, intestine, cartilage, lung, kidney, pancreas, spleen, lung, heart, brain/nerve, skin, and eye) were obtained from the literature. Optimized values for ε_{s1}, ε_{s2}, ε_{∞}, τ_1, and τ_2 in Equation 10.14 were obtained by nonlinear least squares matching to the measured data for fat and muscle (Table 10.9), with τ_1 and τ_2 being the average of the optimized values for fat and muscle. All other tissues have properties falling roughly between these two types of tissues. This was done to facilitate volume averaging of the tissue properties in cells of the heterogenous human model. Having τ_1 and τ_2 constant for all tissues, allowed linear (volume) averaging of the ε values for each tissue in a given cell to calculate ε values for that cell.

TABLE 10.9

Debye Constants for Tissues, $\tau_1 = 46.2 \times 10^{-9}$ s and $\tau_2 = 0.91 \times 10^{-10}$ s (Average of Optimum for Fat And Muscle)

Tissue	ε_∞	ε_{s1}	ε_{s2}
Muscle	40.0	3948	59.09
Bone/cartilage	3.4	312.8	7.11
Blood	35.0	3563	66.43
Intestine	39.0	4724	66.09
Liver	36.3	2864	57.12
Kidney	35.0	3332	67.12
Pancreas/spleen	10.0	3793	73.91
One-third lung	10.0	1224	13.06
Heart	38.5	4309	54.58
Brain/nerve	32.5	2064	56.86
Skin	23.0	3399	55.59
Eye	40.0	2191	56.99

10.4.2.5.2 Induced Currents and SAs

The $(FD)^2TD$ formulation has been used to calculate coupling of an ultrashort pulse to the heterogenous model of the human body. From the calculated internal fields, the vertical currents passing through the various layers of the body are calculated by using the following equation:

$$I_z(t) = \delta^2 \sum_{i,j} \frac{\partial D_z}{\partial t} \tag{10.25}$$

where δ is the cell size ($=1.31$ cm), and the summation is carried out for all cells in a given layer. The layer-averaged absorbed energy density or SA and the total energy W absorbed by the whole body can be calculated using the following relationships:

$$\mathrm{SA}|_{\text{layer } k} = \frac{\delta t}{N_k} \sum_{i,j,t} \frac{E(i,j,k,t)}{\rho(i,j,k)} \frac{\partial D(i,j,k,t)}{\partial t} \tag{10.26}$$

$$W = \delta t \delta^3 \sum_{i,j,k,t} E(i,j,k,t) \frac{\partial D(i,j,k,t)}{\partial t} \tag{10.27}$$

In Equation 10.26 and Equation 10.27, δt is the time step ($=\delta/2c = 0.02813$ nsec) used for the time domain calculations, N_k is the number of cells in layer k of the body, and $\rho\,(i,j,k)$ is the mass density (in kg/m^3) for each of the cells in the corresponding layers.

A typical time domain, UWB pulse with a peak amplitude of 1.1 V/m is shown in Figure 10.23. It is interesting to note that the pulse has a rise time of about 0.2 nsec and a total time duration of about 7 to 8 nsec. The Fourier spectrum of the pulse is shown in Figure 10.24. Most of the energy in the pulse is concentrated in the 200- to 900-MHz band with the peak of the energy being at about 500 MHz.

For purposes of illustration, the results that follow assume the incident fields to be vertically polarized, since this polarization is known to result in the strongest coupling for standing individuals [146]. Also, a uniform plane wave illumination of the whole body is assumed by the incident fields. The $(FD)^2TD$ procedure is used to calculate the temporal

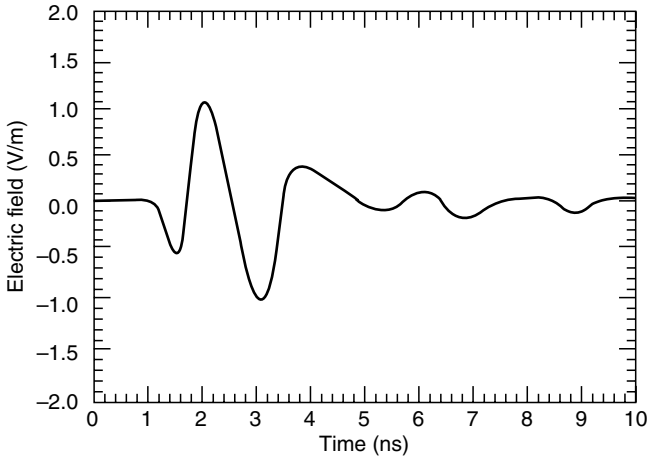


FIGURE 10.23
A representative UWB EMP. Peak incident field = 1.1 V/m.

variations of total vertical currents for the various sections of the body for both the shoe-wearing grounded and ungrounded exposure conditions of the model. The current variations for a couple of representative sections such as those through the eyes and the bladder are given in Figure 10.25a and b, respectively. The calculated peak currents for the various sections are on the order of 1.1 to 3.2 mA/(V/m). It is interesting to note that there is very little difference in the induced currents, whether the model is grounded or not. This is due to the fact that most of the energy in the pulse is at frequencies in excess of 300 MHz, where the effect of the ground plane on the induced currents or the SARs is minimal.

In Figure 10.26, the peak current for each section of the body is plotted with a section resolution of 1.31 cm. The maximum peak sectional current of 3.5 mA, which is equal to 3.2 mA/(V/m), occurs at a height of 96.3 cm above the bottom of the feet. A very similar result also had been observed for calculations using isolated and grounded models of the human body for plane wave exposures at frequencies of 350 to 700 MHz, where the highest induced currents on the order of 3.0 to 3.2 mA/(V/m) were calculated for sections of the body that are at heights of 85 to 100 cm relative to the feet.

The SA and the total absorbed energy for exposure to the UWB pulse can be calculated using Equation 10.26 and Equation 10.27. The total energy absorbed by the body exposed

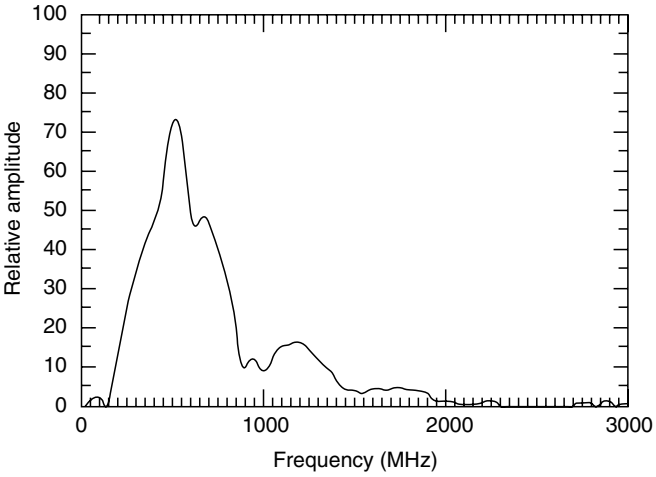


FIGURE 10.24
Fourier spectrum of the EMP of Figure 10.23.

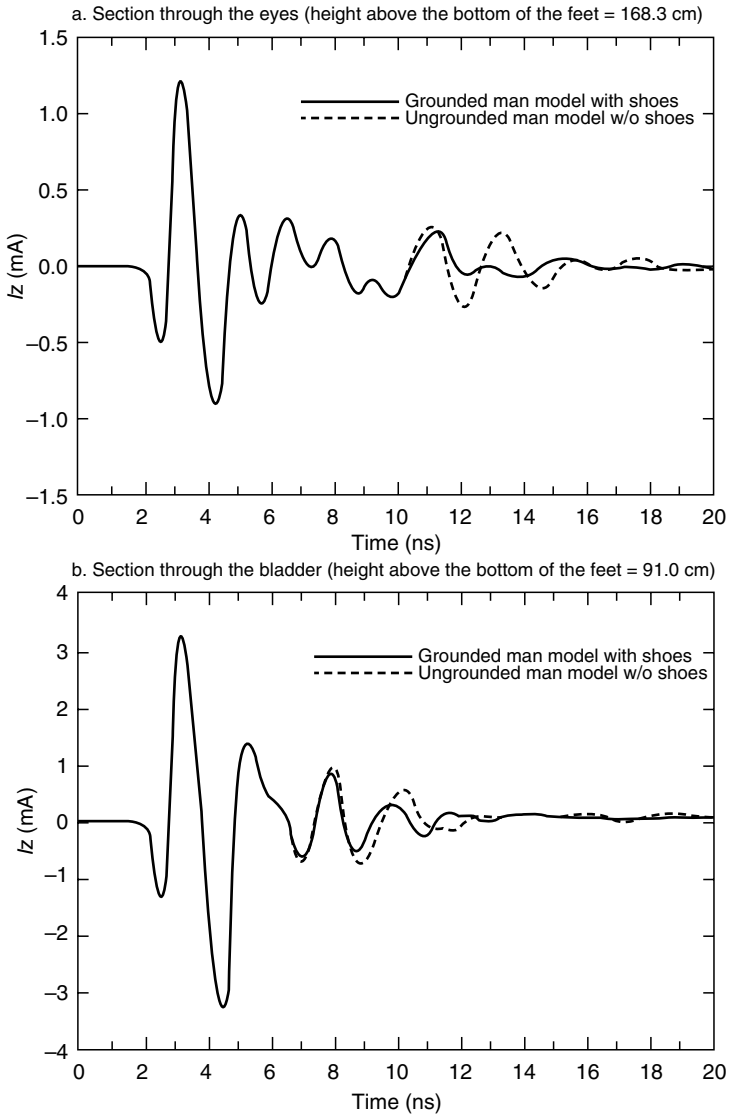


FIGURE 10.25
Currents induced for the various sections of the body for shoe-wearing grounded and ungrounded conditions of exposure. $E_{peak} = 1.1$ V/m.

to a single pulse of the type shown in Figure 10.23 is 2.0 and 1.91 pJ for isolated and shoe-wearing grounded conditions, respectively.

10.4.2.6 Absorption in the Head of Cellular Phone Users

The widespread use of cellular mobile telephone systems has brought about an increased concern for possible adverse health effects from the RF field emitted by the handset. Indeed, exposure standards have been mandated by various national bodies to limit human exposure to cell phone radiations. These RF exposure standards provide specifications in terms of power deposition per unit mass, that is, SAR induced in the user's head, with which cell phones must comply [100,101].

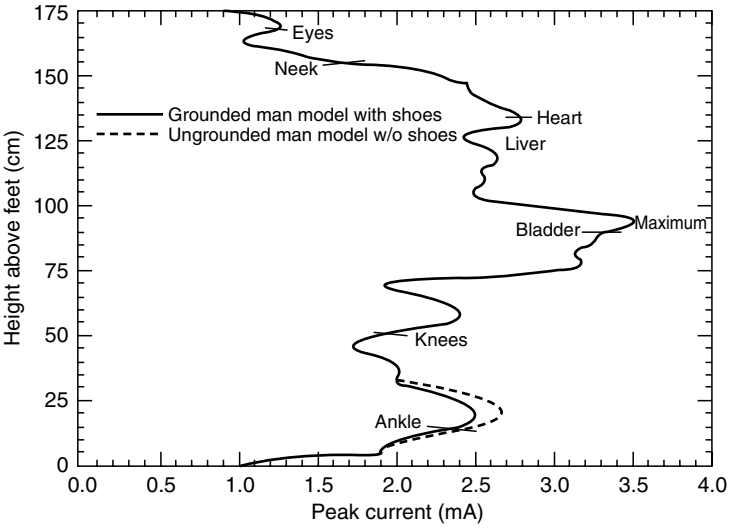


FIGURE 10.26
Peak currents induced for the various sections of the body for shoe-wearing grounded and ungrounded conditions of the model. $E_{\text{peak}} = 1.1$ V/m.

Laboratory procedures for compliance testing of mobile phones are based on experimental measurements, performed according to published protocols [147,148]. In these tests, real phones and phantom head models, shells filled with a material with dielectric properties equivalent to those of the brain tissue at the frequencies of interest, are used. Clearly, the phantom is a simplified model of the human head and is specifically designed for compliance testing. Consequently, it is not suited for an accurate analysis of the SAR distribution in various tissues and organs of the head. A detailed analysis of the distribution of the power absorption would be required to obtain a better understanding of SARs inside the head. Such information is needed for the necessary extrapolation of results from *in vivo* and *in vitro* experimental studies devoted to investigating the effects of RF radiation on humans. They would provide the exposure data needed in epidemiological studies aimed at evaluating any possible dose–effect relations.

Increasingly, advances in computational bioelectromagnetics have made detailed evaluation of SAR distribution inside the human head possible through the use of accurate and realistic models of the human head and the source, that is, the mobile phone, and the use of suitable numerical methods such as the FDTD technique.

The first numerical studies were performed by simulating the phone radiating element as a half-wavelength dipole or a quarter-wavelength monopole mounted on a box [149–154]. These antenna models, and the last in particular, can only be used as a rough model of the retractable antenna, which at the beginning was in nearly all cell phone handsets. However, at present, the need for more and more compact terminals and for dual-band operation has given rise to new antenna types. In particular, two types of antennas have been developed: planar integrated antennas and helical antennas. While half-wavelength dipoles and monopoles can be easily implemented inside an FDTD code, modeling of helix or planar antennas can become a rather difficult task.

The difficulties in modeling helical structures with the FDTD method were revealed in some recent studies. For example, only rather large structures have been studied employing a pure FDTD scheme [155,156]. For smaller structures, published reports had either employed equivalent sources [157] or a hybrid MoM–FDTD technique [158,159]. While these reports show some problems and drawbacks, investigations using FDTD, properly

modified through the use of a graded mesh, have obtained good agreement with MoM and experimental results [160,161]. In these studies, both near-field and radiation patterns of dual-band cell phones equipped with a helical antenna have been reproduced. Moreover, the SAR distributions inside the VH model of the head have been computed, showing a higher penetration depth at 900 MHz and higher superficial SARs at 1800 MHz. Moreover, approximately 80% and 50% of the radiated power was absorbed inside the head at 900 and 1800 MHz, respectively. For a phone in contact with the ear and tilted to bring its axis along the ear–mouth direction (the so-called cheek position), radiating an average power of 250 mW at 900 MHz and 125 mW at 1800 MHz, peak 1-g SARs of 1.65 and 1.08 W/kg were obtained in the head at 900 and 1800 MHz, respectively. In the same examples, the peak 1-g SARs in the brain were 0.13 and 0.06 W/kg at the two considered frequencies, respectively.

Planar antennas can be mounted on the top, lateral, or back sides of the phone [162–165]. Shorted patch antennas typically have a 10-dB bandwidth between 5% and 10% that can be increased to about 12% by parasitically coupling another printed radiator in the vertical direction (stacked patch). For comparison, the bandwidth is about 30% for the monopole antenna [163]. In this case, an important consideration is the influence of the hand wrapped around the handset. For a cell phone equipped with a planar antenna, the hand has a detuning effect on the antenna resonant frequency and causes a reduction of the bandwidth; both are evident where the hand masks the antenna. About 30% of the radiated power was absorbed by the hand, while for the monopole the hand absorption was only 15% [162]. For a radiated power of 250 mW at the frequency of 900 MHz and a head–handset separation of 2 cm, the computed peak 1-g SAR was 0.95 W/kg for a laterally mounted planar inverted F antenna (PIFA), and the result was 0.49 W/kg for a monopole antenna [162]. When a phone equipped with a side-mounted PIFA was kept in contact with the ear, the peak 1-g SAR increased to 1.4 W/kg [164]. Note that the back-mounting configuration gave rise to a substantial (up to three times) reduction in the peak SAR [162].

Another important task for an accurate evaluation of the power absorption in the head is the model adopted for the phone case. The typical approach, followed in the literature, consists of representing the case as a box, that is, a plastic-coated metal parallelepiped [149–165]. In order to model the correct shape of cell phones, both CAD files [166] and topometric sensors [167] have been used. However, in most previous studies, the internal structures of the phone have been modeled simply as a homogenous perfect conductor. Recently, CAD files have been used also to model the internal structures (printed circuit board, battery, keypad and buttons, etc.) of the phone [168]. An alternate approach to a suitable numerical model of the mobile phone was proposed by Pisa et al. [169]. It starts with a simplified model, which includes only the main phone parts (antenna, keyboard, internal box, plastic coating, etc.) having ''realistic'' dimensions and electric properties. The realistic parameters are then tuned by using an optimization procedure, which minimizes a functional that depends on the differences between the measured and simulated electric and magnetic fields in front of the phone and on the SAR inside a cubic phantom. As an example for the applicability of the proposed optimization method, a numerical model of a commercial phone, operating at 900 MHz, was implemented, and the power deposition in the VH model of the human head was computed for various phone–head distances. The results in terms of peak SAR in various head organs and tissues and for various phone–head distances are presented in Table 10.10. The SAR_{1g} and SAR_{10g} show a monotonic decrease when the phone–head distance increases, while the peak SARs inside the head tissues reach their maxima when the phone is kept at specific distances from the head. This behavior is due to the fact that with the telephone pressed against the head, the power absorption is confined to a limited region in front of the

TABLE 10.10

Peak SAR Averaged over 1 g (SAR_{1g}) and 10 g (SAR_{10g}) and Peak SAR as Averaged over 1 g in Various Organs and Tissues, for Different Distances between the Phone and the Visible Human Phantom for a Radiated Power of 250 mW at 900 MHz

	SAR_{1g} (W/kg)	SAR_{10g} (W/kg)	$SAR_{1\ brain}$ (W/kg)	$SAR_{1\ eye}$ (W/kg)	$SAR_{1\ skin}$ (W/kg)	$SAR_{1\ muscle}$ (W/kg)	$SAR_{1\ fat}$ (W/kg)	$SAR_{1\ gland}$ (W/kg)
$d = 0$ mm	1.450	0.600	0.125	0.0102	0.504	0.223	0.142	0.448
$d = 2$ mm	0.740	0.500	0.123	0.0101	0.504	0.244	0.162	0.493
$d = 6$ mm	0.670	0.470	0.174	0.0100	0.482	0.278	0.165	0.471
$d = 8$ mm	0.630	0.450	0.109	0.0103	0.460	0.280	0.160	0.445
Cheek position ($d = 0$ mm) optimized	0.810	0.410	0.088	0.0360	0.171	0.447	0.301	0.420
Cheek position ($d = 0$ mm) nonoptimized	2.568	0.888	0.177	0.0578	0.315	0.721	0.400	0.664

antenna feed point, whereas by moving the handset away from the head, a greater portion of the head is exposed. When the distance was further increased, the SAR decreased monotonically as a result of the decay in field intensity. This study also showed that the use of inaccurate phone models (last row in Table 10.10) could give rise to SARs, averaged over 1 g, up to three times higher than those computed for the optimized model [169].

Faced with a rapid saturation of the cellular phone market, many cell phone manufacturers and service providers are turning their attention toward youths in promoting handsets that are cheap, with inexpensive service plans, or both [170]. An issue of particular interest is the possible difference in power absorption between children and adults. To answer this question, the first problem to be addressed is the realization of an accurate numerical model of a child's head. Because of ethical concerns, the availability of anatomical models of children has been limited. The common approach for obtaining a model of the child has been the reduction of the dimensions of the voxel size of adult models. Sometimes, this reduction was performed by employing different scaling factors for the different parts of the head. It appears that dielectric constants for children may be considerably higher than adults [171]. However, since the detailed data for the dielectric properties of tissues in children are scarce, they are usually assumed to be equal to those of adults or generically increased by a constant factor in most models. Nevertheless, using these models, some papers have reported increases of up to 50% in the peak 1-g SARs in the child head, compared to an adult head, for exposure to cell phones operating at frequencies around 835 and 1900 MHz [151,172]. A similar increase has been observed in the peak 1-g SARs obtained in the brain. A possible explanation of these results is the larger depth of penetration of power in the child models as compared to the adult one [151,172]. Other papers devoted to the investigation of differences between child and adult exposure to cellular phones have shown no significant difference in peak 1-g SAR between adults and children [173,174]. There are several possible explanations for the discrepancy. It has been suggested that the contradictory results may be due to the different phone excitation schemes used by different authors [175]. The disparity in distances of separation between the antenna and the head also was suggested as a pivotal factor in determining the reported discrepancies [170].

In an effort to help resolve the discrepancies, the SAR distributions induced in two child's head models, an isotropic scaling of the VH head (child size, CS) and an

TABLE 10.11

Peak SAR Averaged over 10 g (SAR_{10g}) and Peak SAR as Averaged over 1 g in Various Organs and Tissues, for Radiated Powers of 250 mW at 900 MHz and 125 mW at 1800 MHz in Children and Adults

		SAR_{10g} (W/kg)	$SAR_{1\ skin}$ (W/kg)	$SAR_{1\ muscle}$ (W/kg)	$SAR_{1\ bone}$ (W/kg)	$SAR_{1\ csf}$ (W/kg)	$SAR_{1\ brain}$ (W/kg)
900 MHz	VH	0.67	2.00	0.67	0.20	0.34	0.16
	CS	1.18	4.02	1.03	0.31	0.45	0.25
	CL	1.03	1.15	0.41	0.14	0.23	0.20
1800 MHz	VH	0.39	0.99	0.30	0.08	0.12	0.08
	CS	0.29	0.87	0.30	0.08	0.13	0.09
	CL	0.27	0.91	0.30	0.06	0.15	0.10

tanisotropic scaling of the VH head (childlike, CL), have been computed and compared with SAR distributions induced in the VH by a mobile phone equipped with a back-mounted dual-band patch antenna [176]. Some of the results are presented in Table 10.11. It can be seen that the peak SAR_{10g} showed an increase of about 50% and a reduction of about 25% for the child models compared to the adult model at 900 and 1800 MHz, respectively. Moreover, as the brain is closer to the mobile phone in the case of CS and CL heads, the SAR_{1g} in the brain of children is slightly more significant than that for the adult.

Other exposure scenarios also have been investigated, including head exposure inside a car and cell phones not placed in contact with the ear. In some studies, the influence of the metallic and dielectric structures of a car on SAR induced by a cellular phone inside an adult head was analyzed [155,177–179]. Studies performed by modeling the whole car have shown that the main influence on SAR distribution was due to structures that were very close to the head [178,179]. In particular, the presence of a vertical glass wall in parallel with the antenna axis did not significantly influence the SAR distribution, while a metallic wall can cause up to an 80% increase in the peak 1-g SAR [155,177]. The presence of a reflecting wall placed horizontally over the head, simulating the roof of a car, rendered the SAR distribution more uniform, increasing the lower values and reducing the higher ones [155].

Cellular phones commonly are used in contact with the ear. However, when they are used with a headset, they can be positioned at different body locations. Moreover, unintentional exposures also might occur for a subject standing close to someone using a cellular phone, for example, in a crowded environment. The peak SAR produced by a phone placed slightly above the navel of the VH model has been calculated by using the FDTD method, and the results have been compared to those of a flat phantom—modeled as a multilayered transmission line—whose thickness was varied statistically [180]. The exposure of a human subject to a half-wavelength dipole placed at various positions at a distance of 9 mm from the body surface also has been investigated [181]. In particular, 11 different locations have been considered, that is, in front of the right ear and left ear, the nose, eye, heart, lung, shoulder, stomach, hip, lower back, and the groin. The computed results showed that the maximum values of SAR_{1g} and SAR_{10g} occurred, in all cases, when the phone is close to the ear. For all other positions, corresponding to possible locations of the phone when used in conjunction with a headset, peak 1-g SAR values were at least 30% lower than those obtained in the common ear position.

10.5 Temperature Elevations Induced in Biological Tissues by EM Power Absorption

10.5.1 Introduction

EM energy impinging on the human body induces currents and fields inside the body. A major biological response from absorption of EM energy in the RF and microwave frequency range is the elevation of tissue temperature. Consequently, most internationally recognized guidelines for limiting human exposure to EMFs in the RF and microwave range use SAR as the basic dosimetric metric [100,101]. Likewise, the vast majority of studies available in the literature, addressing the topic of human exposure to EMFs, focus their attention on the dosimetric problem of quantifying induced power absorption inside the exposed subject. A central premise of these exposure guidelines is to protect exposed subjects against temperature increases exceeding the threshold for induction of adverse thermal effects. Therefore, an increasing number of investigators are beginning to address the problem of human exposure to EMFs with a thermal analysis to estimate the temperature increment induced inside the exposed subject.

Another domain in which a thermal analysis can be very useful, or even essential, is that of therapeutic applications where EMFs are deliberately used to cause predefined temperature increases in specific target tissues in the body. Some of the applications include hyperthermia cancer treatment and microwave tissue ablation. In such cases, performing a numerical electromagnetic and thermal study of the applicator in its intended operating environment, inside the body, can be a valuable aid in designing the applicator, in establishing the clinical protocol (i.e., power to be delivered, time of application, etc.), and for treatment planning purposes.

In the following, an overview of the available analytical formulations to characterize heating induced by EMFs is presented. Some numerical implementations, suitable to study the thermal problem in realistic situations, are summarized with specific examples.

10.5.2 Bio-Heat Equation

The bio-heat equation (BHE) was originally proposed by Pennes in 1948 to analyze temperature distributions in a resting forearm [182]. Subsequently, it has been modified to study phenomena of heat transport and exchange for the whole body [183,184]. It is an analytical model that describes the temperature distribution $T = T(\mathbf{r},t)$ inside the body. One of the more general formulations of the BHE is given here for temperature rises associated with exposures to EMFs:

$$\nabla \cdot (K(\mathbf{r})\nabla T) + A(\mathbf{r},T) + Q_{\mathrm{v}}(\mathbf{r}) - R_{\mathrm{L}}(\mathbf{r}) - B(\mathbf{r},T)(T - T_{\mathrm{B}}) = C(\mathbf{r})\rho(\mathbf{r})\frac{\partial T}{\partial t}\,(\mathrm{W/m^3}) \qquad (10.28)$$

The five terms on the left side of Equation 10.28 represent heat accumulation (or loss) per unit time and per unit volume at a point inside the body. Specifically, the various ways through which heat is transferred, produced, or removed from the tissue are:

- Heat transfer through internal conduction, where K (W/(m°C)) is the tissue thermal conductivity
- Metabolic heat production (A [W/m^3])
- Electromagnetic power deposition (Q_{v} [W/m^3])

- Respiratory heat losses in the lungs (R_L [W/m^3])
- Heat exchange due to capillary blood perfusion, which is proportional to blood flow and is represented by the parameter B (W/(°C m^3)), and the difference between blood and tissue temperature ($T_B - T$); note that T_B is a function of time (i.e., $T_B = T_B(t)$)

The right side of Equation 10.28 denotes the temperature increase (or decrease) per unit time. The thermal capacitance per unit volume is given by the product between the tissue specific heat, C (J/(kg°C)) and density, ρ (kg/m^3).

It should be mentioned that the BHE assumes that heat exchange with blood takes place exclusively via capillary perfusion. In reality, heat exchange also occurs with large blood vessels. This mechanism does not take the form of a distributed exchange throughout the tissue volume, like the $B(T - T_B)$ term in the BHE, but instead, the form of a localized exchange at the blood vessel walls. To account for it would require the introduction of an additional term in the BHE [185,186]. Moreover, it would require precise knowledge of the structure of the vasculature inside the biological body, which is not always available. However, this mechanism only alters temperature distribution near large blood vessels and does not significantly affect the overall temperature distribution, especially the maximum temperature increases elsewhere in an exposed body [187]. Therefore, this mechanism can generally be neglected without significant loss of accuracy, if the principal purpose is to assess safety compliance of a given exposure situation, from the thermal point of view. On the other hand, proper inclusion of large blood vessels may be important when planning hyperthermia or ablation treatments. The presence of a large blood vessel in the target region may cause temperature elevations to remain below the minimum threshold required for effective treatment.

A first step in using the BHE to compute the temperature increases induced by exposure to EMFs is the evaluation of SAR or local power deposition. In fact, $Q_v = \rho$ SAR is the exogenous heat source responsible for the alteration in temperature profiles inside the exposed subject. Once the Q_v term is determined, the BHE would provide the time evolution of temperature, provided that appropriate initial and boundary conditions are imposed, as discussed later. In this manner, the BHE allows assessment of both the transient response and steady-state temperature increases.

An implicit assumption in the above discussion is that the electromagnetic and thermal problems are independent and can be investigated sequentially. This is equivalent to assuming that electromagnetic transients are irrelevant and therefore the steady-state SAR distributions can be used as the input for the thermal analysis, and that changes in tissue temperature do not alter the field distribution inside the tissue. Concerning the first assumption, the time constants of the electromagnetic and thermal processes are of orders of magnitude different, with the EMF reaching steady state at most after a few microseconds, while thermal constants inside living biological tissues are of the order of a few minutes under usual circumstances. This means that electromagnetic transients can indeed be neglected for the thermal analysis. The second assumption, instead, deserves some more attention. In fact, dielectric constants of biological tissues are temperature dependent, and therefore, the EMF distribution could change as heating proceeds and temperature increases. However, this effect may be neglected so long as the temperature elevation is small, that is, on the order of a few degree Celsius, as is expected for common EMF exposures. If temperature increase is large and the induced variation in dielectric constants is no longer negligible, for example, when heating food in a microwave oven, the electromagnetic and thermal problems must be solved in a coupled manner, iteratively updating the electromagnetic solution as heating progresses [188–190].

10.5.2.1 Initial Conditions

The BHE is a partial differential equation in time and space; its solution requires the specification of both initial and boundary conditions. For studies involving RF- and microwave-induced heating inside the human body, the initial temperature distribution typically is set to the physiological norm, computed as the steady-state solution of Equation 10.28 in the absence of external power deposition ($Q_v = 0$). Thus, the resulting equation is

$$\nabla \cdot (K(\mathbf{r})\nabla T) + A_0(\mathbf{r}) - R_L(\mathbf{r}) - B_0(\mathbf{r})(T - T_{B0}) = 0 \ (\mathrm{W/m^3}) \tag{10.29}$$

In this case, thermal parameters do not depend on temperature and are set to their physiological values at approximately 37°C. Similarly, the physiological value at rest is used for blood temperature. Note that Equation 10.29 does not contain time derivatives and, therefore, does not require any initial condition to be solved.

10.5.2.2 Boundary Conditions

Boundary conditions are needed to account for the heat exchange between the body surface, namely, the skin, and the external environment, in both the general and the steady-state formulations of the BHE as represented by Equation 10.28 and Equation 10.29, respectively. The simplest boundary conditions that can be applied are the adiabatic condition, that is, a thermally insulated surface, or the Dirichelet boundary condition, that is, an enforced surface temperature. Adiabatic conditions can be used to model tissue surfaces in close contact with highly insulating materials, such as the catheters used to insert antennas employed in hyperthermia or ablation treatment. In contrast, Dirichelet boundary conditions can be used for surfaces in close contact with a circulating fluid kept at a constant temperature (forced convection).

Adiabatic and Dirichelet boundary conditions are rather simple but they are not suitable for representing the general heat exchanges that take place at the skin. A general boundary condition, obtained by imposing the continuity of the heat flow perpendicular to the surface of the body, can be expressed as [191]:

$$-K(\mathbf{r})(\nabla T \cdot \mathbf{n}_0)_S = H(T_s - T_A) + \mathrm{SW}(T)(\mathrm{W/m^2}) \tag{10.30}$$

where S is the skin surface and $\mathbf{n}_0$ is the outward unit vector normal to S. The terms on the right side of Equation 10.30 represent the two ways in which heat is exchanged with the environment. In particular, the first term describes heat loss due to convection, and it is proportional to the difference between skin temperature (T_S) and ambient air temperature (T_A) through the convection coefficient H (W/(m^2°C)). The last term represents heat loss due to sweating (SW).

A few words are needed about radiative heat exchange. If one assumes the body surface is surrounded by objects that are all at the same ambient temperature T_A, the expression for heat exchange through radiation from the body surface to the environment, per unit area, is given by [192,193]:

$$Q_r = e\sigma(T_s^4 - T_A^4)(\mathrm{W/m^2}) \tag{10.31}$$

where e is the surface emissivity, σ is Stefan–Boltzmann's constant, and the temperatures are expressed in degrees Kelvin (K). Under normal conditions, T_S and T_A do not differ significantly from about 300 K, and Equation 10.31 can be approximated as [193]:

$$Q_r = H_r(T_s - T_A)(W/m^2) \tag{10.32}$$

where H_r is an equivalent convection coefficient. Therefore, the convective term in Equation 10.32 can effectively model both convective and radiative heat exchanges, by using an overall convection coefficient that also takes into account the equivalent convection parameter H_r in Equation 10.32. There are cases, however, in which the surrounding objects are at different temperatures. In such circumstances, the problem becomes very complex and a possible solution, based on the use of an RT method to connect mutually visible surfaces and consider radiant heat transfer between them, has been proposed [194]. However, the simple approach of an equivalent convection is generally sufficient for an accurate analysis of the thermal problem.

It is worthy of mention that the convective boundary condition also can be used to represent an adiabatic condition by simply setting the convective coefficient to zero. It can also represent an approximate Dirichelet boundary condition, by using a very high convective coefficient and setting T_A equal to the imposed surface temperature.

10.5.3 Thermoregulatory Responses

The temperature of the human body is regulated to within a narrow range of about 37°C, in its core. Under normal circumstances, this is accomplished through an exquisite thermoregulatory mechanism involving sweating and vasodilatation (see Chapter 5 by Black for more details on thermoregulation [285]). The thermoregulatory mechanism is activated whenever the temperature $T(\mathbf{r})$ in specific parts of the body, where thermal sensors are placed, shifts from its basal value $T_0(\mathbf{r})$. In particular, the basal temperature distribution $T_0(\mathbf{r})$, which corresponds to a state of ''thermal comfort,'' is the one obtained in a naked subject when the external air temperature T_A is about 30°C (in a dry environment) [184,195].

Since a part or all of the absorbed electromagnetic energy is converted into heat inside the human body, computations of tissue temperature must take into account the thermoregulatory mechanisms in response to the heat input from RF and microwave absorption, starting from a state of thermal comfort [195]. Specifically, the presence of thermoregulatory mechanisms causes some of the terms in Equation 10.28 and Equation 10.30 to vary with body temperature. The first term that shows a dependence on temperature in Equation 10.28 is metabolic heat production, which may be characterized by the following equation [196]:

$$A(\mathbf{r},T(\mathbf{r})) = A_0(\mathbf{r})(1.1)^{(T(\mathbf{r})-T_0(\mathbf{r}))} \tag{10.33}$$

where A_0 is the basal metabolic rate in the tissue. Equation 10.33 shows that metabolic heat production depends only on local tissue temperature. It must be noted that this dependence is not related to thermoregulation but rather to the fact that metabolic processes are slightly accelerated when the temperature increases.

With regard to the variation of blood flow, there are two different, but essential, phenomena: one for internal tissue perfusion and the other for peripheral (skin) perfusion. For blood perfusion to the internal tissues, the regulation depends only on local tissue temperature [196,197]. Thus, in a simple model, blood perfusion could be assumed to be at its basal value B_0 until the local temperature reaches 39°C. When the local temperature exceeds 39°C, the blood perfusion starts to increase linearly with temperature in order to enhance the local heat removal process, until the local temperature rises to above a value of about 44°C. At this point, the increasing rate of blood perfusion arrives at a maximum. Accordingly, the internal blood perfusions are modeled by the following expressions:

$$B(\mathbf{r},T(\mathbf{r})) = B_0(\mathbf{r})\ T(\mathbf{r}) \leq 39^{\circ}\mathrm{C} \tag{10.34}$$

$$B(\mathbf{r},T(\mathbf{r})) = B_0(\mathbf{r})[1 + S_B(T(\mathbf{r}) - 39)]\ 39^{\circ}\mathrm{C} < T(\mathbf{r}) < 44^{\circ}\mathrm{C} \tag{10.35}$$

$$B(\mathbf{r},T(\mathbf{r})) = B_0(\mathbf{r})(1 + 5S_B)\ T(\mathbf{r}) \geq 44^{\circ}C \tag{10.36}$$

The above model of the internal temperature regulation mechanism is rather simple. A more complex temperature control model, instead, would include regulation of blood perfusion in the skin through vasodilatation. In particular, two different signals are used as feedback to regulate vasodilatation: one is the hypothalamic temperature increase ($T_H - T_{H0}$), used as an indicator of the elevation of the body core temperature, and the other is the average skin temperature increase $\overline{\Delta T}_s$, defined as follows:

$$\overline{\Delta T}_s = \frac{\int_S (T(\mathbf{r}) - T_0(\mathbf{r}))\,dS}{S} \tag{10.37}$$

where S is the skin surface of the body. The two feedback signals are assigned different weights, with a greater importance given to the hypothalamic temperature, and then used, together with local skin temperature, to regulate skin blood flow according to [183,184]:

$$B(\mathbf{r},T(\mathbf{r})) = \left[B_0(\mathbf{r}) + F_{HB}(T_H - T_{H0}) + F_{SB}\overline{\Delta T_S}\right]2^{(T(\mathbf{r})-T_0(\mathbf{r}))/6} \tag{10.38}$$

where F_{HB} and F_{SB} are the weights of the hypothalamic and skin temperature signals, respectively.

From the above discussion, it can be noted that blood acts as a heat transfer agent, taking heat away from the inner body parts, whose temperature is higher than that of the blood, and bringing this heat to the body periphery. There, heat is passed to the skin layers, whose temperature is lower than that of the blood, and dissipated through sweating and evaporation. During microwave irradiation, the net heat exchange, between blood and the various body tissues, is different from zero, and consequently the blood temperature T_B varies according to the following equation:

$$Q_{BTOT} = C_B\rho_B V_B \frac{\partial T_B}{\partial t}(\mathrm{W}) \tag{10.39}$$

where Q_{BTOT} is the net rate of heat acquisition of the blood from the body tissues, C_B and ρ_B are the blood specific heat and mass density, respectively, and V_B is the total blood volume, assumed equal to about 5 L [198]. When the thermal equilibrium is reached, the net heat exchange is null, and therefore blood temperature stays at a constant value, slightly higher than the basal one.

The feedback mechanism that regulates sweating (SW in Equation 10.30) is very similar to that regulating peripheral blood flow and can be described as follows [183,184]:

$$\mathrm{SW}(\mathbf{r},T(\mathbf{r})) = \left[\mathrm{PI} + F_{HS}(T_H - T_{H0}) + F_{SS}\overline{\Delta T_S}\right]2^{(T(\mathbf{r})-T_0(\mathbf{r}))/10} \tag{10.40}$$

where PI represents *perspiratio insensibilis* (insensible perspiration), that is the basal evaporative heat loss from the skin.

In fact, this model still represents a simplification of the thermoregulatory system of the human body, which is very complex. For example, the skin from different parts of the body does not have the same sweating behavior, as implied by Equation 10.40, and there exist other internal temperature sensors, besides the hypothalamus. Notwithstanding these limitations and the great variability in thermoregulatory behavior among different subjects, the model can be considered a good starting point to assess thermal responses in a human subject exposed to an EMF. It must also be observed that in most practical situations, induced thermal elevations are very small and thermoregulatory responses may not be invoked, so that basal physiological values for thermal parameters may be assumed for the BHE.

10.5.4 Numerical Methods for Solving the Thermal Problem

The combination of the BHE and the thermal boundary condition represent a complicated problem, which can become nonlinear if thermoregulatory mechanisms are considered. Analytical solutions of this problem, neglecting thermoregulation, can be obtained only for simplified body geometries and exposure conditions, which allow an analytical determination of the SAR distribution. For example, an analytical solution in stratified media may be obtained as an expansion in eigenfunctions, which are applicable to planar, cylindrical, and spherical multilayer geometries [199,200]. Also, an analytical solution for the case of a multilayer slab has been investigated in terms of Green's functions [201]. More complicated solutions, able to take into account thermoregulatory mechanisms, have also been developed, based on a simplified cylindrical segment approximation of the human body [183,184,202,203]. In particular, the thermal behavior of the human body is simulated by means of two systems: a controlling system and a controlled one. The controlled system, modeled by the BHE, determines the temperature distribution inside the body, while the controlling system provides feedback signals able to modify the thermal parameters of the controlled one in order to maintain a constant body core temperature (thermoregulation). The principal limitation of this approach stems from modeling the body as a few homogenous cylindrical segments, each having a uniform SAR and temperature distribution.

When studying more realistic and detailed geometries, like an anatomically based body model, analytical or cylindrical segment solutions are no longer feasible, and a numerical approach becomes necessary. One possibility is the development of a finite element solution of the BHE [204,205]. However, the most common approach is to use a finite difference scheme, which will be discussed in some detail in the following. One of the main reasons for preferring a finite difference solution, besides its computational efficiency, is that it allows a very simple link with the FDTD method, which is the most popular numerical method for SAR computations. Earlier finite difference solutions of the BHE, used in conjunction with cubic-cell models of the human body, comprised only a few hundred voxels. They used an implicit formulation to avoid the restrictions on the size of the time step. Since these solutions required matrix inversions, they were computationally intensive [16]. As more detailed body models, comprising thousands of voxels, became available, new finite difference solutions were developed. These techniques, based either on explicit or on alternate direction implicit (ADI) formulations, are discussed in the following.

10.5.4.1 Explicit Finite Difference Formulation

One approach to obtain a finite difference explicit formulation of the BHE is based on the thermal balance approach [98]. The body under consideration is divided into cubic cells of

side δ, and the temperature is evaluated at the center of each cell. Temperatures are computed at equal-time steps, δt. In the following, the expression $T^n(i,j,k)$ represents temperature computed at time $n\delta t$ in the (i,j,k) cell. The finite difference formulation is derived by imposing the thermal balance to each cell [192], such that

$$Q_{\text{tot}}^{n,n+1}(i,j,k) = \Gamma(T^{n+1}(i,j,k) - T^n(i,j,k))(\text{J}) \tag{10.41}$$

where $Q_{\text{tot}}^{n,n+1}$ is the total heat accumulated (positive) or lost (negative) in the cell during the time interval $[n\delta t - (n+1)\delta t]$, $(T^{n+1} - T^n)$ is the variation of the cell temperature in the same time interval, and $\Gamma = C\rho\delta^3$ is the thermal capacitance of the cell. The heat $Q_{\text{tot}}^{n,n+1}$ is accumulated (or lost) in the cell through the five mechanisms present in the BHE, and, for boundary cells, also through convection to external air and sweating (Equation 10.30).

Heat transfer through internal conduction is governed by Fourier's law. For the (i,j,k) cell, the heat $Q_{\text{K}}^{n,n+1}$ entering the cell through conduction from the $(i-1,j,k)$ cell in the time interval $[n\delta t - (n+1)\delta t]$ can be derived by exploiting the well-known analogy between heat conduction and electrical current conduction [185,192]. In particular, if K_1 and K_2 are the thermal conductivities of the two cells under examination, heat flows through the series connection of two thermal conductances, equaling $K_1\delta^2/(\delta/2)$ and $K_2\delta^2/(\delta/2)$, respectively. Therefore, heat flowing from the center of the $(i-1,j,k)$ cell to the center of the (i,j,k) cell, through the boundary face, experiences an overall thermal conductance equal to $2K_1K_2\delta^2/((K_1+K_2)\delta)$. As a result, we obtain:

$$Q_K^{n,n+1}(i,j,k) = \frac{2K_1K_2}{K_1+K_2}\delta^2\frac{T^n(i-1,j,k) - T^n(i,j,k)}{\delta}\delta t \tag{10.42}$$

An expression similar to Equation 10.42 holds for heat exchanged with the other neighboring cells.

The contributions of metabolic heat production and electromagnetic power deposition are volumetric heat sources, and therefore the contribution they give to $Q_{\text{tot}}^{n,n+1}$ can be immediately derived and is expressed by Equation 10.43 and Equation 10.44, respectively:

$$Q_A^{n,n+1}(i,j,k) = A(i,j,k)\delta^3\delta t \tag{10.43}$$

$$Q_{Q_v}^{n,n+1}(i,j,k) = Q_v(i,j,k)\delta^3\delta t \tag{10.44}$$

Respiratory losses in the lungs are taken into account by subtracting the volumetric loss R_L from the metabolic heat production A in the corresponding cells for the lung.

Finally, the contribution to $Q_{\text{tot}}^{n,n+1}$ due to capillary blood perfusion takes the form of a volumetric term and can be represented, as in metabolic heat production and exogenous heat deposition, as:

$$Q_B^{n,n+1}(i,j,k) = B(i,j,k)((T_B - T^n(i,j,k))\delta^3\delta t \tag{10.45}$$

For boundary cells in contact with air, heat flow through the face is governed by convection rather than conduction. For a generic cell (i,j,k), considering a face in direct contact with air, the heat $Q_{\text{H}}^{n,n+1}$ entering the cell through convection in the time interval $[n\delta t - (n+1)\delta t]$ is:

$$Q_H^{n,n+1}(i,j,k) = H(T_A - T^n(i,j,k))\delta^2\delta t \tag{10.46}$$

Heat losses due to sweating at the skin surface (SW) are converted to a volumetric heat loss term and are directly subtracted from the metabolic heat production term A in the skin cells.

Note that in Equation 10.42, Equation 10.45, and Equation 10.46, the temperature has been referred to the time instant $n\delta t$ in order to obtain, at the end, an explicit formulation. Starting from the equations given above, general explicit formulations that hold for each cell can be derived. (See the paper by Bernardi et al. [98] for additional details)

10.5.4.1.1 Stability Criterion

Explicit finite difference formulations are straightforward to implement and are computationally efficient, but they have a limitation on the maximum time step δt that can be used without incurring numerical instability.

The stability criterion for the previously mentioned finite difference scheme can be obtained through Fourier's analysis, which yields the following restriction on δt, derived for internal cells (no convective contributions) [206]:

$$\delta t \leq \frac{1}{6(K/C\rho\delta^2) + (B_0/2C\rho)} \tag{10.47}$$

Because of the typical values of thermal parameters and convection coefficients for the human body, the stability criterion for the peripheral voxels, where some of the faces exchange heat through convection rather than conduction, is less stringent than that of Equation 10.47. Consequently, Equation 10.47 may be safely assumed as the stability criterion for the overall scheme.

10.5.4.2 ADI Formulation

While the explicit finite difference formulation of the BHE has been applied to many simulations, it becomes computationally unaffordable when very small cell sizes are used or when high thermal conductivity materials are present in the domain under study. This stems from the extremely small time steps δt that would be required according to Equation 10.47. In such cases, the ADI formulations can be used [207]. ADI is a general method, developed for numerical solution of parabolic equations. It combines unconditional stability, typical of implicit methods, with the computational efficiency due to the tri-diagonal nature of the resulting matrices [208–210]. Note that the Fourier heat conduction equation is a typical parabolic equation. While the BHE is no longer parabolic, because of the presence of the term related to blood flow, ADI can still be applied, but it loses its unconditional stability. In any case, for time steps on the order of a few seconds, the scheme has proved to be stable in typical applications. It can yield reductions on the order of tenfold or more [207] in execution time, over the classical explicit formulation.

The basic idea behind the ADI technique is to extend to the 3-D case the 1-D Crank–Nicolson's scheme, which averages the outcome from the explicit and the implicit formulations to obtain second-order accuracy both in space and in time variables [192]. In particular, Crank–Nicolson's scheme can be extended to the full 3-D case, by using a sequence of approximate Crank–Nicolson solutions along the three axes, indicated as $T^*(i,j,k)$, $T^{**}(i,j,k)$, and $T^{***}(i,j,k)$, the last one being used as the final estimate for $T^{n+1}(i,j,k)$.

The first approximate solution is obtained using Crank–Nicolson's scheme along the x axis only, while backward differencing is used along y and z:

$$\frac{K}{\rho C}\frac{1}{2}\left(\frac{T^*(i-1,j,k)-2T^*(i,j,k)+T^*(i+1,j,k)}{(\delta x)^2}+\frac{T^n(i-1,j,k)-2T^n(i,j,k)+T^n(i+1,j,k)}{(\delta x)^2}\right)$$
$$+\frac{K}{\rho C}\frac{T^n(i,j-1,k)-2T^n(i,j,k)+T^n(i,j+1,k)}{(\delta y)^2}$$
$$+\frac{K}{\rho C}\frac{T^n(i,j,k-1)-2T^n(i,j,k)+T^n(i,j,k+1)}{(\delta z)^2}$$
$$=\frac{T^*(i,j,k)-T^n(i,j,k)}{\delta t}-\frac{A_0+Q_v+B_0T_B}{\rho C}$$
$$+\frac{B_0}{\rho C}\frac{T^*(i,j,k)+T^n(i,j,k)}{2} \tag{10.48}$$

Extending subsequently Crank–Nicolson's solution along the y axis and the z axis, the following expressions are obtained for the second and third estimates:

$$\frac{K}{\rho C}\frac{1}{2}\left(\frac{T^*(i-1,j,k)-2T^*(i,j,k)+T^*(i+1,j,k)}{(\delta x)^2}+\frac{T^n(i-1,j,k)-2T^n(i,j,k)+T^n(i+1,j,k)}{(\delta x)^2}\right)$$
$$+\frac{K}{\rho C}\frac{1}{2}\left(\frac{T^{**}(i,j-1,k)-2T^{**}(i,j,k)+T^{**}(i,j+1,k)}{(\delta y)^2}+\frac{T^n(i,j-1,k)-2T^n(i,j,k)+T^n(i,j+1,k)}{(\delta y)^2}\right)$$
$$+\frac{K}{\rho C}\frac{T^n(i,j,k-1)-2T^n(i,j,k)+T^n(i,j,k+1)}{(\delta z)^2}$$
$$=\frac{T^{**}(i,j,k)-T^n(i,j,k)}{\delta t}-\frac{A_0+Q_v+B_0T_B}{\rho C}$$
$$+\frac{B}{\rho C}\frac{T^{**}(i,j,k)+T^n(i,j,k)}{2} \tag{10.49}$$

$$\frac{K}{\rho C}\frac{1}{2}\left(\frac{T^*(i-1,j,k)-2T^*(i,j,k)+T^*(i+1,j,k)}{(\delta x)^2}+\frac{T^n(i-1,j,k)-2T^n(i,j,k)+T^n(i+1,j,k)}{(\delta x)^2}\right)$$
$$+\frac{K}{\rho C}\frac{1}{2}\left(\frac{T^{**}(i,j-1,k)-2T^{**}(i,j,k)+T^{**}(i,j+1,k)}{(\delta y)^2}+\frac{T^n(i,j-1,k)-2T^n(i,j,k)+T^n(i,j+1,k)}{(\delta y)^2}\right)$$
$$+\frac{K}{\rho C}\frac{1}{2}\left(\frac{T^{n+1}(i,j,k-1)-2T^{n+1}(i,j,k)+T^{n+1}(i,j,k+1)}{(\delta z)^2}+\frac{T^n(i,j,k-1)-2T^n(i,j,k)+T^n(i,j,k+1)}{(\delta z)^2}\right)$$
$$=\frac{T^{n+1}(i,j,k)-T^n(i,j,k)}{\delta t}-\frac{A_0+Q_v+B_0T_B}{\rho C}$$
$$+\frac{B_0}{\rho C}\frac{T^{n+1}(i,j,k)+T^n(i,j,k)}{2} \tag{10.50}$$

Starting from the above expressions, it is possible to derive the general ADI formulation that holds for each internal cell. (See the paper by Pisa et al. [207] for additional details.) The formulation can also be adapted to boundary cells, where convective heat exchange must be considered, by introducing a fictitious external node.

10.5.5 Temperature Elevations in Subjects Exposed to EM Fields

When an EM field impinges on the biological body, a fraction of the incident power is absorbed by the body and is converted into heat in the body tissue. Thus, the absorbed energy can cause temperature increases in various body organs and tissues. If the temperature increase is small, it has little effect and is controlled by the thermoregulatory mechanisms of the body. However, if the temperature increment is large, it can produce irreversible biological damage. For example, a temperature increase of about 4.5°C for more than 30 min would produce neuronal damage [211]. Experiments performed on the rabbit eye indicated that a threshold increase of 3°C to 5°C in the lens can induce cataract formation [212,213]. The temperature increase necessary to induce thermal damage to the skin is about 10°C [214,215], while it is 8°C for muscle tissues [216]. Also, experiments performed using laboratory animals have shown various physiological and behavioral effects when the body core temperature rises more than 1°C to 2°C [100]. (See also Chapter 5 by Black [285].)

Moreover, most RF protection standards have adopted basic restrictions in order to keep the thermal increments below some agreed upon level. In particular, the value of 4 W/kg averaged over the whole body (SAR_{WB}) had been adopted by exposure guidelines as the threshold for the induction of adverse thermal effects associated with an increase of the body core temperature of about 1°C in animal experiments. Restrictions on local SAR were introduced in order to limit local temperature increments, since the ratio of the local peak to whole-body averaged SAR can be as high as 20:1 for exposure to a uniform plane wave [217]. However, it is important to note that tissue heating during EM exposure is strongly influenced not only by the power dissipated in the local tissue volume, but also by the way in which absorption is distributed in the surrounding area, by the thermal characteristics of the tissue and its neighbors, and, finally, by the heat exchange with the external environment. The correlation between local SAR values and temperature increases and between SAR and temperature distributions is not straightforward. There have been many studies dealing with thermal increments due to exposures both to the far field of radiating sources and to the near field of cellular phones. In the following some of these studies will be summarized and discussed.

10.5.5.1 Temperature Increments in the Human Body Exposed to the Far Field of Radiating RF Sources

In the past, temperature elevations due to EM power absorption in the human body have been evaluated using several models. The earlier studies were based on a simplified cylindrical segment approximation of the human body [183,184,202,203]. In these studies, the thermal behavior of the human body was simulated by means of two systems: a controlling system and a controlled one. The controlled system, modeled by the BHE, determines the temperature distribution inside the body, while the controlling system provides feedback signals able to modify the thermal parameters of the controlled one in order to maintain a constant body core temperature (thermoregulation). These studies are limited to modeling the body as few homogenous cylindrical segments, each one having a uniform SAR and temperature distribution. A subsequent study [197] used a cubic-cell model with tissue inhomogeneity and took into account the thermoregulatory mechanisms in the BHE. In this case, the BHE was solved using an implicit formulation, which

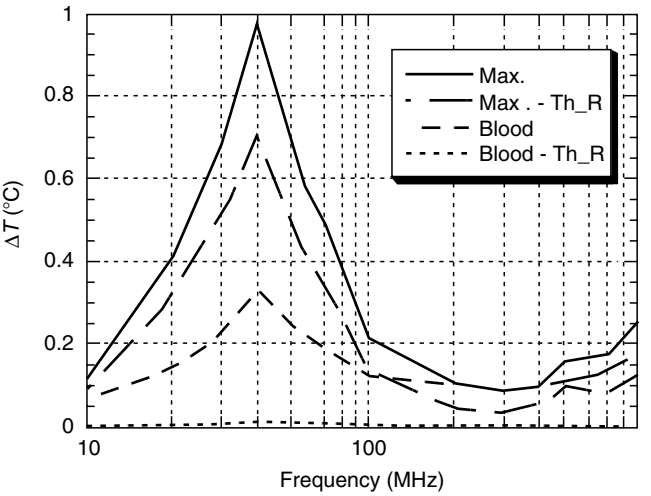


FIGURE 10.27
Maximum temperature increases (ΔT) in the body and blood of a subject wearing shoes, as a function of frequency, with or without thermoregulation (Th_R) for a P_{inc} equal to the limits set by ICNIRP [101].

avoided the restriction in the size of the time step. The explicit formulation requires a computationally intensive matrix inversion. Lately, explicit formulations of the BHE have been developed to study thermal responses in anatomically accurate body models [196,218,219]. In most of these studies, only limited body regions were considered, and thermoregulation mechanisms were neglected.

More recently, the electromagnetic and thermal problems have been combined in a detailed anatomical model of the human body (5-mm resolution) [98]. The FDTD method was used to compute the EMF distribution inside the exposed body, while an explicit finite difference formulation of the BHE, together with an accurate model of the human thermoregulatory system, were developed to compute the corresponding temperature increase.

For an incident power density equal to the maximum permissible value in the International Commission on Non-Ionizing Radiation Protection (ICNIRP) exposure guidelines for the general public [101], Figure 10.27 shows the maximum temperature increase ΔT_{max} obtained inside the body and in the blood as a function of frequency for a subject wearing shoes, both with and without thermoregulation [98]. It can be seen that the highest ΔT values are obtained at 40 MHz. It is also interesting to note that when thermoregulation is considered, the increase in blood temperature is practically zero, while the maximum temperature rise in the body can reach 0.72°C. This happens since blood temperature is very close to the body core temperature, which thermoregulation tends to keep as constant, while the maximum temperature increments are usually found in the superficial tissue layers.

It is worth noting that at 40 MHz, the maximum temperature increase (i.e., 0.72°C in the presence of thermoregulation) is found in the muscle tissues of the ankle. The threshold for the induction of thermal damage in muscle is about 45°C [216], which corresponds to a temperature increase of about 8°C. This temperature differential coincides with the safety factor of 10 promulgated by ICNIRP [100] for occupational exposure in limiting the power density from inducing a thermal effect. Moreover, a safety factor of 50 can be deduced from the temperature increase obtained at 10 MHz and in the frequency range between 100 and 900 MHz, where the maximum temperature increases are less than 0.16°C.

Figure 10.28 shows the distribution of the maximum temperature increase for each horizontal layer of the body at 40 MHz (a) and 900 MHz (b), for an incident power density of 1 mW/cm.^{2} At 40 MHz, the maximum temperature increases are obtained at the level

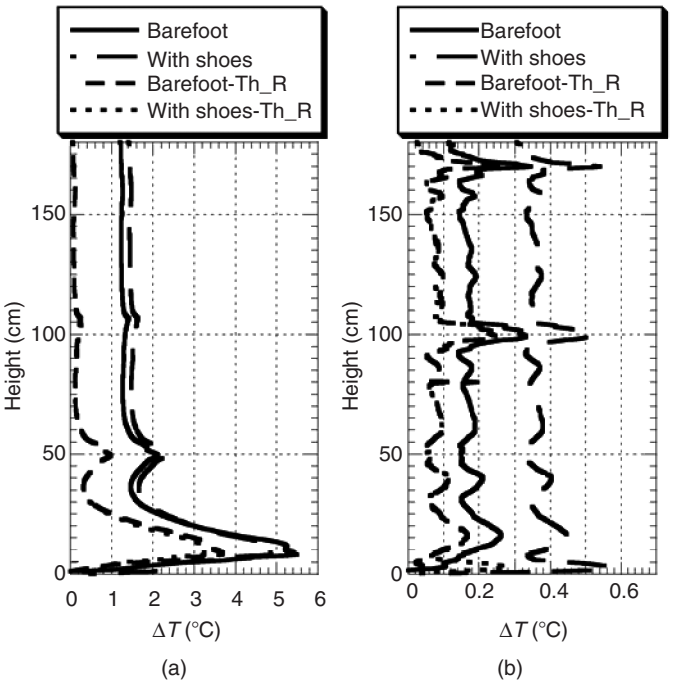


FIGURE 10.28
Layer peak temperature increase (ΔT) in the absence or presence of thermoregulation (Th_R) for a grounded subject barefoot or with shoes ($P_{inc} = 1\,mW/cm^2$). (a) $f = 40\,MHz$ and (b) $f = 900\,MHz$.

of the ankles, where the maximum local SARs also are located. The result showed that the presence of the shoes could influence temperature change. Since shoes are isolators from the thermal point of view, they prevent heat flow from going to the ground through them and provoking higher heating within the body. The only exception is in the ankle section, where heating was higher in the barefoot model because of the higher SAR values, at 40 MHz.

Also, the presence of the thermoregulatory mechanisms reduced the temperature increase almost uniformly along the body. Figure 10.28 illustrates clearly the role of blood convection in heat exchanges. In fact, even without active thermoregulation, heat could be spread from the point where its deposition is relatively high (e.g., the ankle at 40 MHz) to the rest of the body, by an increase in the temperature of the circulating blood. Therefore, even if power absorption is limited to one body region, temperature elevations may occur throughout the body. This is clearly visible at 40 MHz, where, although power absorption is mainly confined to the ankle region, in the absence of thermoregulation significant temperature elevations (about 1.4°C, $P_{inc} = 1.0\,mW/cm^2$—see Figure 10.28a) can be observed in the brain. The corresponding elevation in blood temperature elevation is about 1.46°C. It is interesting to note that at 900 MHz, in the absence of active thermoregulation, the brain temperature elevation (0.5°C, $P_{inc} = 1.0\,mW/cm^2$—see Figure 10.28b) is higher than blood temperature elevation (0.35°C), as a result of power deposition inside the brain.

10.5.5.2 Temperature Increments in the Head of a Cellular Telephone User

One consequence of RF power absorption in the human head exposed to the field emitted by a cellular phone is temperature increase in the head. In practical situations, in addition to RF power deposition, there are two other causes for temperature increase. The first one is the contact between the phone case and the user's head (ear and cheek, in particular), which blocks the convective heat exchange between the skin layers and the air. It causes

the temperature to rise in tissues around the contact zone. Obviously, this heating is independent of the radiated power, and indeed it was observed also for a wired phone. The second cause for temperature increase is the heating of the phone itself, because of the power dissipated in the internal circuitry, especially the power amplifier. This heating is transferred to the head tissues via thermal conduction.

Studies on temperature rises in the human head, associated with the field emitted by the cell phone, are usually conducted by using anatomically based head models, a numerical solution of the electromagnetic problem, and finite difference formulations of the BHE [161,164,172,187,220–223]. For example, the dissipation in the power amplifier was simulated by adding a power deposition of 250 mW at 900 MHz and 125 mW at 1800 MHz, uniformly distributed inside the upper part of the phone with a 50% efficiency [161]. The heating effects due to SAR, phone contact, and power dissipation in the amplifier were considered separately and were subsequently added together in order to obtain the temperature elevation. The maximum temperature elevations obtained in the ear and in the brain of a user's head are given in Table 10.12 for 900 and 1800 MHz. The ambient air temperature was assumed to be 24°C and a time interval of 15 min, approximating the duration of a long phone call. Although a steady state would not have been reached, the temperature elevation after 15 min is expected to be very close to the steady-state value [164].

The data shown in Table 10.12 reveal some interesting aspects. First, the temperature elevation induced inside the brain by SAR alone was less than 0.1°C, especially when the phone was kept in the ''cheek'' position. This configuration resulted in a marked reduction in power deposition inside the brain. Table 10.12 also shows that the mere contact of the cellular phone with the ear and cheek, even in a standby mode, in which no RF power is radiated, can cause a temperature elevation in the ear reaching as high as 1.5°C. This is due to the highly insulating properties assumed for the phone plastic shell. A negligible maximum temperature elevation of about 0.01°C, instead, is obtained in the external brain region. If the contribution from power dissipation in the amplifier is included, the induced temperature elevations are not significantly altered. It must be noted, however, that this result arises from consideration of power dissipation in the power amplifier alone. In the real situation, additional power dissipation is present in the internal circuitry of the handset, besides the power amplifier, and hence slightly higher temperature elevations may be observed [221].

Note: Results are for visible human (VH) adult, isotropically reduced child size (CS), and anisotropically reduced child-like (CL) numerical phantoms.

TABLE 10.12

Temperature Elevations Induced in the User's Head, after 15 min, by a Phone Equipped with a Dual-Band Monopole-Helix Antenna (Average Radiated Power: 250 mW at 900 MHz and 125 mW at 1800 MHz)

Frequency (MHz)	Position	Heating Cause	ΔT_{max} (°C)	$\Delta T_{maxbrain}$ (°C)
900	Vertical	SAR	0.221	0.061
	Cheek	SAR	0.136	0.023[a]
		Contact	1.543	0.012[b]
		Contact + power dissipation	1.544	0.012[b]
		Contact + power dissipation + SAR	1.581	0.023[a]
1800	Vertical	SAR	0.155	0.036
	Cheek	SAR	0.085	0.011[a]
		Contact	1.543	0.012[b]
		Contact + power dissipation	1.543	0.012[b]
		Contact + power dissipation	1.549	0.012[b]

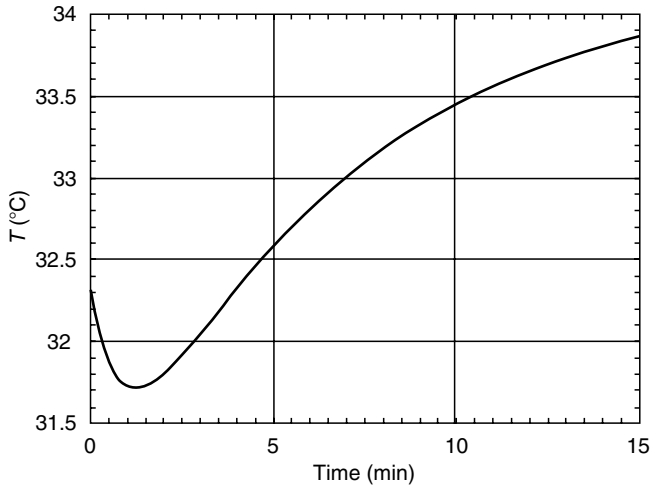


FIGURE 10.29
Time evolution of the temperature at a point on the ear in direct contact with a nonradiating phone.

The effect of the phone contact on the temperature evolution in the ear region is shown in Figure 10.29. It can be seen that when the phone was put in contact with the ear, the ear temperature experienced a quick decrease. This is because the phone was initially at ambient temperature (24°C), which was lower than the ear temperature. However, soon afterward, the heat supplied by the blood and conducted from the neighboring tissues stopped the decrease. Indeed, the temperature started to elevate, going beyond the initial value, because of the suppressed convective exchange with air.

When all heating sources are considered simultaneously, the results indicate that the maximum temperature elevation in the ear was almost entirely due to the contact effect, with only a very slight contribution due to SAR deposition in the ear region. However, the situation was completely different in the brain region. In fact, the heating effects due to SAR and phone contact tend to heat different parts of the brain. The contact-effect heating occurred in the lower external brain region, and the SAR-induced heating appeared mostly in the upper external brain region. Therefore, these two heating effects are not additive in the brain, and when they are simultaneously present, as opposed to the case when only one is considered, the result is that the portion of the brain affected by heating becomes larger. The peak temperature increase in the brain is therefore governed by the more significant of the two heating causes. At 900 MHz, SAR is more dominant, while at 1800 MHz, because of the lower radiated power, the two heating effects are comparable. Note that the ANSI/IEEE safety guidelines, which restrict the 1-g averaged spatial peak SAR to 1.6 W/kg, are associated with maximum temperature rises in the brain between 0.03°C and 0.09°C. These values are about 50 times lower than the threshold for thermal damage. The ICNIRP safety guideline of a 10-g averaged spatial peak SAR equal to 2 W/kg, results in maximum temperature rises in the brain between 0.1°C and 0.2°C, which is about 25 times lower than the threshold value.

10.6 Thermal Therapeutic Applications of Microwave Energy

Recent advances in technological development and in the understanding of EMF interaction with biological materials and systems have launched a broad range of biomedical applications. The following is a brief overview of computational techniques involved in

the development of ablative and hyperthermia therapies, including microwave cardiac ablation, endometrial ablation, and hyperthermia treatment of cancer. All of these therapeutic applications involve the use of microwave technologies to produce localized depositions of electromagnetic energy and, as a result, a rise of the local temperature in biological tissues. The target tissue temperature for the ablative treatments is about 65°C [224,225], whereas for the hyperthermia treatments, it is about 43°C [226]. The ablation treatments include the treatment for cardiac arrhythmias and for endometrial disorders such as menorrhagia. In all cases, the distribution of temperature increase must be carefully controlled in order to avoid excessive temperature increase in the surrounding healthy tissue. (See also Chapter 12 by Chou [284].)

10.6.1 Ablation for Cardiac Arrhythmias

Cardiac arrhythmias are mainly due to the presence of abnormal electrical sources or current paths in the cardiac tissues and are usually treated by destroying the tissue substrate where the electrical anomaly is localized [227–230]. This was performed by surgical resection initially, and later on by delivering a high-intensity DC shock with a defibrillator [227,230]. However, the high voltages and currents associated with the DC shock resulted in uncontrollable cardiac damages and severe complications. Subsequently, the use of RF EMFs to heat and destroy the arrhythmic tissue was proposed [230], and the advantages of microwave technology were demonstrated [228,229].

The RF ablation of cardiac tissue is usually performed using a unipolar arrangement, in which a catheter electrode placed into the heart delivers RF current to a large dispersive ground electrode on the skin surface of the patient. The RF current that flows from the catheter to the ground electrode following radial paths generates heat. While flowing from the catheter, the RF current density decreases as the second power of distance; consequently, the heat generation decreases according to the fourth-power law with the distance from the electrode. With this arrangement, the lesion (ablated tissue) is restricted to a small region (usually about 2 to 3 mm in diameter) contiguous to the catheter electrode, and the lesion dimensions cannot be extended by increasing the delivered power [225,227,229–231]. In microwave ablation, a catheter antenna is inserted into the cardiac chamber and is used to deliver MW power [225,228]. Since MW power deposition inside tissue decays with distance by following a second-power law, deeper lesions can be obtained compared to RF ablation [229,232–234].

In cardiac ablation treatments the lesion is usually defined as the region where temperature exceeds 65°C, which represents the threshold for irreversible damage of this tissue. This region must be large enough to ablate all the abnormal tissue responsible for the arrhythmia. Catheter antennas used for MW ablation have included monopoles [235,236], dipoles [229,237,238], and helices [232,239]. The design of a MW catheter antenna is a crucial point in MW ablation treatments and requires a complete study of the performance of the antenna imbedded in blood and in contact with the cardiac tissue. Performance parameters usually analyzed include the radiation pattern in the tissue; antenna impedance, which governs the bandwidth of the antenna; surface current suppression, in order to prevent heating of tissue along the catheter feeding cable; and dimensions of the induced lesion [240,241].

The design and performance evaluation of the microwave ablation antennas can be conducted by using computational tools and tested through *in vitro* or *in vivo* experimental studies [229,233,238,242]. Numerical tools allow the analysis of antenna performances under different operating conditions, and the evaluation of both electromagnetic power deposition and temperature increase in the tissue. In particular, the numerical evaluation of temperature increase induced inside the cardiac tissue allows the evaluation of blood flow influence on the induced lesion. This evaluation is of fundamental importance since the

D = 2.4 mm, D_1 = 1.4 mm, D_2 = 0.87 mm, D_3 = 0.3 mm

L_1 = 3 mm, L_2 = 0.5 mm, L_3 = 1.5 mm, L_4 = 1 mm

FIGURE 10.30
The cap-choke microwave catheter antenna.

presence of high blood flow rates inside the heart chambers provides a very effective heat removal process at the heart tissue surface so that the blood flow strongly limits the efficiency of both RF and MW ablation systems. Several numerical studies of SAR and temperature increase have been performed with the FEM [236,243–245] as well as the FDTD [246].

Figure 10.30 shows a cap-choke antenna mounted on an RG/178BU flexible coaxial cable operating at 2450 MHz [238]. The structure was realized by connecting an annular cap to the inner conductor of the cable, and a cylindrical coaxial choke to the outer conductor. A junction, filled with high-temperature epoxy resin, was used to separate the cap from the choke. Figure 10.31 shows the same antenna inserted in a two-layer cylindrical model of the heart. The heart model was used to study the influence of antenna position (touching or pressed into the cardiac muscle) and of blood flow (high or low) on the induced lesion. As an example, some computed results are presented in Table 10.13 for the amount of power to be delivered to the cardiac tissue to obtain lesions of different depths, under four operating conditions for an exposure duration of 60 sec [246].

10.6.2 Ablation for Endometrial Disorders

While still in the beginning stage, microwave and RF thermal ablation of the endometrium have been suggested recently as efficient and cost-effective alternatives to surgical resection as a treatment for dysfunctional uterine bleeding [247–251]. Techniques presently in

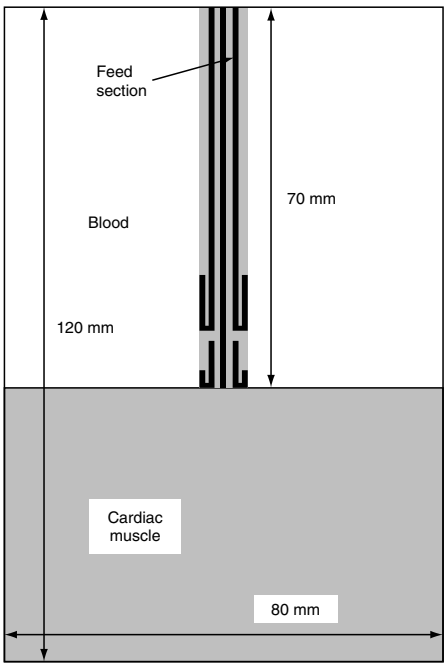


FIGURE 10.31
Cross section of the two-layer numerical model. The antenna's radial dimensions are not in scale.

[a] $\Delta T_{maxbrain}$ located in the upper external brain region.
[b] $\Delta T_{maxBRAIN}$ located in the lower external brain region.

TABLE 10.13

Microwave Power Required to Produce a Given Lesion Depth for Different Operating Conditions (Exposure Duration: 60 sec)

	Power (W)			
Lesion Depth (mm)	**Touch Low Perfusion**	**Touch High Perfusion**	**Pressed Low Perfusion**	**Pressed High Perfusion**
1	2.5	4.0	2.0	2.5
3	6.2	10	5.0	6.2

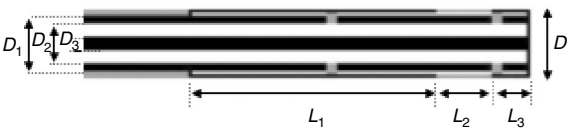
use include electrosurgery resection and Nd:YAG laser coagulation under direct hysteroscopic visualization [247,248,252–256]. The reported rates of complete amenorrhea are between 25% and 70% [253,256]. The variability arises principally from the unpredictable nature of induced thermal injury and perforation of the uterine wall [253]. Quantitative measures and patients' subjective reports of microwave endometrial ablation suggest a higher rate of satisfaction, acceptability, and life quality improvement [257,258].

In endometrial ablation, as in cardiac ablation, the design of the catheter antenna should be carefully tested to ensure the desired temperature increase (up to an increase of about 40°C in this case) in the tissue of interest. A sleeved-slot antenna designed for endometrial ablation operation at 915 MHz is depicted in Figure 10.32. The antenna configuration is similar to that of the catheter antenna for cardiac ablation, and is mounted on an RG8U coaxial cable. Figure 10.33 shows a comparison of the axial SAR distribution obtained from an FDTD analysis and from temperature measurements made in a cylindrical phantom filled with a muscle-equivalent material [259]. Two radial distances from the antenna axis, 2.5 and 7.5 mm, are shown. The SAR data obtained experimentally were normalized to the ones obtained from the FDTD simulation with 1.0 W of radiated power.

Figure 10.34 presents the lesion depth, defined as the region around the antenna where the temperature increase was greater or equal to 38°C (final temperature 75°C), as a function of the time of the exposure at different radiated powers. The curves were obtained by considering an antenna inserted in a cylindrical phantom filled with muscle-equivalent material. They simulate an antenna touching the endometrial tissue to be ablated. The lesion dimensions were evaluated as the depth from the antenna outer conductor. These curves can serve as guides in clinical trials where the antenna feeding power and time of exposure are key parameters to be chosen for a desired lesion dimension.

10.6.3 Microwave Interstitial Hyperthermia for Cancer Treatment

Hyperthermia cancer therapy is a treatment procedure in which tumor temperatures are elevated to above 43°C [226]. Investigations performed on cell cultures, tumor-bearing animals, and human patients have clearly shown that hyperthermia affords preferential



D = 12 mm, D_1 = 9.8 mm, D_2 = 7 mm, D_3 = 2.6 mm
L_1 = 45 mm, L_2 = 10 mm, L_3 = 7 mm,

FIGURE 10.32
A microwave catheter antenna for endometrial ablation.

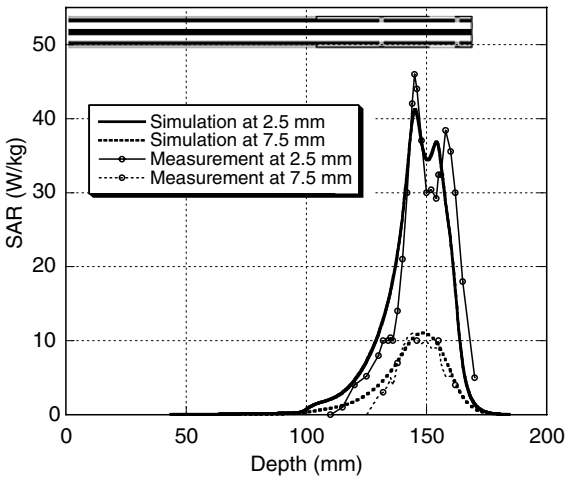


FIGURE 10.33
Comparison of axial SAR distributions obtained from FDTD and from temperature measurements made in tissue phantoms for the endometrial sleeved-slot antenna. The data are shown for radial distances of 2.5 and 7.5 mm.

killing of malignant cells, enhances the cytotoxic effects of many anticancer drugs, and potentiates the cell-killing ability of ionizing irradiation [260–266].

An important aspect of the development of applicators for microwave hyperthermia is the production of required temperature distributions in superficial and deep-seated tumors, that is, to produce temperatures in excess of 43°C in the tumor tissue, in order to guarantee the destruction of the malignant cells, while maintaining the temperature in the healthy tissue below 42°C to avoid thermal damage. In microwave hyperthermia, the antenna must provide efficient power delivery, good impedance matching at the frequency of operation, and a uniform SAR distribution in the tumor region. However, if the region to be treated is large compared to the field penetration depth, the required SAR uniformity cannot be achieved with a single microwave antenna, and the use of antenna

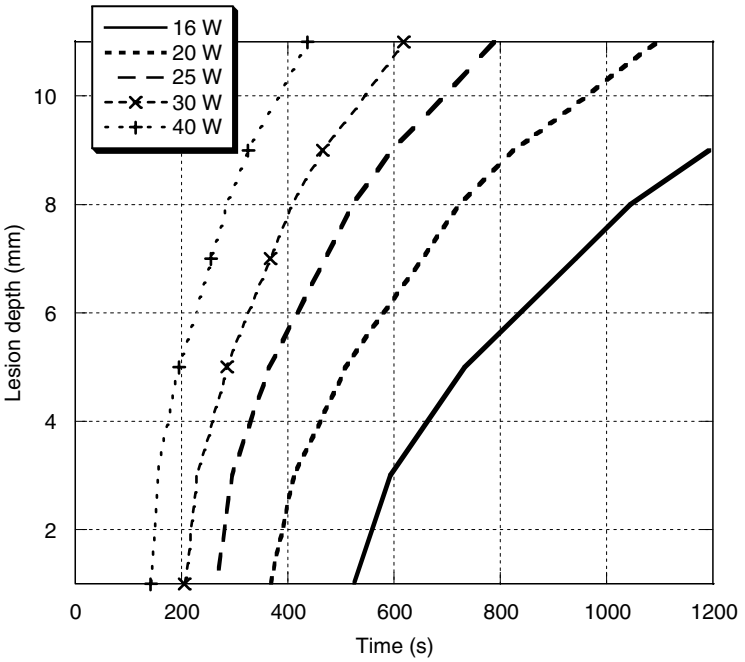


FIGURE 10.34
Endometrial lesion depth as a function of exposure duration for different radiated powers.

arrays becomes necessary. The following paragraphs present some computational results for thin catheter antennas designed for interstitial hyperthermia treatment of brain tumors.

Many investigations have been conducted on electromagnetic power deposition with regard to hyperthermia treatment for cancer. Most earlier studies were conducted analytically, modeling the catheter dipole antenna and surrounding tissue with a lossy transmission line [267–270]. Later, numerical and experimental studies were conducted on several antenna types, with the aim of optimizing antenna performances [270–274]. Considerable attention was devoted to arrays of antennas that have been studied both experimentally [275–277], by measuring the rate of temperature change caused by the radiated power, and theoretically, using antenna theory approaches [275,276,278] or approximate numerical procedures [277,279]. Indeed, antenna arrays have proved to be more suitable for increasing the region of uniform SAR deposition. More recent studies calculated, besides the electromagnetic power deposition, also the corresponding temperature increase. In fact, thermal analysis is a fundamental step in evaluating the effectiveness of the microwave applicator since it allows the assessment of the region where the temperature is above the threshold, and estimation of the required input power. Temperature distributions produced by interstitial antennas in tumor tissues have been experimentally evaluated by using microwave radiometry [277] and computed by using finite difference explicit solutions of the BHE [280,281]. A numerical solution of the BHE allows the analysis of the influence of different parameters such as blood flow on the temperature increase [280] and the development of clinical protocols [281].

Recently, an ADI solution of the BHE has been developed to study a 3-D array of catheter antennas inserted into a brain-equivalent phantom [282]. The antenna considered (Figure 10.35) was a sleeved-slot antenna mounted on a UT-34 coaxial cable [259,283]. An equilateral triangular array of the sleeved-slot antennas was studied in a phantom of brain-equivalent tissue in order to assess its capability in heating tumor regions of various dimensions [282]. Figure 10.36a shows the SAR distribution for 15-mm spacing among the antennas in the array; while in Figure 10.36b, contour plots at $\Delta T = 6^{\circ}\mathrm{C}$ for various radiated powers and for a 15-mm spacing are presented. The graphs shown in Figure 10.36a and b are for a horizontal plane passing through the antenna slot [282].

Results such as those in Figure 10.36 can provide guidance to clinical protocols regarding the input power and optimal geometry (array spacing) for achieving an efficient tumor heating. For example, there is a minimum input power below which three separated regions around the three interstitial antennas constitute the region with temperatures above 43°C. Once this power is exceeded, a simply connected domain is obtained.

It is interesting to note that blood flow is remarkably low in the necrotic core of tumor tissues compared to normal tissue. Moreover, the rate of blood flow in normal tissue increases during hyperthermia. These phenomena may be investigated by varying the blood perfusion parameter in the BHE. Computer simulations, performed by varying the blood perfusion parameter from 5% to 200% of the nominal value, showed that the heat removal mechanism becomes less efficient as the blood flow is decreased, and the effective region of hyperthermia therapy is enlarged [282]. Consequently, the reduced blood flow in the necrotic tumor core and the increase in blood flow in normal tissue can serve to facilitate hyperthermia therapy.

10.7 Concluding Remarks

Knowledge of internal electric and magnetic fields, induced current densities, and SARs is fundamental in the study of biological responses, health effects, and medical applications

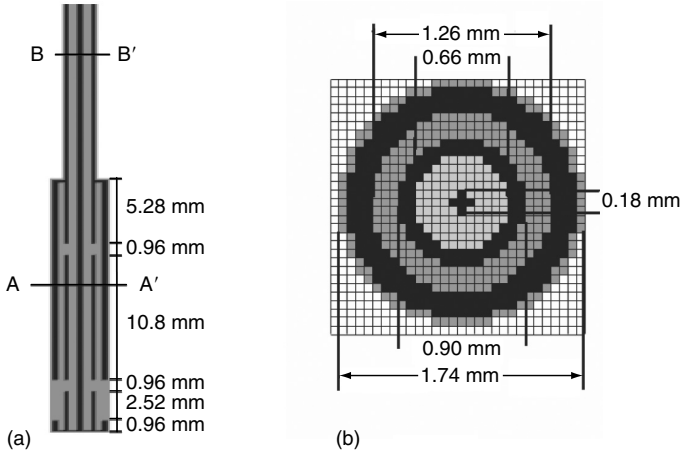


FIGURE 10.35
Longitudinal (a) and horizontal AA′ (b) sections of the sleeved-slot antenna.

of EMFs. Complexities of biological tissues and of the incident fields make closed-form analytical solutions impractical, and computer methods are needed to predict the internal fields and their distributions. Great strides have been made during the past decade in the area of numerical dosimetry using anatomically based models of the human body. Among the most valuable of the numerical methods for predicting field intensities and SAR calculations are the impedance method for use at lower frequencies, where quasi-static approximations may be made ($<\sim$40 MHz for the human body), and the FEM and FDTD methods, which may be used at any frequency of interest. For numerical calculations, the FDTD method requires a computer memory and computation time that is proportional to N. This is a considerable advantage over the computing methods, such as MoM or MoM–FFT. This chapter described the salient features of these methods and the many bioelectromagnetic exposure conditions for which they have been applied. Because of the limitations on the length of the chapter, only a few of the important recent applications of some of these methods were presented in some detail.

Note that numerical methods have matured to a level that they are being increasingly used by researchers in many laboratories for dosimetric calculations for important and

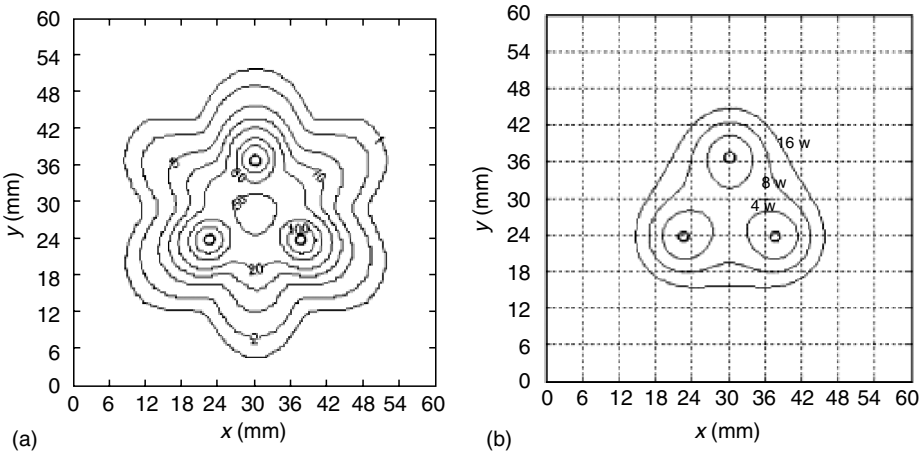


FIGURE 10.36
SAR distribution (a) and contour plots at $\Delta T = 6^{\circ}$C for various radiated powers (b), on a horizontal plane passing through the antenna slot, for 15-mm spacing among the antennas in the array.

meaningful bioelectromagnetic problems. Some of the future developments will involve improving the efficiencies of the various codes by techniques such as use of the expanding grid rather than the regular grid, elimination of the relatively shielded interior regions of the modeled space at higher frequencies, and use of truncated models of the body at microwave frequencies where there is a lack of coupling between the various regions of the body. Because of accurate modeling of the tissue heterogeneities and shapes, these models have and will continue to play an important role in emerging technologies with bioelectromagnetic concerns. Some of the likely applications are personal wireless and mobile communications systems, automotive devices such as electric automobiles and collision avoidance systems, medical devices such as MRIs, implantable pacemakers and defibrillators, applicators for hyperthermia, and other minimally invasive therapeutic and surgical procedures.

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11

Experimental EMF Exposure Assessment

Sven Kühn and Niels Kuster

CONTENTS

11.1 Objectives and Limitations

Experimental electromagnetic field (EMF) exposure assessments can be divided into two categories: (1) densitometry, that is, quantification of the incident EMF or the field characteristics at the location of exposed bodies but without their presence, and (2)

dosimetry, that is, quantification of the EMF induced in biological tissues or bodies. In most cases of compliance evaluation, verification that the actual exposure is below a certain value is paramount to accurate determination of the individual exposure. However, highly accurate predictions are needed for some medical applications, for instance, hyperthermia. The focus of this chapter is on dosimetry for frequencies above 10 MHz, often referred to as radio frequency (RF) dosimetry. At lower frequencies, experimental dosimetry is usually limited to measurement of the incident magnetic fields.

11.1.1 Dosimetry

Dosimetry is the science of quantifying the three-dimensional (3–D) distribution of EMF inside tissues and organs of biological bodies. The term is also applied with media having dielectric characteristics similar to biological bodies, for example, cell cultures, tissue-simulating liquids, etc. The induced field is the only field parameter that can interact with biological processes and therefore is referred to as the primary quantity.

Dosimetry usually refers to the assessment of the induced fields on a macro level, that is, the averaged induced fields across cells. Microdosimetry refers to the evaluation of fields across membranes, proteins, etc. This is a new field facing various basic problems such as material models and transitions between classical and quantum electrodynamics. Since the field of microdosimetry has not yet matured and since microdosimetry can be directly developed from locally averaged induced fields in the frequency range considered (<300 MHz), the term dosimetry in this chapter refers to marcodosimetry only.

The distribution of induced fields, particularly at RF, is a complex function of numerous parameters such as frequency, incident field strength, incident angle, field impedance, incident field distribution, polarization, size and shape (posture) of the biological body, tissue distribution, dielectric characteristics of the tissues, etc. In general, the dynamics of the induced field strength range over several orders of magnitude. In other words, the strength and distributions of the fields induced by the same incident exposure greatly vary with anatomy and body orientation with respect to the field and posture.

It is practically impossible to measure the fields noninvasively or *in vivo*; thus, measurements can only be obtained postmortem. The limitations [1] associated with postmortem evaluations include (1) accessibility to only certain tissues, (2) dielectric changes (e.g., lower tissue temperature and decreased blood content), (3) field distortions by the invasively introduced probe, and (4) large uncertainties associated with obtaining accurate measurements near and across tissue boundaries [2,3]. Only the integrated, totally absorbed power can be determined relatively easily by the calorimeter method (see Section 11.3.2.4).

Progress in computational electromagnetics along with the exponential growth of computational power and memory have facilitated determination of the field distributions in full anatomical human bodies with resolutions much smaller than 1 mm^3 (see Chapter 10 on RF modeling by Lin). The lossy and low-resonance properties of complex anatomical structures pose no special challenges for numerical methods (Figure 11.1). Limitations are only due to inadequate phantoms providing insufficient spatial resolution, for example, to accurately represent the scull [3].

Nevertheless, experimental dosimetry is often superior to numerical approaches for the compliance testing of commercial devices. Sources usually consist of highly resonant structures tightly assembled with other electronic and metallic structures. It is difficult to predict with reasonable and known uncertainty whether and how distortion of resonances and excitations of secondary structures might occur through simulations, especially when also considering the scattered fields of biological bodies. Small differences can

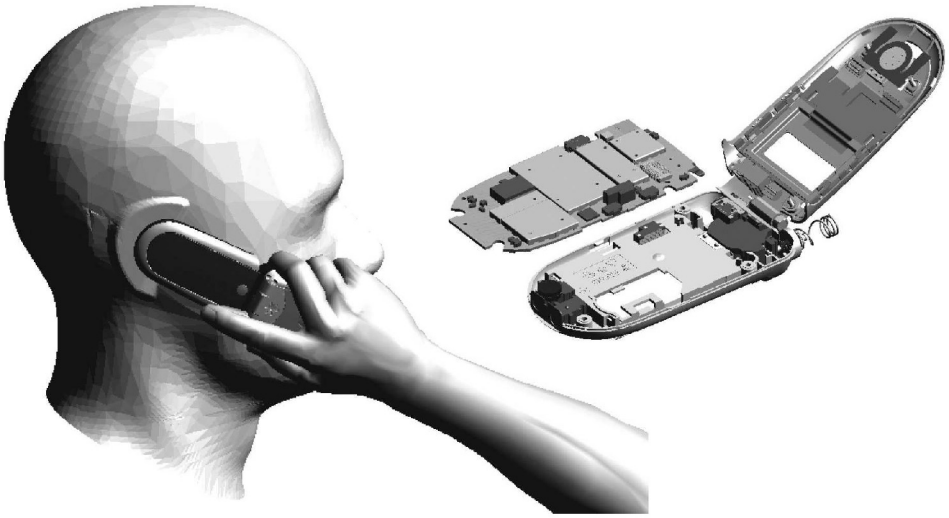

FIGURE 11.1
The latest advances in numerical techniques enable the computation of realistic scenarios without restrictions regarding spatial resolution and material description. The remaining difficulties are material parameters and manufacturing tolerances.

easily result in deviations of more than a factor of 2 from reality. Only when the structure is electromagnetically well-defined can good correspondence between simulations and measurement generally be achieved, that is, with an uncertainty smaller than 20% [4]. On the other hand, experimental techniques allow testing of the physical device under test (DUT) and do not require verification of the computational model.

The detailed information of the field distributions inside anatomical bodies obtainable by numerical methods is often irrelevant, since it cannot be generalized. For safety considerations, the upper boundary of exposure for the entire population rather than individual exposure is relevant. Hence, worst-case phantoms are often applied to assess the upper exposure boundary for specific exposure conditions, for example, from mobile transmitters. Since the degree of freedom for these phantoms is relatively large, they can be chosen homogenously (see Section 11.4.1). Recent evaluation of the procedures for mobile phone compliance testing has confirmed that conservative assessments are possible with a simplified experimental technique using homogenous phantoms [4–6].

During the past decade, considerable progress has been achieved in experimental dosimetric assessment. Since the late 1990s, experimental techniques have been routinely applied for evaluating transmitters operating in the closest vicinity of the body. They have proven to be more reliable, cheaper, and faster. A summary of these techniques and procedures is provided in this chapter. However, dosimetric assessments are limited to homogenous phantoms or to a few tissues in biological bodies. These assessments are normally applied for testing compliance with the basic restrictions or for the validation of results obtained by computational techniques.

11.1.2 Densitometry or Incident Exposure Assessment

Experimental dosimetry requires sophisticated instrumentation, significant expertise, and time. It is impractical for *in situ* exposure assessments. Therefore, easy to apply techniques and methods using a worst-case approach have been developed to determine compliance

with potentially hazardous induced fields by determining the incident fields. The worst-case concept derives the conditions for maximum induced fields inside the human body for an incident field strength in terms of the polarization, field distribution (plane wave), field impedance (plane wave), size, and posture of the human body and its dielectric properties. The induced fields are lower than a value X if the local maximum incident field strength of the E field and H field is below the value Y. Attempts to alter this conservative approach have yielded alternatives with an insufficient scientific and engineering basis (see Section 11.5).

Assessment of the incident exposure is simple for plane wave or far-field conditions. Under these conditions, the E field vector is perpendicular to the H field vector, and both are orthogonal to the direction of propagation. The ratio of the E and H fields is equal to the wave impedance Z at any location:

$$Z = \frac{E}{H} \tag{11.1}$$

and in free space

$$Z_0 = 377\,\Omega \tag{11.2}$$

Furthermore, the amplitude is constant over the entire volume of the absent exposed body. In these cases, it is necessary to measure only one component (E or H field) at one location in space. Unfortunately, far-field conditions rarely occur. However, far-field conditions are approximately met locally by changing the amplitude in space at distances larger than the extension of the reactive near-field zone:

$$r > \frac{2D^2}{\lambda}, \quad D \sim \frac{\lambda}{2} \tag{11.3}$$

$$r > \frac{\lambda}{2\pi}, \quad D \ll \frac{\lambda}{2} \tag{11.4}$$

where r is the radius or distance from the transmitting antenna/structure, λ the wavelength, and D the largest antenna dimension.

In other words, for distances meeting the requirements of Equation 11.3 and Equation 11.4, only the maximum of the field components must be determined to demonstrate compliance.

For any distance smaller than the requirements of Equation 11.3 and Equation 11.4, the maximum of both components must be spatially scanned to reliably predict that the maximal induced fields are below a certain limit. Fine volume scanning of transmitter antennas in the very near field yields greater uncertainty and is more time-consuming than dosimetric measurement in homogenous phantoms. Since such near-field assessments are more conservative than specific absorption rate (SAR) evaluations, they are rarely conducted in the context of exposure assessments.

11.2 Fundamental Quantities of EMF

The basic quantities necessary for electromagnetic exposure assessment are summarized in Table 11.1.

TABLE 11.1

Quantities, Symbols, and Units Used in Experimental Exposure Assessment

Symbol	Quantity	Unit
$\vec{E}$	E field (vector)	V/m
$\vec{H}$	E field (vector)	A/m
S	Power density (scalar)	W/m^2
$\vec{S}$	Pointing vector, $\vec{S} = \vec{E} \times \vec{H}$	W/m^2
W	Energy density	W/m^3
SAR	Specific absorption rate	W/kg
ΔT	Temperature increase	K
J	Current density	A/m^2
$\bar{\varepsilon}$	Complex permittivity, $\bar{\varepsilon} = \varepsilon_0 \cdot \bar{\varepsilon}_r$	F/m
ε_0	Permittivity of free space, $\varepsilon_0 = 8.854 \times 10^{-12}$	F/m
$\overline{\varepsilon_r}$	Complex relative permittivity, $\overline{\varepsilon_r} = \varepsilon_r' - j\varepsilon_r''$	
σ	Conductivity	S/m
μ	Permeability, $\mu = \mu_r \cdot \mu_0$	H/m
μ_0	Permeability of free space, $\mu_0 = 4\pi \times 10^{-7}$	H/m
μ_r	Relative permeability	
c	Specific heat capacity	J/(kg K)
ρ	Mass density	kg/m^3

11.2.1 Primary Quantities: Basic Restrictions

Restrictions on exposure to time-varying electric fields, magnetic fields, and EMF that are based directly on established health effects are termed basic restrictions (see Chapter 8 on standards by Van Deventer et al. [68]). Depending on the frequency of the field, the physical quantities used to specify these restrictions are either the current density (J) or the SAR. The dosimetric quantities used in current guidelines [7–10] are J for frequencies up to 10 MHz and the SAR for the frequency range from 100 kHz to 10 GHz. J is related to the internal electric field by Ohm's law:

$$J = \sigma E \tag{11.5}$$

E is the internal electric field, and σ is the complex conductivity of the tissue.

SAR is the ratio of the average rate of the absorbed power to the absorbing mass. It is defined as follows:

$$\mathrm{SAR} = \frac{\mathrm{d}}{\mathrm{d}t}\left(\frac{\mathrm{d}W}{\mathrm{d}m}\right) = \frac{\mathrm{d}}{\mathrm{d}t}\left(\frac{\mathrm{d}W}{\rho \mathrm{d}V}\right) \tag{11.6}$$

where dW is the incremental energy dissipated in an incremental mass dm included in an incremental volume dV and ρ is the mass density. SAR can also be calculated directly from the electrical loss, which is proportional to the mean square of the locally induced electric field strength E:

$$\mathrm{SAR} = \frac{\sigma E^2}{\rho} = \frac{J^2}{\sigma \rho} \tag{11.7}$$

and to a temperature increase by:

$$\mathrm{SAR} = c\frac{\mathrm{d}T}{\mathrm{d}t} \tag{11.8}$$

where c is the local specific heat capacity of the tissue. Equation 11.8 is valid only if the exposed body is in thermal equilibrium or in a steady thermal state at the beginning of the exposure, and either heat exchange processes can be neglected during the measurement interval or the processes are known to correct dT correspondingly. Current safety standards [7–10] for limiting EMF exposure provide maximum limits for basic restrictions for the uncontrolled/general public as well as for controlled/occupational exposure over the whole considered frequency range. The standards are ambivalent with respect to the quantity SAR. The debate among experts is whether SAR is a dosimetric quantity only relevant as a surrogate for thermally based models of EMF interaction or whether it can describe effects in addition to those related to temperature. SAR is directly related to the induced internal E fields as well as to the current density (Equation 11.7) but only directly related to the induced H fields for special cases.

11.2.2 Derived Quantities: Reference Levels or Maximum Permissible Exposure

The derived quantities are the electric field strength (E), magnetic field strength (H), magnetic flux density (B), and power density (S). As discussed in the previous sections, these quantities were derived from the basic restrictions using experimental or computational methods and represent conservative limits for worst-case exposure scenarios. Derived limits are called reference [7] or maximum permissible exposure levels [8,9]. Compliance with these quantities implies compliance with the basic restrictions. However, if the reference quantities exceed the derived limits, the relevant basic restrictions are not necessarily exceeded. In such cases, compliance can be demonstrated by dosimetric means.

In summary, reference levels are easy to assess if the plane wave or far-field conditions are met (see Section 11.1.2) and the resulting SAR and induced current densities are below the corresponding basic restrictions under all circumstances. Typical reference limits for occupational/controlled and general public/uncontrolled exposure are given in Refs. [7–10].

11.3 Experimental Techniques

11.3.1 Field Probes

E field probes have been used for microwave measurement since the early 1970s. The first power meters were developed by Aslan [11] and Rudge [12]. Aslan used a thermocoupling model consisting of two pairs of thin-film, vacuum-evaporated electrothermic elements that functioned as both an antenna and a detector. Rudge employed two small diode-loaded dipoles as sensor elements. The first prototype of an isotropic, miniature field probe was introduced by Bassen et al. [13] in 1975. Additionally, fiber optic field probes had already been proposed in the 1970s [14]. Comprehensive overviews of field probes are reported in Refs. [2,15].

11.3.1.1 Broadband E *Field Probes*

Diode-based field probes are well established and commonly used for dosimetric assessment. These probes consist of an appropriate field sensor, a detector, transmission lines, and read-out electronics (Figure 11.2). Three mutually orthogonal diode-loaded dipoles with an isotropic receiving pattern constitute the probe. To achieve good spatial resolution and broadband performance, electrically short dipoles are employed:

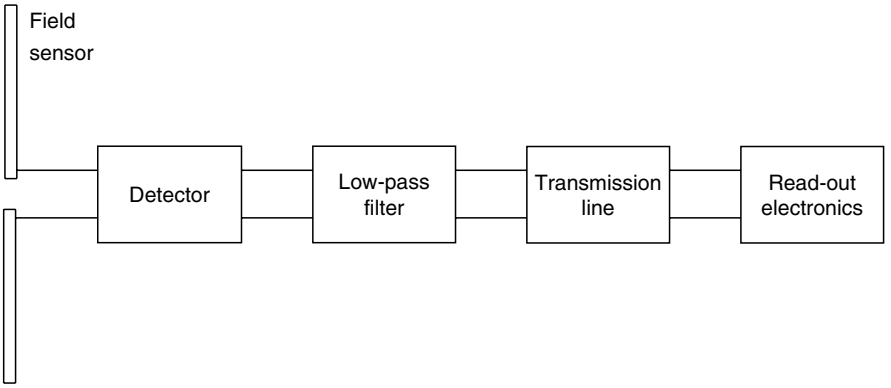

FIGURE 11.2
Simplified schematic of a broadband field probe.

$$\beta h = \frac{2\pi h}{\lambda} \ll 1 \tag{11.9}$$

where h is the length of a dipole arm, β the propagation constant, and λ the wavelength [15]. A flat frequency dependence cannot be achieved if the length of the probe is larger than a fraction of the wavelength ($< 0.05\lambda$). However, this limitation can be overcome by gradually resistive dipoles [16].

Typical isotropic E field probe sensors are shown in Figure 11.3. An RF detector diode (usually Schottky type) is located in the center of the dipole arms. If the detector diode is operated in the square-root law region, the diode current is proportional to the RF power delivered over the dipole to the detector diode. The detector diode is connected with a highly resistive line to the data acquisition electronics. The transmission lines must be designed precisely to eliminate distortions, such as parasitic sensor elements and scattering, which cause degradation of the pattern and unwanted polarization characteristics of the actual receiving antenna. High-resistive transmission lines are ideal for minimizing field perturbation and pickup effects. A detailed investigation of transmission line design

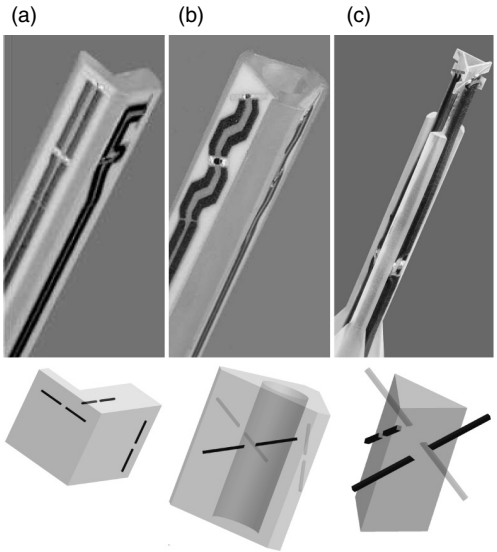

FIGURE 11.3
E field probe configurations: (a) E field probe for measurements in air with one sensor aligned to the probe axis and two orthogonally, (b) dosimetric probe for E field measurements in tissue-simulating liquids allowing integration of an optical proximity sensor in its center, and (c) miniature dosimetric probe with interleaved dipoles. (From IT'IS Foundation. With permission.)

can be found in Smith [17]. Current probe designs apply either thin-film ($R \sim 10\ \mathrm{M\Omega/m}$) [14] or thick-film ($R \sim 500\ \mathrm{M\Omega/m}$) [18] techniques.

The induced fields are recorded by the read-out electronics. The electronics typically consist of a measurement amplifier and an analog digital converter. The read-out field values are then optically forwarded. The optical transmission provides a galvanic decoupling and reduction of field-perturbing conductive parts near the DUT.

In addition to *E* field probes, *H* field probes are also available, the basic theory of which can be found in Whiteside and King [19]. *H* field probes and *E* field probes are basically similar, except for the field sensor element, that is, *H* field probes employ a small loop element instead of a dipole sensor. The disadvantages of loop-based sensors include a strong frequency dependence and currents induced by both *H* and *E* fields. Different methods for flattening the frequency dependence of loop probes have been proposed in Refs. [2,20]. The ratio of the voltage induced in a circular loop with diameter *d* by the *E* field and the *H* field is [19]:

$$\frac{V_E}{V_H} \simeq -\mathrm{j}2\pi\frac{d}{\pi} \tag{11.10}$$

Therefore, for electrically small loops only, that is, $d/\lambda \ll 0.01$, the current will mainly be determined by the magnetic field. In Poković [2], lossy covers were proposed to suppress the *E* field sensitivity of the loop.

In contrast to dipole-based sensors, thermocouple probes are true square-root law [a1]detectors. Such sensors are, for example, used in free space field probes by Narda [21]. These sensors are, however, impractical for dosimetric and near-field applications because of their generally lower sensitivity and dynamic range.

Thermistors are also true square-root law detectors and also small. They can have higher resolution than thermocouples but need more frequent calibration.

Based on the setup of these isotropic field probes, the measured field magnitude is yielded from the root sum square of the three orthogonal components:

$$|X| = \sqrt{|X_1|^2 + |X_2|^2 + |X_3|^2}\ X \in \{E,H\} \tag{11.11}$$

This summation is carried out regardless of any phase differences between the respective components. Hence, if maximum hold peak detectors are applied, the field reading represents the upper bound of the field magnitude.

The output signal of the probes just described is dependent on the following parameters:

- Frequency, modulation, and field strength
- Polarization, direction, and field gradients
- Material boundaries near the probe sensors
- Sources of interference (noise, static and low-frequency fields, vibration, temperature, etc.).

Therefore, it is necessary to quantify the influence of these parameters. Calibration under well-defined conditions is carried out to characterize the most crucial parameters for each probe individually. A detailed summary of different calibration methods for field probes and characterization of the parameters contributing to the measurement uncertainty is given in Poković [2]. All possible influences must be included in the resulting uncertainty assessment, since the conditions during the actual application of the probes differ

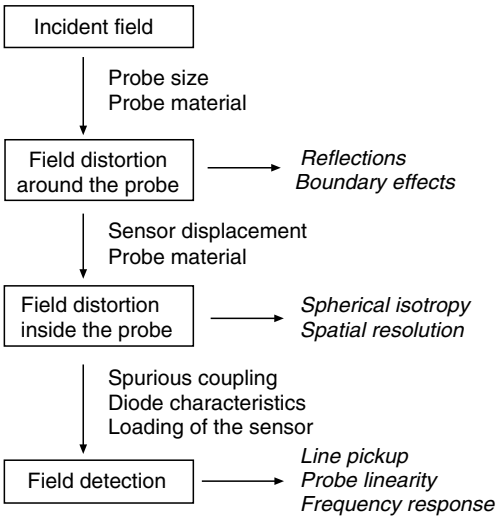

FIGURE 11.4
Impact of the constructional details on the probe characteristics.

considerably from the calibration scenario. Figure 11.4 provides an overview of different probe construction parameters that contribute to the probe characteristics.

Modern dosimetric field probes are available in the frequency range from 10 MHz up to 6 GHz. They have an isotropy error lower than ± 0.5 dB and sensitivities in the range of 1–10 $\mu W/g$ [22]. Modern probes have very small sensor tip dimensions (2.5 mm) and high spatial resolution, allowing measurements very close to material boundaries. A probe with reduced size (tip diameter 1.0 mm) was introduced by Poković et al. [23] and enables accurate dosimetric measurements for frequencies exceeding 10 GHz. Although this probe consists of only a single sensor element, isotropy is obtained by 120° rotation around the probe axis and an appropriately aligned sensor element. Probes for determining both the electrical and the magnetic field vector information are presented by Poković et al. [24]. This technique is based on measurements of five or more field components in space and reconstruction of the ellipse parameters by a combination of a downhill simplex and a Givens updating algorithm.

11.3.1.2 Electro-Optical Sensors

In contrast to RMS sensors, it is possible to measure fields over a broad frequency band in the time domain by exploiting electro-optic methods. Recent advances in semiconductor and photonic crystal research have provided the foundation for the next generation of near-field measurement equipment based on electro-optical methods. The basic concept of electro-optic probes is shown in Figure 11.5.

The most important electro-optic effects for measuring EMF are the Pockels effect and the quantum confined Stark effect (QCSE). The Pockels effect describes the refraction index dependence on the induced E field of anisotropic dielectric crystals such as cadmium telluride (CdTe) [25] or lithium nobiat ($LiNbO_3$) [26,27]. H field-sensitive crystals have also been determined, for example, cadmium manganese telluride (CdMnTe) [25]. The QCSE is based on the change of the absorption spectrum of a semiconductor structure under the influence of the electric field. Sensors exploiting the Pockels effect are reported in Refs. [25–27]. A detailed summary of electro-optic phenomena, materials, and applications can be found in Agullo-Lopez et al. [28]. Alternatively, the signal from the field sensor can modulate a small laser diode rather than the external electro-optical modulation.

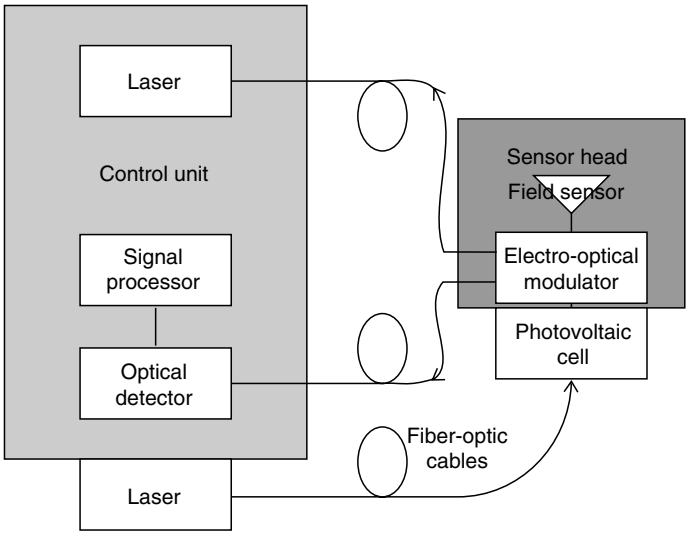

FIGURE 11.5
Principle of an electro-optic probe for EMF measurements.

The most common modulators are the Mach–Zehnder interferometer (MZI) as well as the already mentioned method of the direct modulation of the laser-diode current. The MZI (Figure 11.6) splits the light of a single-mode fiber into two parallel branches of $LiNbO_3$ waveguides. The feedpoints of the dipole are connected to electrodes that are located between the parallel branches, resulting in the antipodal modulation of the phase of the light. For recombined light, the phase modulation results in an intensity modulation. Sensitivities of 1–10 mV/(m Hz) can be reached. The upper cutoff frequency of these sensors is primarily determined by the length of the branches. For high sensitivity, the transit time through the interferometer must be much lower than the periodic time of the signal being measured. In Refs. [26,27], interferometers with a 3-dB bandwidth of 10 GHz were realized. A possibility to overcome this limitation could be the application of traveling wave modulation [29].

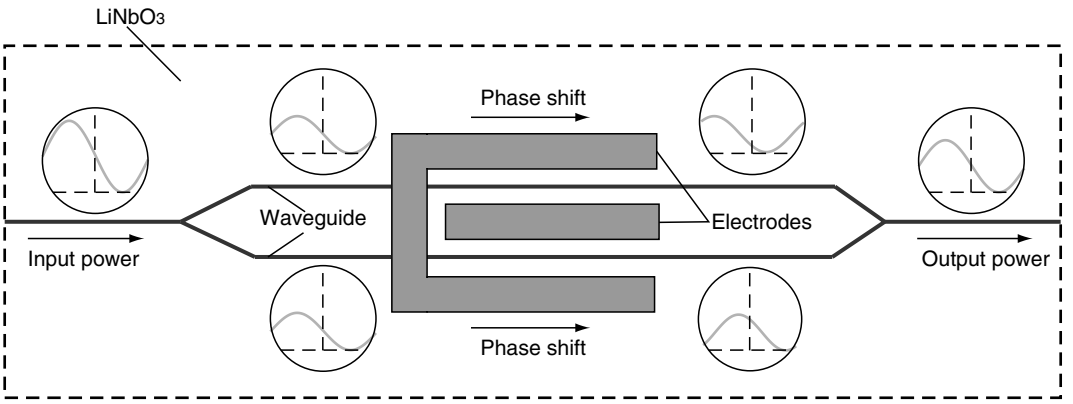

FIGURE 11.6
Schematic of an MZI. The light through the waveguide is modulated antipodally by the electrodes by changing the refractive index of the $LiNbO_3$ substrate.

Another approach reported in Ref. [25] uses only nonconductive parts in the sensor tip. Different types of crystals that are sensitive to electric and magnetic fields are used. Linear polarized light passing through the electro-optic crystal is reflected on a dielectric mirror and passes through the crystal again, where the polarization is changed. A beam-split polarizer transduces the ellipticity change into a change of the optical intensity. Sensors with a sensitivity of 10–400 V/m and 0.1–0.8 A/m in the frequency range from DC to 2 GHz were realized.

For modulation using QCSE, semiconductors with pn- or pin-junction structures are used. A varying reverse bias over the junction modulates the electric field and consequently the absorption and reflection spectra of the semiconductor as well. If the modulator is operated at a constant frequency, different reflection and transmission characteristics of the light and an intensity modulation result.

In addition to passive modulation (QCSE), direct modulation of a vertical cavity surface emitting laser (VCSEL) [30–32] has recently been applied. The current through the laser is directly modulated by the measurement signal. The VCSEL is especially suitable for modulation because of its high bandwidth, low threshold current, and low noise.

The MZI is the most popular modulation method among the three mentioned, and several commercial products are available based on this technology. Disadvantages include the limited ability to reduce its size as well as the bandwidth limitations. Passive modulators are relatively simple to manufacture as integrated circuits. Although passive modulators are inferior to MZI regarding sensitivity, the development of miniature field probes applying the VSCEL technology is currently the most promising approach.

11.3.2 Temperature Instrumentations

11.3.2.1 Temperature Probes

The locally induced SAR can also be assessed by temperature measurements, as summarized in Equation 11.8. A typical temperature rise curve as applied for SAR measurements is shown in Figure 11.7. Two types of temperature probes exist: those based on thermistors and those based on optical effects. The requirements for temperature probes for SAR assessments are:

- *Small size:* The probe must be small to resolve high temperature gradients, without disturbing the temperature distribution as well as the RF field.
- *Nonconductive materials:* Only electrically nonconductive materials prevent heating of the probe by induced currents and are transparent to EMF.
- *Low noise level:* Especially for dynamic temperature measurements, for example, SAR, small differences must be detected accurately. Therefore, the noise level should be much smaller than 10 mK.
- *Short reaction time:* A short reaction time is essential for SAR measurements, since the temperature rise (dT/dt) is only proportional to the SAR if heat diffusion does not occur. An appropriate probe must have reaction times much lower than 100 msec [33].

Temperature probes for SAR measurement using thermistors were first described by Bowman [34]. These probes utilize high-resistance thermistors that are connected through high-resistance lines to the read-out electronics. In Burkhardt et al. [35], a temperature probe based on a VITEK thermistor (BSD Medical Devices, U.S.A.) is presented. This probe has a noise level of 5 mK, a sensitivity of 5 mK/sec, and a tip diameter of

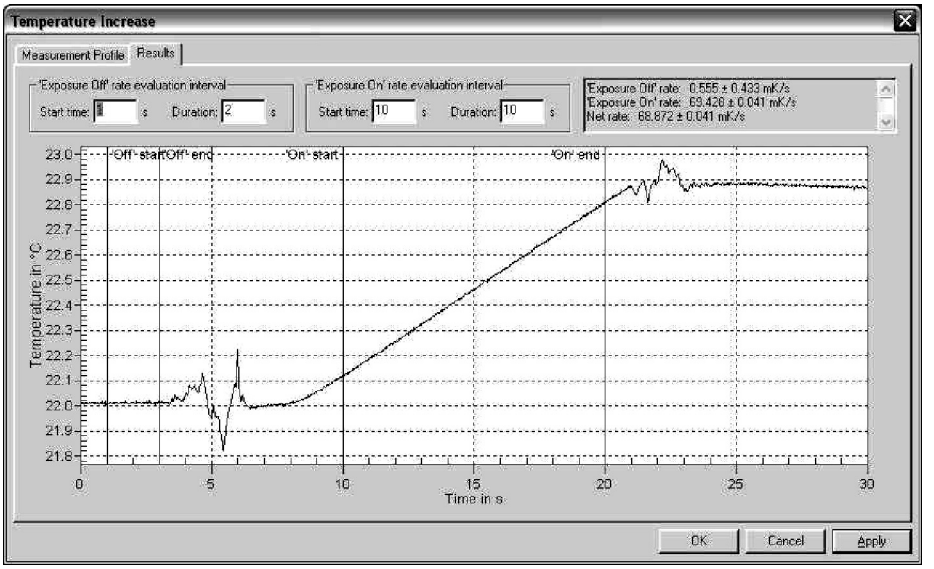

FIGURE 11.7
Typical temperature rise curve for SAR assessment. The linear part of the rise curve is applied for the calculation of the SAR. (Acquired using DASY4 from SPEAG, Switzerland.)

1 mm; however, it has a relatively slow response time of 240 msec. In Schuderer et al. [36], a novel temperature probe design for dosimetric assessments was introduced. The probe provides a spatial resolution of 0.02 mm^3, noise level of 4 mK, a sensitivity of 0.5 mK/sec, as well as a response time of only 10 msec.

In addition to the thermistor concept, temperature probes based on thermo-optical effects are also available. These probes are applied in high-voltage transformers, industrial microwave ovens, and hyperthermia treatment. One of the exploited effects is the decay rate of a phosphorescent layer at the tip of a fiber optic cable [37]. These modern commercially available probes have a noise level of 0.1 K and reaction times of 250 msec. Another exploited effect is the interferometric application of a cavity that is filled with materials that have highly temperature-dependent refraction indices. These probes reach sensitivities of 2–3 mK/sec [35].

11.3.2.2 Infrared Photography

The measurement of temperature by black body-equivalent radiation (infrared photography) is an alternative to invasive measurements using temperature probes. The resolution of infrared thermographs can be very high (<1 mm), and the sensitivity of affordable systems has continuously improved over the years. This was also one of the first methods to measure SAR [38], since the surface radiation can be recorded quickly using infrared cameras without perturbation of the incident field. Infrared cameras were also used to measure the temperature of Global System for Mobile Communications (GSM) mobile phones [39]. The technique has several disadvantages:

- It has limited sensitivity compared to temperature or dosimetric probes.
- It is limited to surfaces.

- The thermal radiation characteristics of the materials must be determined accurately.
- The background radiation must be homogenous.
- Evaporation and convection can cause substantial errors and must be controlled.
- Different aspect angles of the camera can cause different results.

11.3.2.3 Microcapsulated Thermo-Chromic Liquid Crystals

A novel idea to assess 3-D temperature distributions optically and in quasi real time was proposed by Suzuki et al. [40]. Microcapsulated thermo-chromic liquid crystals are suspended uniformly in a gel with the dielectric properties of human muscle tissue. The temperature of the gel is determined by measuring the light scattered from a laser beam that scans through the liquid. The technique has a limited dynamic range and sensitivity.

11.3.2.4 Calorimeters

Calorimetry specifies methods for measuring heat due to biological, chemical, or physical processes that are endothermic or exothermic. Calorimetric methods are suitable for determining average whole-body SAR, but they cannot reveal SAR distributions.

Calorimetry can be subdivided into two types:

- *Direct calorimetry:* The heat is determined directly using calorimeters.
- *Indirect calorimetry:* The amount of expressed heat is determined indirectly by measuring the amount of oxygen consumption and relating it to the oxicaloric equivalent of the reaction.

Basically, calorimetric dosimetry analyzes the heating and cooling processes of an exposed sample. Typical calorimeters used in microwave dosimetry are the Dewer flask calorimeter and the twin-well calorimeter [41].

11.3.3 Measurement Antennas

Different types of broadband matched antennas are usually applied for the frequency-selective exposure assessment of external fields. These measurement antennas are matched to 50 Ω to be compatible with standard RF measurement equipment. They are usually applied for far-field measurements of emissions by cellular telephony base stations, broadcast services, etc. Common broadband RF measurement antennas such as horn or logarithmic periodic antennas have a certain directivity. For example, for an antenna with a 45° beam width, more than 18 measurement directions are necessary for each polarization, since the receiving patterns do not have the shapes of square sectors. This reduces the applicability of these antennas for complex propagation scenarios, that is, locations where the received field is not dominated by a direct line of sight propagation path but by multipath reception. Tuned dipole antennas do not show a directivity in the radial direction, but they lack broadband operation. Conical [42] and biconical [43] antennas have the advantage of nondirectiveness in the radial direction and generally good broadband characteristics. If, for example, the ADD3D method [44] is applied in combination with a conical dipole antenna, the measurement orientations for a fully isotropic scan can be reduced to three different directions. In this case, the

isotropy is obtained by an antenna alignment similar to near-field probes, such that the resulting field is:

$$|E| = \sqrt{|E_1|^2 + |E_2|^2 + |E_3|^2} = \sqrt{|U_1|^2 + |U_2|^2 + |U_3|^2} \cdot AF \tag{11.12}$$

where AF is the frequency-dependent antenna factor in linear quantities (1/m) and U_i is the antenna output voltage at the three different antenna orientations. To obtain the antenna output voltages, a measurement receiver (see Section 11.5.1) connected via a well-characterized cable is applied. The antenna output voltage is:

$$|U_{i_{\text{antenna}}}| = |U_{i_{\text{receiver}}}| \cdot \text{ATT}_{\text{cable}} \tag{11.13}$$

where $|U_{i_{\text{receiver}}}|$ is the voltage measured with the receiver and $\text{ATT}_{\text{cable}}$ the attenuation of the cable in linear units. Other sources of attenuation, for example, attenuators to reduce the Voltage standing wave ratio (VSWR) of the measurement antenna, must be similarly considered.

11.4 Near-Field Scanners

11.4.1 Scanners for Dosimetric Compliance Testing

In dosimetric compliance tests, exposures from RF transmitters operating in close proximity to the body, for example, mobile phones or body-worn wireless devices, are compared to the basic restrictions (see Section 11.2.1). This is a complex task, since the exposure greatly depends on the device design, the position of the device with respect to the body, the external and internal anatomy, as well as the effect of the backscattered field on the device (Figure 11.8). In order to obtain a reliable assessment with acceptable effort, the standards must determine the maximum or 90th percentile exposure for the entire

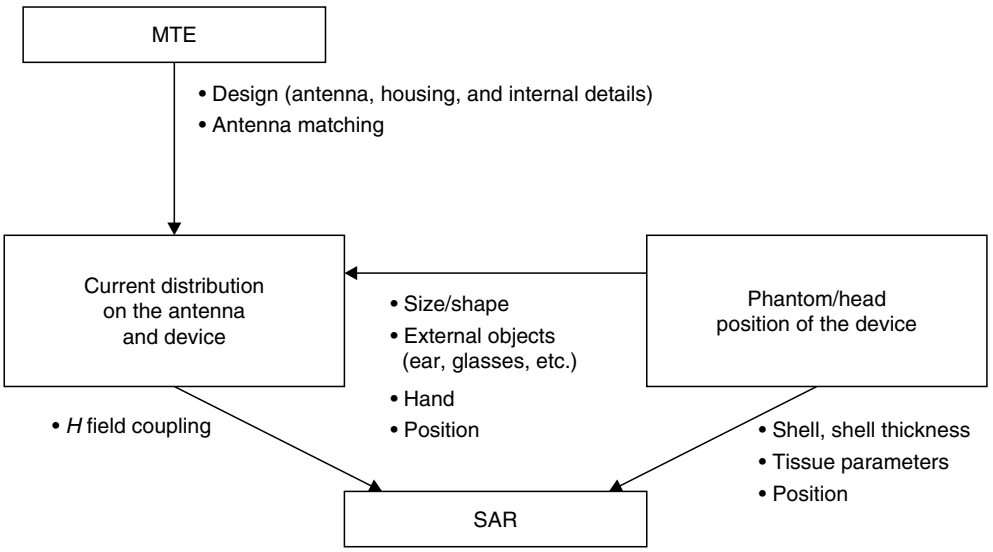

FIGURE 11.8
Overview of impact parameters for dosimetric compliance testing of mobile terminal equipment (MTE).

population that may be operating the DUT. Measurement standards have been developed by different organizations, for example, by the International Electrotechnical Commission (IEC), the Institute of Electrical and Electronics Engineers (IEEE), the Association of Radio Industries and Businesses (ARIB), Korea Electromagnetic Engineering Society (KEES), and others.

In general, a dosimetric evaluation requires the measurement of several hundreds of points distributed over a complex 3-D phantom. The task is divided into (1) searching for the location of the maximum absorption on a 2-D grid and (2) determining the peak spatial SAR value on a fine 3-D grid. Especially at high frequencies, these points must be determined with high accuracy to achieve low measurement uncertainty despite high attenuation and large spatial field variations. Automated dosimetric assessment systems are utilized to perform these compliance tests. A typical configuration of a dosimetric assessment system is shown in Figure 11.9 and Figure 11.10. A computer-controlled six-axis positioner with excellent positioning repeatability of ± 0.2 mm is used to move the dosimetric E field probe within the scanning grid, which can be adaptive, for example, along a surface that is being detected during the scanning job. The different field probe designs have already been discussed in Section 11.3.1. Phantoms, for example, the specific anthropomorphic mannequin (SAM) phantom, elliptical phantom, etc., and tissue-simulating liquids (see Table 11.2) have been developed and validated with respect to the 90th percentile requirements [45]. A detailed description is provided by Schmid et al. [18]. Because of the strong curvature of the SAM phantom, sufficient accuracy can be obtained only when the measurements are taken with the probes aligned normal to the phantom boundary. The most elaborated components, procedures, and algorithms are employed (Figure 11.10), and an expanded total uncertainty ($k = 2$) for the compliance test of less than 20% can be achieved with even better repeatability.

It should be noted that this approach provides reliable conservative estimates of the maximum peak spatial SAR that might occur in the user population but little information about the exposure of specific tissues.

11.4.2 Fast Dosimetric Scanners

Dosimetric compliance tests of near-field sources are extremely time-consuming, especially as all configurations with all accessories must be evaluated. SAR patterns provide

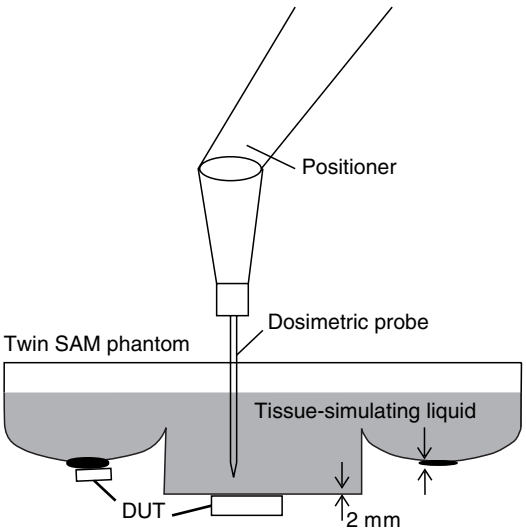

FIGURE 11.9
A dosimetric assessment systems consists of a computer-controlled positioner, a dosimetric field probe, and a phantom (left and right head, flat region for system validation) filled with tissue-simulating liquid.

FIGURE 11.10
DASY4 dosimetric assessment system. (From SPEAG, Switzerland.)

further valuable information such as (1) the output power under loaded conditions as indicated by a different peak spatial SAR if the absorption pattern is not altered and (2) changes in the internal RF path, for instance, by poor contacts, as indicated by a modified SAR pattern. Therefore, fast SAR scanners are desirable for precompliance testing as well as for research and development. Such scanners would also be greatly beneficial for

TABLE 11.2

Electric Parameters of Head and Body Tissue Equivalent Liquids at Various Frequencies

	Head		Body	
Frequency (MHz)	ε_r	σ (S/m)	ε_r	σ (S/m)
150	52.3	0.76	61.9	0.80
300	45.3	0.87	58.2	0.92
450	43.5	0.87	56.7	0.94
835	41.5	0.90	55.2	0.97
900	41.5	0.97	55.0	1.05
915	41.5	0.98	55.0	1.06
1450	40.5	1.20	54.0	1.30
1610	40.3	1.29	53.8	1.40
1800–2000	40.0	1.40	53.3	1.52
2450	39.2	1.80	52.7	1.95
3000	38.5	2.40	52.0	2.73
5800	35.3	5.27	48.2	6.00

quality assurance purposes, when integrated into production lines (every device tested for compliance, output power, and RF performance).

An algorithm to extrapolate peak spatial SAR values from the 2-D area scan performed at the phantom surface was presented by Kanda et al. [46]. Another algorithm reducing the measurement time of an area scan lasting 5–10 min was proposed by Merckel and Fleury [47].

Two additional approaches have been presented to further accelerate the assessment. The first approach, using a scanner based on incident *H* field measurements, is described in the next section. The second approach is based on a sensor array implanted in a solid flat phantom (Figure 11.11). The phantom is filled with a broadband tissue-simulating gel (300 MHz up to 6 GHz), with sensors located 4 mm below the surface. The density of the sensor array (15 mm) is sufficient to reliably assess the exposure. The measured SAR values of all sensors are acquired and integrated in parallel, such that the total assessment time is less than 3 sec, even for TDMA (Time Division Multiple Access) signals with complicated frame structures.

11.4.3 Incident Near-Field Scanners

In the reactive near field, field gradients are generally very high, and the field impedance differs greatly from the far-field impedance and rapidly changes over short distances. Hence, both *E* and *H* fields must be assessed, based on requirements regarding spatial resolution and isotropy that are similar to those of dosimetric scanners. In addition, distortions by reflections from instrumentation must also be carefully evaluated and included in the uncertainty budget.

General purpose scanner systems are equal or similar to those used for dosimetric evaluations, except that *E* and *H* field probes optimized for free space are used instead of

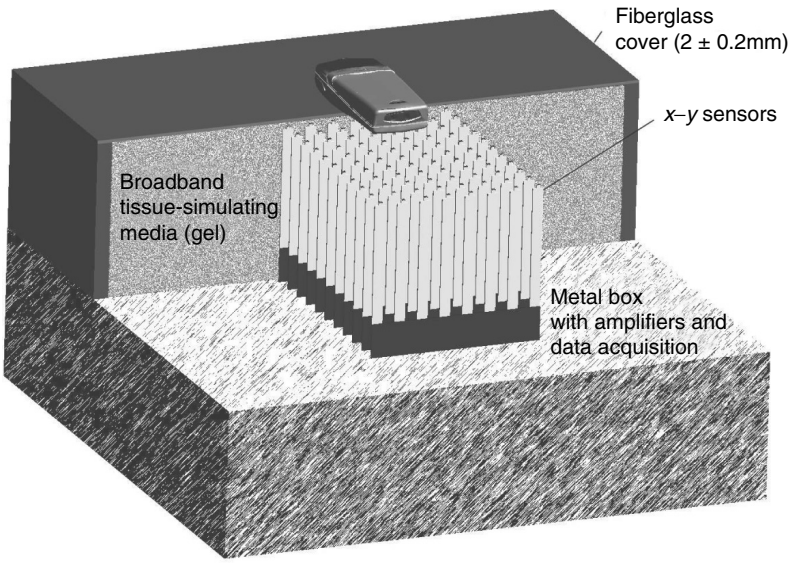

FIGURE 11.11
The concept of a fast dosimetric scanner based on a dense array of sensors completely immersed in a broadband tissue-simulating medium. In order to provide a quick response, the signals of all sensors must be amplified and integrated in parallel for the frame structure and to increase the signal-to-noise ratio. The high-resistive sensor leads are vertical to minimize field distortions.

dosimetric probes. Since the scan procedures do not need to follow complex surfaces, three-axis systems [48] are also suitable. However, such evaluations are rarely used to test compliance with safety limits, since the limits are significantly more conservative and the measurement resources, time required, and uncertainty budget are higher than for dosimetric assessments. Nevertheless, such measurements are valuable for the validation of numerical results [49] or to test compliance with interference limits in the close near field, for example, for hearing aids [50].

A specialized near-field scanner was proposed and developed to test the precompliance of mobile handsets with safety limits [51]. Its underlining concept is based on the primary interaction mechanism of near-field exposure [52], that is, the local SAR is approximately proportional to the square of the incident magnetic field at the surface of the phantom:

$$\mathrm{SAR} = \alpha H_s^2 \tag{11.14}$$

The magnetic field is scanned in a reference plane above the DUT using a loop antenna array. The factor α is determined by relating a traditional compliance measurement inside the phantom to the magnetic field scan in free space for a certain DUT. The system can predict the SAR within 30 sec. The main disadvantage of such a system is that it does not simulate a realistic load to the antenna of the DUT.

11.5 Incident Field Evaluations in the Far Field of Transmitters

Evaluation of the exposure in the far field of a transmitter is usually conducted for fixed transmitters such as radio and TV broadcast antennas, radar sites, or cellular base stations. Exposure assessments are carried out in areas that are generally accessible or restricted to qualified working personnel. Compliance is tested with the reference limits by assuming free space field impedance, that is, by E field evaluation. As described in Section 11.1.2, only one measurement point is required under real far-field conditions. However, actual environments usually involve nearby reflectors, that is, a scanning procedure or statistical knowledge about the field distribution is needed to determine the maximum exposure.

Broadband instant measurements are often insufficient, since the evaluated transmitters do not always operate at maximum power, for example, in the case of base stations, the transmitted power is dependent on the traffic. In such cases, information on the maximum exposure with respect to the measured exposure must be available and soundly applied to extrapolate the worst-case exposure. Table 11.3 lists the parameters that are necessary to extrapolate the worst-case exposure and to reduce the uncertainty of the actual measurement campaign. It is easier to determine the measurement methods when additional parameters are known. General sources of error are:

- Field perturbation by measurement personnel, for instance, reflection and absorption of EMF due to the body of the measurement engineer
- Application of the measurement antenna, for example, nonobservance of antenna directivity and polarization
- Application of ineffectively decoupled cables, for instance, acting as secondary antennas

TABLE 11.3

Important Parameters of RF Transmitter Sites Assessed in the Far Field

Site Parameter	Explanation
Location	The location of the transmitter with respect to the measurement point
Line of sight/nonline of sight	Determines if a prevalent propagation path may be expected
Type of site	Single- or multiple-antenna site
Antenna directivity	Antenna beam characteristics
Antenna radiation direction	The direction the transmitter radiates
Antenna power at measurement	The antenna input power at the time the measurement takes place
Maximum antenna input power	Maximum permissible antenna input power
Frequency	Frequencies at which the site transmits
Communication system	Communication system that is used, that is, which signal characteristics are expected
Other sources of radiation	The field at the measurement point if the assessed transmitter is switched off

- Application of the measurement receiver, for example, incorrect measurement settings
- Selection of the measurement point, for example, measurement points that are not feasible to give the maximum EMF exposure, measurement points close to bodies that influence the measurement antenna's calibration.

Different methods for assessing EMF exposure in the far field have been proposed. One approach is the scanning method. This method requires the engineer to slowly move the measurement antenna with varying polarizations and directions through the volume of interest [53]. The measurement receiver operates in maximum hold mode during the assessment, that is, the maximum field value is determined and compared to the reference values. Another method is based on the examination of several well-defined points in the area of interest. In this case, the antenna is mounted on a tripod, and the different directions and polarizations are examined at the considered points [54]. The first method is conservative but sensitive to the position of the measurement operator with respect to the antenna. The second method can be performed with the measurement engineer further away, but the number of measurements in the volume is small. A combination of both methods is presented in Coray et al. [55], that is, first the region is scanned for the field maximum in the area of interest, and then an isotropic and frequency-selective measurement is performed at the location of the maximum.

Far-field techniques are also often employed in the near field of transmitters, for example, on transmitter towers. Some standards allow a spatial averaging of E field evaluations [9], the rationale of which is based on the whole-body SAR limit. However, this constitutes a relaxation of the safety concept, since it does not consider H field coupling as the dominant mechanism in the near field nor the limits of peak spatial SAR. Based on current knowledge, such relaxations do not exclude violations of the basic restrictions.

The advantages and limitations of different measurement techniques to assess exposure from unknown transmitters are discussed below.

11.5.1 Broadband Measurements

Broadband measurements are especially applicable for survey measurements. The field is measured and automatically summed over a broad frequency range. No information on

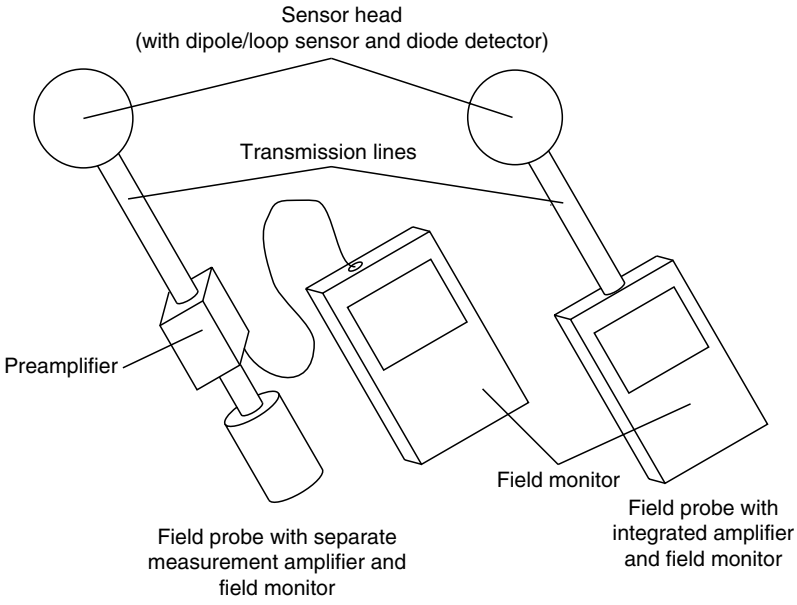

FIGURE 11.12
Schematic of the most common designs of broadband RF survey meters.

the spectral characteristics of the field is available. Therefore, if a broadband meter is used for compliance testing, the measured field value must comply with the lowest permissible limit defined in the measurement range of the meter. Broadband survey meters are relatively inexpensive and easy to apply. Hence, these probes are often used for field measurements.

Figure 11.12 displays typical broadband field survey meter designs. Figure 11.13 displays the frequency response of two broadband probes. The field value measured with probe 1 must comply with the lowest limit in the frequency range from 10 MHz to 1 GHz, whereas probe 2 must comply with the lowest limit between 100 MHz and 10 GHz. The overlapping frequency range is counted twice if the exposure values are added to cover the entire frequency range. Some broadband probes are designed to reflect the frequency dependence of the limits. In all cases, it is advised that the off-band response of

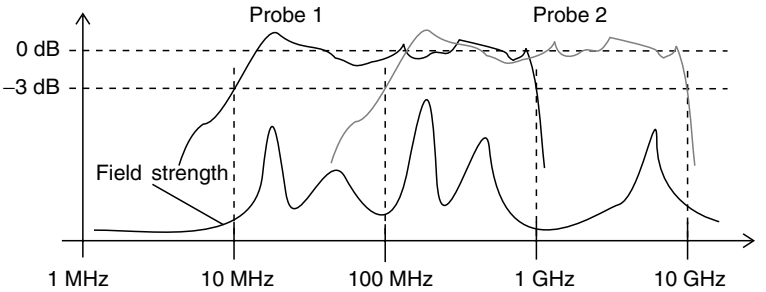

FIGURE 11.13
Frequency response of two broadband field survey meters. The fields in the frequency ranges are summed up. If the fields from probes 1 and 2 are summed again, then the fields in the overlapping frequency range are accounted for twice.

these probe systems be carefully evaluated. If a specific transmitter is the dominant source, compliance testing is greatly simplified [56].

In addition to the frequency response, broadband probes have a certain time-domain transfer function. When pulsed fields are measured, this response must be compensated. However, for this compensation, information on the time-domain characteristics of the measured field is necessary. In summary, the main sources of uncertainty regarding broadband survey meters are:

- Calibration
- Linearity
- Frequency response
- Isotropy
- Time-domain response
- Temperature response

In conclusion, the accuracy of broadband evaluations is significantly limited but generally conservative.

11.5.2 Frequency-Selective Measurements

Frequency-selective measurement techniques can overcome the issue of the unknown spectral composition of the field. However, the execution of the measurement is more complicated, such that insufficiently trained personnel are likely to produce erroneous results.

Measurements in the frequency domain are performed with a measurement antenna, as described in Section 11.3.3, that is connected to a spectrum analyzer (Figure 11.14). The spectrum analyzer mixes the received RF signal down to the base band. A filter is swept in frequency over the considered sweep bandwidth. The signal after the filter is detected using user-definable detectors. Most spectrum analyzers provide video filters for additional filtering (smoothing) of the spectral signal. Setting the sweep and filter parameters can significantly impact the measurement result. Optimal settings for GSM and Universal Mobile Telecommunications System (UMTS) based on a simulation approach were recently presented by Olivier and Martens [57]. The impact of summing up parts of the spectrum because of nonideal filters was investigated by Joseph et al. [58]. Modern analyzers also provide a zero-span mode. The RF signal is mixed down to the base band, and only the time-domain envelope of the signal is displayed afterward. This mode may be applied, for example, to investigate the time-domain characteristics of an unknown communication system. Additionally, it is especially useful to measure pulsed

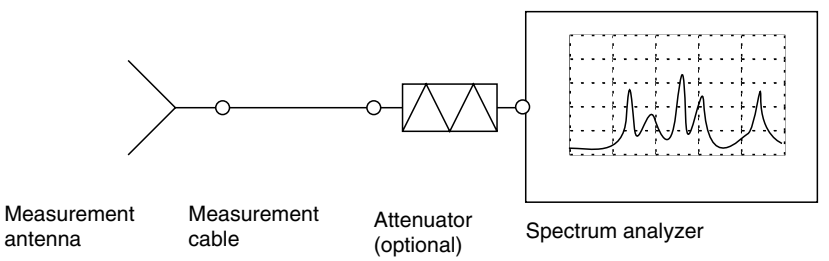

FIGURE 11.14
Schematic of a frequency-selective measurement of EMF.

signal forms, as this signal form is often used in communication systems. In summary, the application of spectrum analyzers is a complex subject. Measurement recommendations dealing with frequency-selective measurements should always describe the spectrum analyzer settings to produce feasible and comparable results. Nevertheless, the measurement engineer should still test the actual applicability of these settings for his particular measurement equipment.

The main sources of uncertainty regarding frequency-selective measurements are:

- Calibration of the spectrum analyzer, cable, and measurement antenna
- Linearity of the spectrum analyzer, cable, and measurement antenna
- Frequency response of the spectrum analyzer, cable, and measurement antenna
- Demodulation method of the spectrum analyzer (detector type)
- Temperature response of the spectrum analyzer, cable, and measurement antenna
- Mismatch between measurement equipment

Although the frequency-selective measurement method overcomes most of the issues regarding broadband survey meters, it is not sufficient to soundly identify the exposure from different transmitters at the same frequency. In this case, measurement receivers should be applied.

11.5.3 Code-Selective Measurements

Code-selective measurements are especially necessary if the exposure from a specific transmitter applies code division multiple access (CDMA), for example, if a UMTS is to be assessed. In the case of UMTS, all base stations usually transmit in a single-frequency band. With a frequency-selective receiver, it is not possible to discriminate between exposure from different base stations, since a single-frequency band is used and the channels are multiplexed in the code domain. Code-selective receivers decode the signal received from a base station, that is, the receiver is able to discriminate between a field strength received from the base station of interest and other noise-like sources. The receiver measures the field received from the base station of interest only if the particular scrambling code is used for decoding. Basically, the same sources of uncertainty must be considered for code- and frequency-selective measurements. However, in contrast to frequency-selective measurements, the modulation of the signal does not increase the uncertainty but rather the possible nonorthogonality of the respective scrambling codes. Many of the typical measurement receivers for UMTS base station measurements (e.g., Rohde and Schwarz TSMU [59], Anritsu ML8720B [60]) provide insufficient sampling rates for swept scanning. Others overcome this limitation, for example, Narda-STS SRM-3000 [61].

11.6 Typical Maximum Peak Spatial SAR Exposures

The daily local RF exposure of the general public has increased by several orders of magnitude with the introduction and proliferation of mobile handsets. This has triggered concern among health agencies and the public, since the highest exposed tissue is the brain. Figure 11.15 and Figure 11.16 display the frequency of worst-case SAR from mobile phones measured according to Refs. [62,63]. Figure 11.15 represents the typical SAR

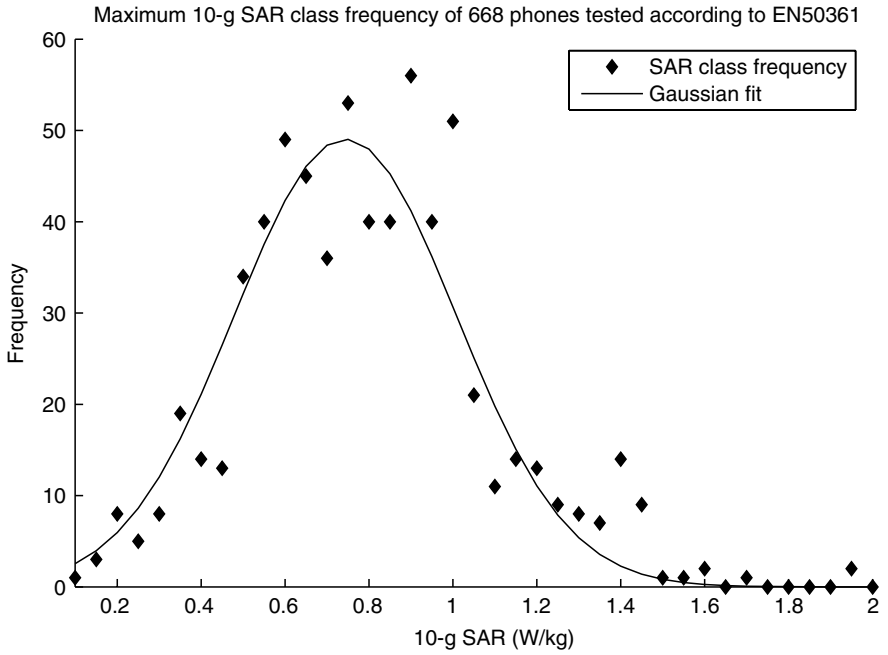

FIGURE 11.15
Statistical distribution of maximum 10-g SAR measured for 668 mobile phones according to EN50361. (From German Federal Office for Radiation Protection, http://www.bfs.de/elektro/hff/oekolabel.html, 2005.)

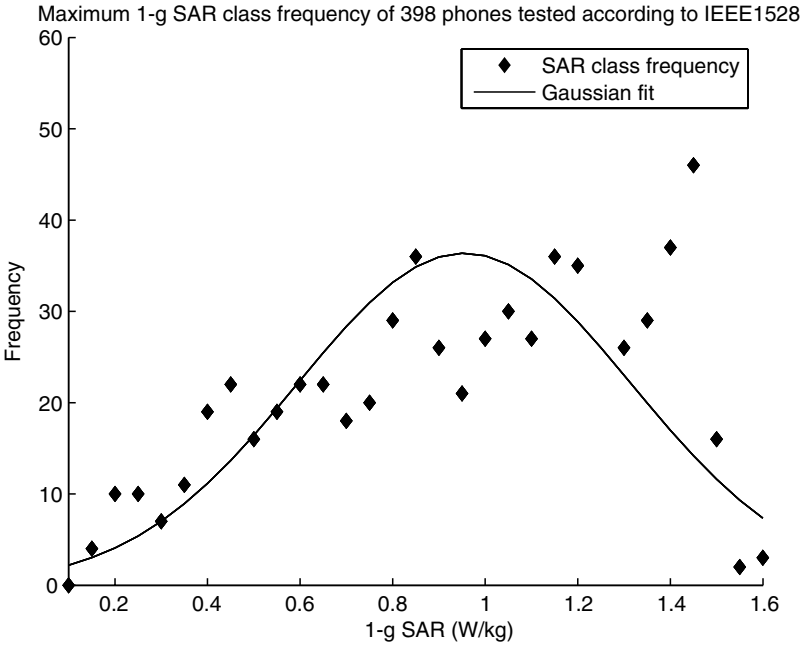

FIGURE 11.16
Statistical distribution of maximum 1-g SAR measured for 687 mobile phones according to IEEE-1528. (From Federal Communications Commission, http://www.fcc.gov/cgb/sar/, 2005.)

TABLE 11.4

Worst-Case Peak Spatial SAR of a Set of Wireless Indoor Devices

Device Class	Frequency Range (MHz)	Worst-Case 10-g SAR (W/kg)
Baby surveillance	40–863	0.077
DECT	1880–1900	0.055
WLAN	2400–2484	0.81
Bluetooth	2402–2480	0.49
PC peripherals	27–40	≤0.005

Note: An absolute worst case for all commercially available products cannot be estimated based on these data.

values for Europe (mean 10-g SAR: 0.74) [64] and Figure 11.16 for North America (mean 1-g SAR: 0.96) [65]. The different averaging masses are due to different legal regulations in Europe and the United States. These values are a considerable percentage of the limits. A recent statistical analysis of the Federal Communications Commission (FCC) SAR database found that the SAR values of newer phones are typically lower than of older phones despite their greatly reduced size.

SAR measurements of devices operated in home and office environments were reported by Kramer et al. [66]. A summary of the maximum SAR values determined in this study for several types of transmitters is given in Table 11.4. It should be noted that under worst-case scenarios, the SAR values measured for WLAN and Bluetooth communication systems are in the same range as those for mobile phones.

11.7 Typical Far-Field Exposures

A study regarding indoor incident field exposure from cellular base station sites was conducted by ARCS (Austria) [55] in the city of Salzburg. Table 11.5 shows two

TABLE 11.5

Results from Indoor Incident *E* Field Measurements Conducted in an Austrian City [55]

Base Station	Distance to Base Station (m)	Cumulative Incident *E* Field (V/m)	Distance to Base Station (m)	Cumulative Incident *E* Field (V/m)
1	196	0.37	374	0.35
2	88	0.51	108	0.89
3	9	0.034	15	0.037
4	16	0.62	8	1.00
5	85	0.94	152	0.75
6	81	1.8	85	1.71
7	4	3.7	25	1.02
8	93	0.19	208	0.19
9	34	0.40	55	0.63
10	39	1.9	76	2.8
11	174	0.59	220	0.45
12	41	0.70	107	0.67
13	2.5	0.67	5.5	0.15

Note: Two cumulative incident field exposure values (sum of incident field exposures from multiple transmitters at one site) at different distances are shown as exemplary for each base station site.

TABLE 11.6

Worst-Case *E* Field of Typical Wireless Indoor Devices at 20-cm and 1-m Distance

Device Class	Frequency Range (MHz)	Worst-Case *E* Field (V/m) (20 cm)	Worst-Case *E* Field (V/m) (1 m)
Baby surveillance	40–863	8.5	3.2
DECT	1880–1900	11.5	2.9
WLAN	2400–2484	3.9	1.1
Bluetooth	2402–2480	3.1	1.0
PC peripherals	27–40	$\leq$1.5	$\leq$1.5

cumulative incident field exposure values (sum of incident field exposures from multiple transmitters at one site) measured at different distances from the considered base station sites. The values are within 0.1 to 1 V/m for distances up to several hundreds of meters. These data also underline that the distance to the base station site has a poor correlation for the incident exposure.

Similar results were reported by Bornkessel and Schubert [67]. This study also included outdoor measurement points and addressed the time dependence, that is, traffic dependence of the exposure from cellular base stations. The results showed a significant time dependence for base stations with multiple traffic channels. In these cases, clearly lower exposure can be expected at night and on weekends.

The incident field exposures from typical devices used in home and office environments were assessed by Kramer et al. [66]. The maximum *E* field exposure values for different device categories are summarized in Table 11.6. The incident field exposure from cellular base stations may be exceeded by the exposure from these devices because of the generally closer distances.

Additionally, an incident exposure of 1 V/m translates to a peak spatial SAR value in the brain that is approximately a factor 10,000 times lower than the maximum exposure by a handset. Thus, exposure by handsets is by far the most dominant source of RF exposure for the general population.

Acknowledgment

The authors wish to thank Prof. Dr. Quirino Balzano, Dr. Urs Lott, and Dr. Katja Pokovic for their critical review of this manuscript. The dosimetric research at the IT'IS Foundation is supported by many institutions, the most significant of which are European and Swiss Funding Agencies, Motorola Inc. (USA), the Mobile Manufacturers Forum (Belgium), MTT (Japan), and Schmid & Partner Engineering AG (SPEAG, Switzerland).

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12

Electromagnetic Imaging of Biological Systems

William T. Joines, Qing H. Liu, and Gary Ybarra

CONTENTS

12.1 Introduction

Two emerging types of electromagnetic imaging are presented: electrical impedance imaging (or tomography, EIT) and microwave imaging (MWI). Both techniques rely on the contrast in electromagnetic properties (complex permittivity) of the tissues to be imaged with that of the neighboring tissue region. Both techniques use an array of sensors

around the region to be imaged. For EIT, a current due to a known voltage is passed between all electrodes within an array to determine the electrical impedance (or admittance) of the imaged tissue. For MWI, a microwave signal is sequentially transmitted through the imaged tissue to all antennas within an array to determine the scattering parameters (ratio of reflected and transmitted signals to the incident signal) of the imaged region. EIT uses a lower frequency (in the kHz or MHz range) so that the imaged region is small compared with the signal wavelength. MWI uses a higher frequency (in the GHz range) so that the imaged region is comparable to the signal wavelength. The MWI frequency is chosen to be low enough to yield an adequate depth of penetration into the imaged tissue, but high enough to allow the use of a number of small, closely spaced antennas in the array. Since antenna size is also comparable to signal wavelength, microstrip patches or waveguide apertures on high-permittivity substrates are often used to reduce the wavelength at the antenna.

Once MWI and electrical impedance imaging are fully developed for clinical use, they have great potential for the early detection of breast cancer. Other imaging methods are now available, but they have certain disadvantages that limit their acceptance as the method of choice for breast cancer screening. Magnetic resonance imaging (MRI) relies on large electrical currents in cryogenically cooled conductors to produce a strong magnetic field. Hardware and safety requirements may continue to make MRI too expensive for widespread use in breast cancer screening. X-ray imaging is now used fairly extensively, but many women dread the discomfort or pain associated with having their breast sandwiched between two hard, flat surfaces in preparation for the screening, and their aversion to this test may prevent them from participating.

For testing patients in the clinic, both MWI and EIT will most likely use the same arrangement as far as the patient is concerned. The patient will lie face down in a comfortable position on a cot or gurney, as illustrated in Figure 12.1. The breast to be screened extends into an opening containing body-temperature liquid that has approximately the same electrical properties as the normal female breast. This liquid is held within a cylindrical or rectangular thin-walled plastic container that is attached beneath the cot. For MWI, numerous small antennas are attached to the entire outer surface of the plastic container. For EIT, numerous small metal electrodes are attached on the inside surface of the plastic container so that the electrodes can flow current through the liquid and the breast tissue under test. These are the techniques, along with numerical modeling,

FIGURE 12.1
Breast imaging arrangement with patient lying comfortably face down.

that we are now using in the laboratory to obtain the results reported herein. Although we describe how we obtain the breast cancer images using phantom (artificial) tissues, we have not yet moved our imaging systems into the clinic to image breast cancer in real patients. The research and development we are now doing are necessary steps that must be taken before successful clinical applications can occur.

12.2 Development of MWI

Active MWI is an emerging technique for several biomedical imaging applications. Besides being economical and easily portable, MWI takes advantage of the high contrast in electrical properties that exists between anomalous and normal tissue over certain ranges of frequency [1–7]. Fortunately for breast cancer imaging, the contrast between normal and malignant tissue appears to be greatest over the approximate frequency range of 600 to 1000 MHz. This frequency range is both low enough and high enough to meet most of the requirements cited earlier.

While the high contrast is advantageous, it does make multiple scattering in the region more pronounced, and this adds to the difficulty of image formation. Although the specific contrasts vary with frequency, there is now a general belief that these contrasts are substantial, especially near 800 MHz (see the references cited in Refs. [8,9] and the review in Fear et al. [10]). For example, according to Joines et al. [6], at 800 MHz, the permittivity relative to air (ε_r) and the electrical conductivity (σ) for malignant breast tissue are approximately $\varepsilon_r \cong 57.2$ and $\sigma \cong 1.08$ S/m, respectively, while they are $\varepsilon_r \cong 16$ and $\sigma \cong 0.16$ S/m, respectively, for normal mammary tissue. The contrast is 3.75 for the relative permittivity and 6.75 for the electrical conductivity. Over the past few years, several research groups have been working on both hardware and software aspects of microwave breast imaging [8,9,11–15] to take advantage of the high contrast in applications of near-field MWI. The reason for the high contrast between malignant and normal tissue may be better understood through a brief examination of the frequency-dependent electrical properties of biological tissue.

12.2.1 Frequency Dependence

The frequency dependence of ε and σ is directly related to the polarization of molecules and structural interfaces caused by an applied electric field within the biological tissue. A specific polarization effect is important in determining ε and σ up to a relaxation frequency, f_r. Above this frequency the induced polarization can no longer change as fast as the applied field. Thus, above f_r the energy storage term (ε) is less, and the energy dissipation term (σ) is greater. Structural or Maxwell–Wagner relaxation, because of cellular membranes and other layered structures within the tissue, is of importance at frequencies below about 100 MHz [16]. Polar or Debye relaxation, because of the rotation of molecules or molecular groups by the applied field, is of importance in determining ε and σ at all frequencies above about 30 MHz. In the 30- to 2000-MHz range, the values of ε and σ versus frequency are highly dependent on the free-water content ($f_r \cong 25{,}000$ MHz) of the tissue. However, bound water (f_r in the 100- to 1000-MHz range) and protein molecules (f_r in the 40- to 300-MHz range) also make significant contributions to ε and σ.

Because most types of polarization can be described formally in the same qualitative manner, the Debye equations often apply very well, even though they were derived for the case of molecular rotation. For a given relaxation frequency, the Debye relations for ε and σ are [17]:

$$\varepsilon = \varepsilon_{\mathrm{H}} + \frac{\varepsilon_{\mathrm{L}} - \varepsilon_{\mathrm{H}}}{1 + \left(\frac{f}{f_{\mathrm{r}}}\right)^2} \tag{12.1}$$

and

$$\sigma = \sigma_{\mathrm{L}} + \frac{(\varepsilon_{\mathrm{L}} - \varepsilon_{\mathrm{H}})2\pi f_{\mathrm{r}}}{1 + (f_{\mathrm{r}}/f)^2} \tag{12.2}$$

where $\varepsilon = \varepsilon_{\mathrm{H}}$ at f well above f_{r} and $\sigma = \sigma_{\mathrm{L}}$, $\varepsilon = \varepsilon_{\mathrm{L}}$ at f well below f_{r}.

Two tissues having different constituencies (e.g., normal and malignant tissues) most likely will have different relaxation frequencies (f_{r1} and f_{r2}). If the operating frequency of an applied electromagnetic wave is between f_{r1} and f_{r2}, then an examination of the Debye equations shows that this is the frequency where the greatest contrast occurs between ε and σ for the two tissues [5].

12.2.2 Scattering Parameters

As stated earlier, to achieve MWI an electromagnetic wave is sequentially transmitted through the tissue region to be imaged and to all antennas within an array surrounding the region in order to determine the scattering parameters (ratio of reflected and transmitted signals to the incident signal) of the imaged region. This is important because the scattering parameters may be measured as well as calculated.

Taking just two antennas in the array, one transmitting and one receiving, the scattering parameters may be simply expressed. The electric field intensity on the transmitter side (E_1) of the region is made up of incident and reflected (scattered) components and likewise, for the electric field intensity on the receiver side (E_2) of the imaged region. This relationship is expressed as

$$E_1 = E_{1\mathrm{i}} + E_{1\mathrm{r}} \tag{12.3}$$

and

$$E_2 = E_{2\mathrm{i}} + E_{2\mathrm{r}} \tag{12.4}$$

where $E_{1\mathrm{i}}$ is a wave incident from antenna 1 into the imaged region, $E_{1\mathrm{r}}$ is reflected into antenna 1 from the region, $E_{2\mathrm{i}}$ is incident from antenna 2 into the region, and $E_{2\mathrm{r}}$ passes from the region and into antenna 2. Since the incident and scattered fields completely determine the transmitted and received signals, it is convenient to express the scattered fields as functions of the incident fields, as

$$E_{1\mathrm{r}} = S_{11}E_{1\mathrm{i}} + S_{12}E_{2\mathrm{i}} \tag{12.5}$$

and

$$E_{2\mathrm{r}} = S_{21}E_{1\mathrm{i}} + S_{22}E_{2\mathrm{i}} \tag{12.6}$$

where the scattering parameters are defined as:

$$S_{11} = E_{1r}/E_{1i}\,|_{E_{2i}=0},\ S_{12} = E_{1r}/E_{2i}\,|_{E_{1i}=0},\ S_{21} = E_{2r}/E_{1i}\,|_{E_{2i}=0},\ S_{22} = E_{2r}/E_{2i}\,|_{E_{1i}=0} \quad (12.7)$$

Thus, S_{11} is the reflection coefficient at antenna 1, under the condition that antenna 2 is terminated in the impedance of its connecting cable (usually 50 Ω), so that no signal enters the region from antenna 2. Under the same condition at antenna 2, S_{21} is the forward transmission coefficient of signals from antenna 1 to antenna 2. Likewise, S_{22} is the reflection coefficient at antenna 2, under the condition that antenna 1 is terminated in the impedance of its connecting cable (usually 50 Ω), so that no signal enters the region from antenna 1. Under the same condition at antenna 1, S_{12} is the reverse transmission coefficient of signals from antenna 2 to antenna 1.

Using the very same concepts and definitions, the scattering parameters for N antennas are expressed as

$$\begin{aligned}
E_{1r} &= S_{11}E_{1i} + S_{12}E_{2i} + S_{13}E_{3i} + \cdots + S_{1N}E_{Ni} \\
E_{2r} &= S_{21}E_{1i} + S_{22}E_{2i} + S_{23}E_{3i} + \cdots + S_{2N}E_{Ni} \\
E_{3r} &= S_{31}E_{1i} + S_{32}E_{2i} + S_{33}E_{3i} + \cdots + S_{3N}E_{Ni} \\
&\vdots \\
E_{Nr} &= S_{N1}E_{1i} + S_{N2}E_{2i} + S_{N3}E_{3i} + \cdots + S_{NN}E_{Ni}
\end{aligned} \quad (12.8)$$

12.2.3 Scattering-Parameter Imaging of Tissue Permittivity

This method of imaging relies on the propagation of electromagnetic waves into and through the region of interest as shown in Figure 12.2. The reflected and transmitted electric fields are referenced to the incident electric field to determine the magnitude and phase delay of the reflection coefficient at the nth port ($S_{nn} = |S_{nn}| \angle\phi_R = E_r/E_i$) and the transmission coefficient from port n to m ($S_{mn} = |S_{mn}| \angle\phi_T = E_t/E_i$) at multiple transmitter–receiver sites around the circumference of the region.

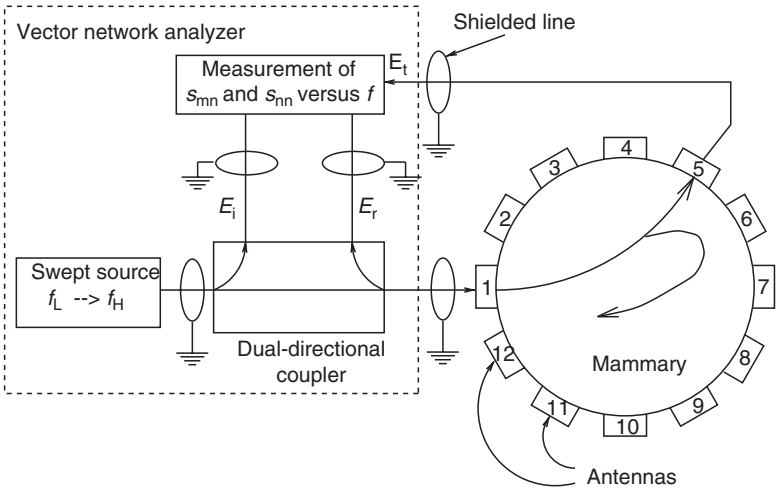

FIGURE 12.2
S-parameter measurement system.

A further visualization of the transmission–reflection method is shown in Figure 12.3, where each antenna on the circumference is a transmitter–receiver and the lines between antennas may be considered average ray paths for transmitted waves. Thus, position 1 in Figure 12.3 transmits to all other receivers at the same time and also receives reflected signals from various points within the target region. Next, position 2 transmits to all positions, and so on around the circumference. Both the amplitude and phase delay of transmitted and reflected signals are functions of the complex permittivity that the particular ray path encounters in traversing or partially traversing the normal and malignant breast tissue regions. The data collected with this method are processed by computer to produce images of subregions of differing permittivity and conductivity within the mammary tissue.

At present, we use a vector network analyzer (HP 8753A, 0.3 MHz to 3 GHz) to perform the measurement functions in Figure 12.2. In a fully developed MWI system, the network analyzer will be replaced with lower-cost, application-specific, individual components.

As an example to illustrate the transmission–reflection imaging method, we use a simplified multiport network theory; a more rigorous full-wave theory will be summarized in Section 12.4. Let d be the distance of an average ray path from a transmitter at port 1 to a receiver at port 7 in Figure 12.3, let Z_0 be the receiver or transmitter impedance, and let Z_M be the intrinsic impedance that the rays encounter in the bulk tissue between transmitter and receiver. From two-port network theory, the reflection coefficient (S_{11}) looking from the transmitter antenna into the bulk tissue is

$$S_{11} = \frac{(Z_M^2 - Z_0^2)\tanh \gamma d}{2Z_0 Z_M + (Z_M^2 - Z_0^2)\tanh \gamma d} = \frac{E_r}{E_i} \tag{12.9}$$

and the transmission coefficient (S_{71}) from port 1 to port 7 is

$$S_{71} = \frac{2Z_0 Z_M \sqrt{1 - \tanh^2 \gamma d}}{2Z_0 Z_M + (Z_M^2 - Z_0^2)\tanh \gamma d} = \frac{E_t}{E_i} \tag{12.10}$$

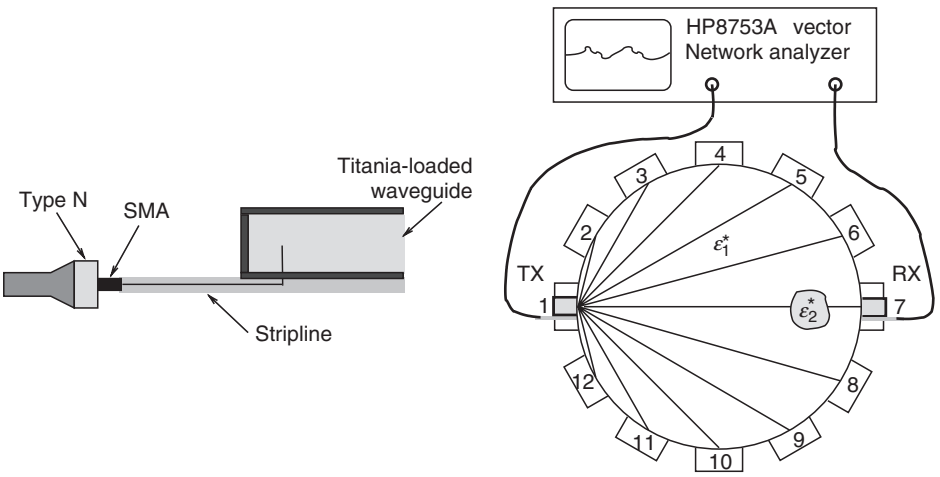

FIGURE 12.3
Top view of the cylindrical plastic container showing some of the antennas in the total array.

where $\gamma = j\omega\sqrt{\mu_0\varepsilon^*}$ is the propagation constant of the bulk tissue, and $\omega = 2\pi f$, where f is the frequency in hertz. Let $Z_M = \sqrt{\mu_0/\varepsilon^*} = 377/\sqrt{\varepsilon_r^*}$ and $Z_0 = 50\ \Omega$, then $Z_0/Z_M = \sqrt{\varepsilon_r^*}/7.54$, and S_{11} and S_{71} become

$$S_{11} = \frac{(56.85 - \varepsilon_r^*)j\tan\left(2\pi f\sqrt{\varepsilon_r^*}d/c\right)}{15.08\varepsilon_r^* + (56.85 + \varepsilon_r^*)j\tan\left(2\pi f\sqrt{\varepsilon_r^*}d/c\right)} = \frac{E_r}{E_i} \tag{12.11}$$

$$S_{71} = \frac{15.08\sqrt{\varepsilon_r^*}\sqrt{1 - j\tan^2\left(2\pi f\sqrt{\varepsilon_r^*}d/c\right)}}{15.08\varepsilon_r^* + (56.85 + \varepsilon_r^*)j\tan\left(2\pi f\sqrt{\varepsilon_r^*}d/c\right)} = \frac{E_t}{E_i} \tag{12.12}$$

where $c = 3 \times 10^8$ m/s. For example, if $d = 0.1$ m, $f = 800$ MHz, and the measured values are

$$S_{11} = 0.200\angle 81.76^\circ = -13.94\,\text{dB}\angle 81.76^\circ \tag{12.13}$$

$$S_{71} = 0.011\angle 86.49^\circ = -39.17\,\text{dB}\angle 86.49^\circ \tag{12.14}$$

then the complex permittivity of the bulk tissue medium at $f = 800$ MHz is determined as

$$\varepsilon_r^* = 36 - j36 = \frac{\varepsilon}{\varepsilon_0} - j\frac{\sigma}{\omega\varepsilon_0} \tag{12.15}$$

where $\varepsilon = 36\varepsilon_0$ and $\sigma = 1.60$ S/m. From our previous measurements [6], normal mammary tissue at 800 MHz would yield $\varepsilon_r^* = 17 - j4$, or $\varepsilon = 17\varepsilon_0$ and $\sigma = 0.18$ S/m. Thus, $\varepsilon_r^* = 36 - j36$ would represent a very large difference in expected tissue properties along the path from port 1 to port 7, which passes through the region occupied by ε_2^* in Figure 12.3. This example is intended to illustrate how the contrast in complex permittivity of a region can not only be measured but also located by coordinate position.

12.2.4 Power, Signal Attenuation, and Signal-to-Noise Ratio

At an operating frequency of 800 MHz, the free space wavelength is $\lambda_0 = 37.5$ cm. In normal breast tissue the wavelength is reduced to $\lambda_{\text{normal}} = \frac{\lambda_0}{\sqrt{\varepsilon_r}} = 9.375$ cm, assuming that the dielectric constant is 16 for normal breast tissue. The distance between any pair of transmitting and receiving antennas is less than 20 cm. Therefore, all measurements are made within a region comparable to the wavelength. The propagation loss between transmitting and receiving antennas is typically in the range of 8 to 16 dB. A typical dielectrically loaded waveguide antenna used for MWI has a 3×3 cm aperture. If the transmitting antenna is operated at a transmitted power of 0 dB m or 1 mW, it results in a transmitted power density of 0.11 mW/cm^2, nine times below the ANSI safety level. The received power is -16 to -8 dB m or 25 to 158 μW. The scattered signal from the tumor is typically 0.01% of of the incident wave. Since the network analyzer's noise level is approximately -90 dB m, the signal-to-noise ratio (SNR) at the receiving antenna is on the order of 30 dB.

12.3 Three-Dimensional Formulation

Currently, there are few methods developed for MWI in three dimensions because of the large computational demand in both forward and inverse problems of inhomogenous media. While two-dimensional (2-D) and 3-D imaging techniques based on the scalar-wave approximation have been developed with some success, breast cancer imaging is inherently a 3-D problem and requires the full 3-D inverse scattering algorithms based on the vectorial Maxwell's equations. In our imaging research we have developed a fast inverse scattering method based on the combination of the contrast source inversion and the fast Fourier transform (FFT) algorithms.

Because of the volumetric inhomogeneities in biological tissues, surface integral equation methods become impractical. Methods based on volumetric techniques are more appealing. We focus on the frequency-domain solution of a volume integral equation (VIE) for inhomogenous media. In a typical inhomogenous tissue medium, both the forward and the inverse scattering problems can be formulated using VIEs. The conventional forward scattering method for VIEs is the method of moments (MoM) [18], but the computational cost is prohibitively high; several 3-D forward problems have been solved in a number of articles [19–22] using this approach. If the VIE involves N unknowns, the MoM has a memory requirement of $O(N^2)$, and a CPU time requirement of $O(N^2)$ or $O(N^3)$ depending on whether the resulting matrix equation is solved iteratively or by direct inversion.

An important improvement over the MoM is a variant of Bojarski's k-space method (see references in Ref. [23]), the so-called conjugate-gradient fast Fourier transform (CG-FFT) method proposed during the 1980s [24,25], which uses iterative the Krylov subspace method [26] combined with FFT or nonuniform FFT [27]. Zhang and Liu [28] recently developed a biconjugate-gradient FFT method based on the weak-form discretization of Zwamborn and van den Berg and showed a significant improvement over the CG-FFT method for wave scattering problems. This method has been further accelerated by the stabilized biconjugate-gradient fast Fourier transform (BCGS-FFT) method for wave scattering by Xu et al. [29]. Recently, the adaptive integral method developed for surface integral equations [30] has been further developed for VIEs to accelerate MoM by using two sets of basis functions to represent near-field and far-field interactions [31].

In the present work, we apply the BCGS-FFT method to MWI by solving the VIE. The problem under consideration is schematically shown in Figure 12.4, where an arbitrary

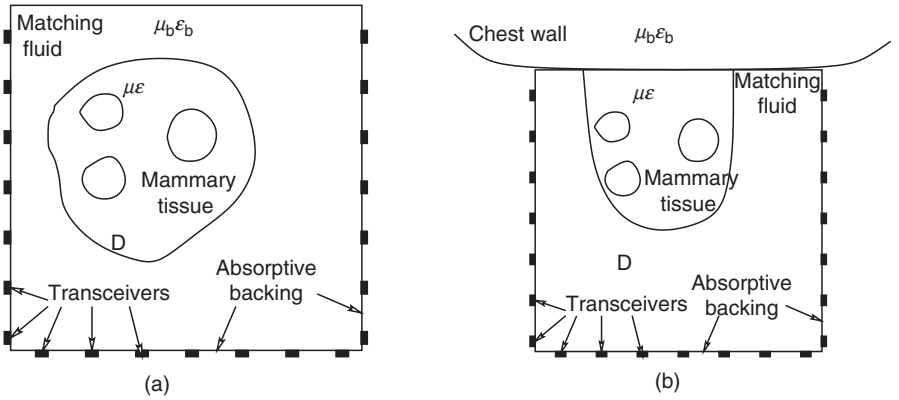

FIGURE 12.4
Imaging chamber from above (a) and from the side (b).

number of antennas are mounted on the plastic container surrounding the phantom model of breast tissue. Specific configurations for simulation will be described in a later section. We calculate the electromagnetic fields both inside the tissue medium and at the receiver array for any source locations. For MWI of breast tissue, the excitation sources (antennas) are in the near-field zone, and the incident field cannot be approximated as a plane wave. Therefore, we include the effects of the finite sources in the near-field zone.

In the following section, we derive from the vectorial Maxwell's equations the VIE for 3-D MWI in the discretized form that we use. Iterative methods for the solution of this discretized linear system are then described. Numerical results are shown to validate the method for MWI.

12.4 Wave Equation and VIE

From Maxwell's equations with an assumed time dependence $e^{j\omega t}$,

$$\nabla \times \mathbf{E} = -j\omega\mu\mathbf{H} \tag{12.16}$$

$$\nabla \times \mathbf{H} = (\sigma + j\omega\varepsilon)\mathbf{E} + \mathbf{J} = j\omega\left(\varepsilon - j\frac{\sigma}{\omega}\right)\mathbf{E} + \mathbf{J} = j\omega\varepsilon^*\mathbf{E} + \mathbf{J} \tag{12.17}$$

$$\nabla \cdot \mathbf{D} = \rho \tag{12.18}$$

$$\nabla \cdot \mathbf{B} = 0 \tag{12.19}$$

we may let

$$\mathbf{B} = \nabla \times \mathbf{A} \tag{12.20}$$

since $\nabla \cdot \nabla \times \mathbf{A} \triangleq 0$ maintains $\nabla \cdot \mathbf{B} = 0$, where $\mathbf{A}$ is the vector potential. Substituting Equation 12.20 into Equation 12.16 yields

$$\nabla \times \mathbf{E} = -j\omega(\nabla \times \mathbf{A}) \tag{12.21}$$

or

$$\nabla \times (\mathbf{E} + j\omega\mathbf{A}) = 0 \tag{12.22}$$

Since $\nabla \times (\nabla\phi) \triangleq 0$, we may let the term in parentheses in Equation 12.22 be the negative gradient of the scalar potential ϕ, and express $\mathbf{E}$ as

$$\mathbf{E} = -\nabla\phi - j\omega\mathbf{A} \tag{12.23}$$

Note that if $\omega = 0$, then $\mathbf{E} = -\nabla\phi$, as expected for static fields. We now invoke the Lorenz condition, which defines the divergence of $\mathbf{A}$ as

$$\nabla \cdot \mathbf{A} = -j\omega\mu\varepsilon^*\phi \tag{12.24}$$

Substituting this condition into Equation 12.23 yields

$$\mathbf{E} = -\mathrm{j}\omega\left[1 + \frac{\nabla\nabla\cdot}{k^2}\right]\mathbf{A} \tag{12.25}$$

where $k^2 = \omega^2\,\mu\varepsilon^*$. Since $\mathbf{E}$ and $\mathbf{H}$ are propagating field intensities that satisfy a wave equation, then $\mathbf{A}$ must satisfy a wave equation obtained as follows. Substitute Equation 12.20 and Equation 12.23 into Equation 12.17 to yield

$$\nabla \times \nabla \times \mathbf{A} \triangleq \nabla(\nabla \cdot \mathbf{A}) - \nabla^2\mathbf{A} = \mathrm{j}\omega\mu\varepsilon^*(-\nabla\phi + \mathrm{j}\omega\mathbf{A}) + \mu\mathbf{J} \tag{12.26}$$

or (again using the Lorenz condition),

$$\nabla^2\mathbf{A} = -\omega^2\mu\varepsilon^*(\mathbf{r})\mathbf{A} - \mu\mathbf{J} \tag{12.27}$$

A solution to Equation 12.27 is in general not available in a closed form because $\varepsilon^*(\mathbf{r})$ is inhomogenous. However, for a homogenous medium with constant complex permittivity ε_b^*, one can find the solution in closed form

$$\mathbf{A}^{\mathrm{inc}}(\mathbf{r}) = \mu\int_V \mathbf{J}(\mathbf{r}')g(\mathbf{r},\mathbf{r}')\,\mathrm{d}V' \tag{12.28}$$

where $\mathbf{r}$, $\mathbf{r}'$, and $\mathbf{R} = \mathbf{r} - \mathbf{r}'$ are vectors from the origin to the field point, from the origin to the source point, and from the source point to the field point, respectively. Green's function in Equation 12.28 for the homogenous medium is given by $g(\mathbf{r},\mathbf{r}') = \mathrm{e}^{-\mathrm{j}k_b R}/4\pi R$, where $k_b = \omega\sqrt{\mu\varepsilon_b^*}$ is the complex wavenumber of the medium. We call this solution $\mathbf{A}^{\mathrm{inc}}$, the vector potential for the incident field in a homogenous background medium. The corresponding incident electric field can be found from Equation 12.25 as

$$\mathbf{E}^{\mathrm{inc}} = -\mathrm{j}\omega\left[1 + \frac{\nabla\nabla\cdot}{k_b^2}\right]\mathbf{A}^{\mathrm{inc}} \tag{12.29}$$

For an inhomogenous medium, even though a closed form solution is not available, one can express the solution in terms of an integral equation through the equivalence principle, as discussed below.

In order to introduce the equivalence principle, the key is to rewrite Maxwell's equations into a second-order partial differential equation for the electric field:

$$\nabla^2\mathbf{E} + k_b^2\mathbf{E} = \mathrm{j}\omega\mu[\mathbf{J} + \mathbf{J}_{\mathrm{eq}}] \tag{12.30}$$

where

$$\mathbf{J}_{\mathrm{eq}} = \mathrm{j}\omega[\varepsilon^*(\mathbf{r}) - \varepsilon_b]\mathbf{E} \tag{12.31}$$

is the volume equivalent electric current density induced in the inhomogenous medium.

Thus, from Equation 12.30, the total field $\mathbf{E}$ can be written as the superposition of the incident field $\mathbf{E}^{\mathrm{inc}}$ due to the primary source $\mathbf{J}$ and the scattered field $\mathbf{E}^{\mathrm{sct}}$ due to the induced source $\mathbf{J}_{\mathrm{eq}}$. Similar to the incident vector potential and incident electric field, the scattered vector potential and scattered electric fields are

$$\mathbf{A}^{\text{sct}}(\mathbf{r}) = \mu \int_V \mathbf{J}_{\text{eq}}(\mathbf{r}')g(\mathbf{r}, \mathbf{r}')\,\mathrm{d}V' \tag{12.32}$$

$$\mathbf{E}^{\text{sct}} = -\mathrm{j}\omega\left[1 + \frac{\nabla\nabla\cdot}{k_{\text{b}}^2}\right]\mathbf{A}^{\text{sct}} \tag{12.33}$$

The total electric field **E(r)** is composed of an incident field plus a scattered field, and it is the scattered field that we need to determine. Thus, combining Equation 12.31 through Equation 12.33, we have

$$\mathbf{E}(\mathbf{r}) - \mathbf{E}^{\text{inc}} = \omega^2\mu\left(1 + \frac{\nabla\nabla\cdot}{k_b^2}\right)\int_V \mathbf{E}(\mathbf{r}')g(\mathbf{r}, \mathbf{r}')[\varepsilon^*(\mathbf{r}') - \varepsilon_b^*]\,\mathrm{d}V' \tag{12.34}$$

where the subscript b denotes a parameter of the background medium (normal tissue and liquid with the same properties). Equation 12.34 is the integral equation representation of the scattered electric field everywhere in space. In particular, for $\mathbf{r} \in V$, Equation 12.34 is a Fredholm integral equation of the second kind. This is the integral equation we solve for the internal electric field **E** for $\mathbf{r} \in V$, from which the field everywhere in the region can be obtained. This type of VIE has been solved by using the MoM [18,20,21]. In our work we will use an alternative discretization method coupled with the Krylov subspace iterative technique to significantly speed up the numerical solution of the problem.

12.4.1 Microwave Imaging

In MWI, scattering parameters are measured using the antennas mounted on the surface of the plastic container in Figure 12.4. The objective of MWI is to reconstruct the distribution of the complex permittivity inside the tissue given the measured scattering parameters.

First, for the MWI system design optimization, the forward problem must be solved. This is to calculate the electric field distribution, given a set of antennas and known distribution of the complex permittivity. In the general problem of microwave interaction with a tissue medium shown in Figure 12.4, an inhomogenous medium with a finite volume V is embedded in an isotropic, homogenous background medium with constant permittivity ε_b, electric conductivity σ_b, and permeability μ_b. This background medium may be air or a matching fluid that is designed to approximately match the electrical properties of the tissue to enhance the SNR in the measurement of the scattered field [9]. The inhomogenous volume V is characterized by nonuniform distributions of permittivity $\varepsilon(\mathbf{r})$ and conductivity $\sigma(\mathbf{r})$; and permeability is assumed constant, that is, $\mu = \mu_b$. The objective is to solve for the electric field everywhere in space due to a finite antenna (usually electrically small because a large array of antennas is needed in an array imaging system). For more details of the BCGS-FFT method, the reader is referred to Refs. [9,28,29,32].

The above discussion is for the forward problem where the distribution of the complex permittivity is known. In reality, for the clinic application of MWI and electrical impedance tomography, we need to solve the inverse scattering problem where the complex permittivity is an unknown distribution. From some limited measurement data collected on the surface of the container, we infer such unknown permittivity distribution by solving the inverse problem through Equation 12.34. In our work, we apply both the distorted Born iterative method and the contrast source inversion method to solve this inverse problem. For details of such inverse solvers, the reader is referred to Refs. [9,33–35].

12.4.2 Electrical Impedance Tomography

This imaging method uses multiple planar electrodes positioned around the region to be imaged, as in Figure 12.5. Impedance or admittance measurements are made between all electrodes, two at a time. Thus, in a parallel-plate capacitor sense, the admittance between any pair of electrodes is the ratio of current to voltage as:

$$Y = \frac{I}{V} = \frac{\int_S \mathbf{J} \cdot d\mathbf{S}}{\int_0^d \mathbf{E} \cdot d\mathbf{l}} = \frac{\int_S (\sigma + j\omega\varepsilon)\mathbf{E} \cdot d\mathbf{S}}{\int_0^d \mathbf{E} \cdot d\mathbf{l}} = (\sigma + j\omega\varepsilon)\frac{A}{d} = j\omega\varepsilon^* \frac{A}{d} \tag{12.35}$$

or $Y = G + j\,\omega C$, where $G = \sigma\,(A/d)$, $C = \varepsilon\,(A/d)$, and $\varepsilon^* = \varepsilon - j\,\frac{\sigma}{\omega}$ is the measured complex permittivity if A/d is known from calibration data. The real and imaginary parts of ε^*, the permittivity ε, and the conductivity σ are the electrical properties of the composite tissue between pairs of electrodes. The factor (A/d) is an effective area-to-distance ratio that may be different for each electrode pair, but this ratio is determined by measuring a material with known electrical properties (such as 0.15 M NaCl at 24°C).

In general, the electric field will be nonuniform but most intense in the region between the electrode pair selected for measurement. The fields between adjacent electrodes will measure properties near the tissue surface, while more diametrically opposed electrodes will measure the composite properties across the tissue region. Such a sequence of measurements is stepped around to include all electrode pairs surrounding the region in 3-D, so that the next set of measurements would be between electrode 2 and all the other electrodes, and so on. Thus, the mapping and imaging of a region are done based on the differing electrical properties within the region.

Impedance imaging is a subject that has been under continuing investigation [36–40]. Research into impedance imaging in our research group began in 1975. We used an open-ended coaxial probe that produced a nonradiating, fringing field to measure the admittance of the material against which the probe was held. This was essentially a two-electrode system that measured the admittance between the inner and outer conductors as given in Zhang and Liu [35]. Moving this noninvasive probe to different positions on the surface of the body, we were able to locate and map out the tumors lying near the skin surface on the bodies of two cancer patients. This work indicated that even

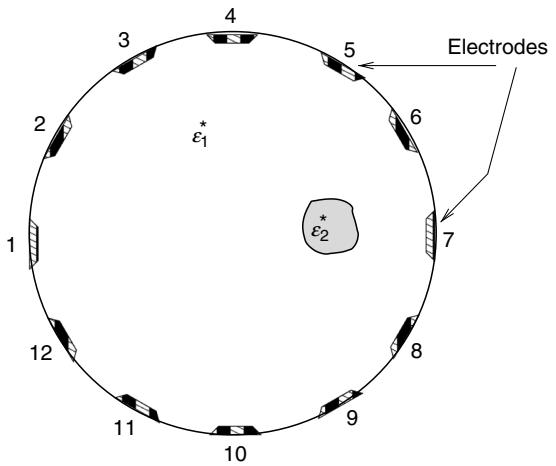

FIGURE 12.5
Configuration of electrical impedance tomography.

when measured through the intact skin, cancerous tissue generally has greater electrical conductivity and permittivity than normal surrounding tissue [41].

The forward and inverse problems of EIT can also be formulated in the same way as for the MWI, that is, using the volume integral Equation 12.34. This is especially convenient if the electrodes are small and can be considered as point electrodes. For finite-size electrodes, in order to apply the boundary conditions on the electrode surface, we use the high-order finite element and spectral element methods to solve the partial differential equations directly in the forward problem. For the inverse problem, we use the distorted Born iterative method [42,43].

12.5 Three-Dimensional Images Reconstructed from Simulated Three-Dimensional MWI Data

Figure 12.6 shows the measurement setup to image two identical spherical anomalies both with $\varepsilon_r = 48$ and $\sigma = 0.8$. The sources and receivers are evenly distributed over the six surfaces of the cuboid. The two spheres of radius 1.1 cm are located at (3.9,0,0) and (−3.9,0,0) cm, respectively. The imaged domain is discretized into $31 \times 31 \times 31$ voxels. The reconstructed ε_r and σ are displayed on three orthogonal slices in Figure 12.7, showing a high fidelity to the ground truth.

12.6 Two-Dimensional Images Reconstructed from Measured Two-Dimensional EIT Data

This section presents three examples of images reconstructed from measured data obtained from a Two-Dimensional EIT system.

12.6.1 Case 1: One Insulator Object Inside the Container

The first example is Case 1, shown in the left panel of Figure 12.9. The difference between the total field and the background field in the right panel of Figure 12.9 is the measured

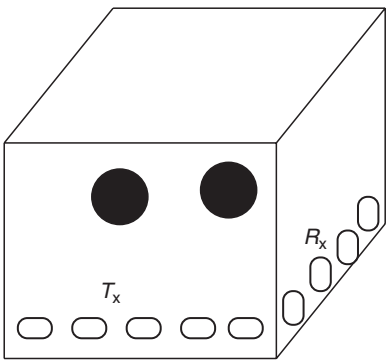

FIGURE 12.6
The setup of Three-Dimensional imaging of two spherical anomalies separated by 7 cm.

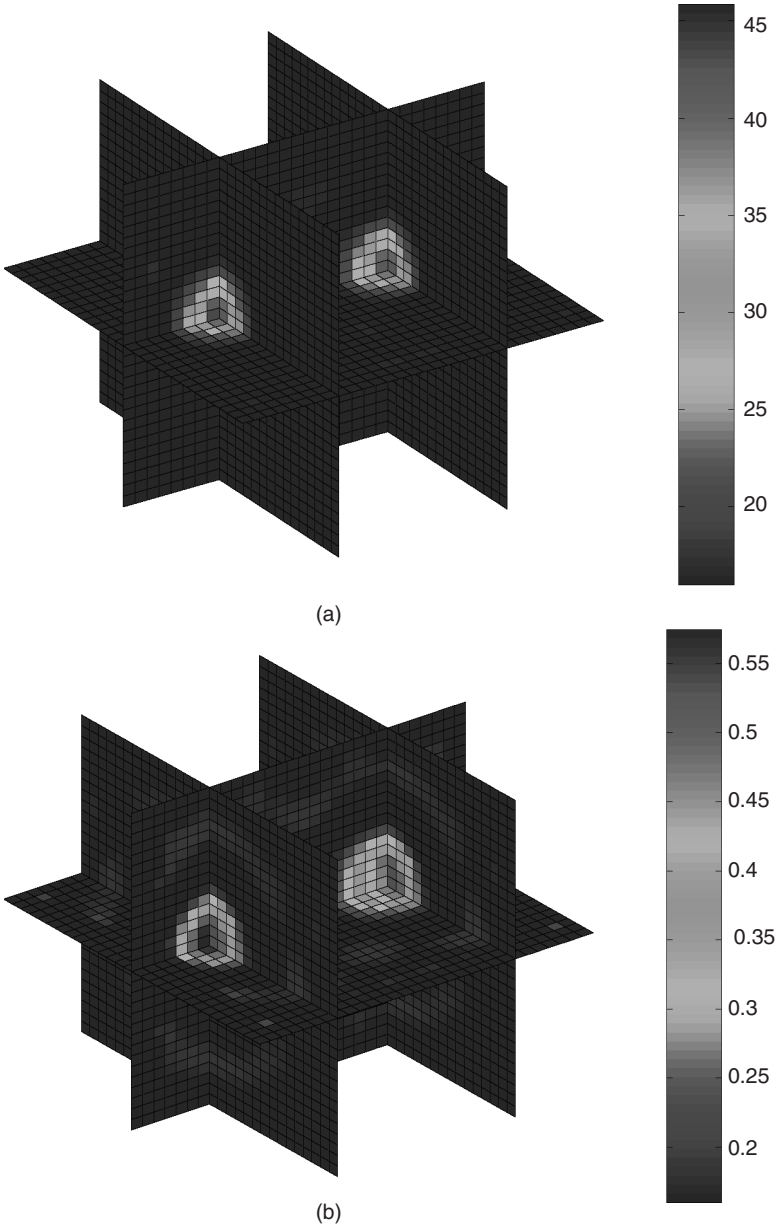

FIGURE 12.7 (See color insert following page 380.)
Inversion for Figure 12.6 on three orthogonal slices through the center of the anomalies. Inverted dielectric constant ε_r (a) and conductivity σ (b).

secondary field. The reconstructed image from this secondary field is shown in the left panel of Figure 12.8. The dotted circle in this figure indicates the ground truth of the object. It is observed that the reconstructed image matches well with the ground truth, although the absolute values of the conductivity of the highly resistive object are not well recovered because of the extreme contrast.

In order to show the misfit between the reconstructed data and the measured data, we take the reconstructed 2-D conductivity map in the left panel of Figure 12.8 and use the

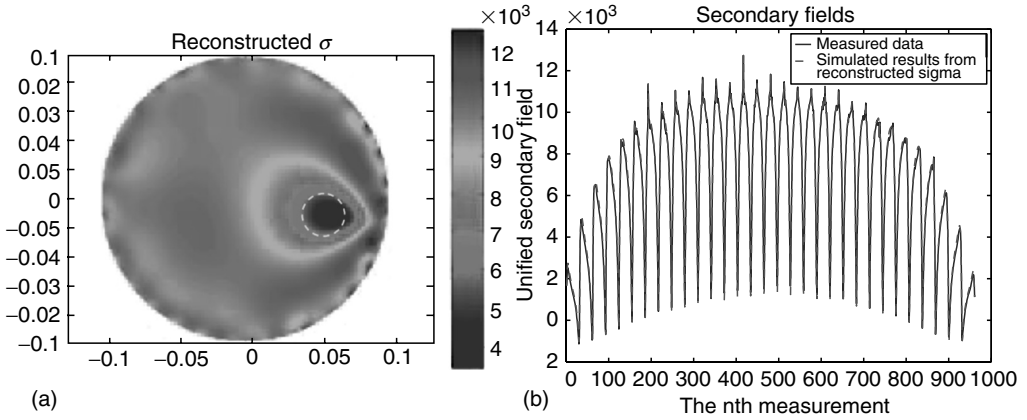

FIGURE 12.8 (See color insert following page 380.)
Left: Image reconstructed from the measured data in Case 1. The dashed circle indicates the ground truth. Right: Comparison of the secondary field between measurements and simulated by forward solver with the reconstructed σ in Case 1.

forward simulator to predict the data corresponding to this image. The comparison between the measured data (blue curve) and the simulated data (red curve) using the reconstructed image is shown in the right panel of Figure 12.8. We observe that these two sets of results have excellent agreement, indicating small data misfit from the reconstructed data.

12.6.2 Case 2: Two Insulator Objects Inside the Container

The setup of the second example (Case 2) is shown in the left panel of Figure 12.10. It is similar to Case 1, except that two insulators (beakers) are inserted into the container. The measured total field and background field are shown in the right panel of Figure 12.10. From the secondary field, the distorted Born iterative method (DBIM) reconstructs the

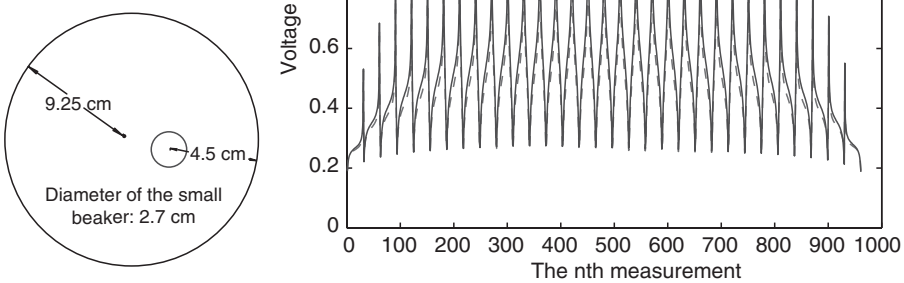

FIGURE 12.9
Left: The setup of Case 1 with one insulator object (beaker). Right: The measured voltage with and without the object in Case 1.

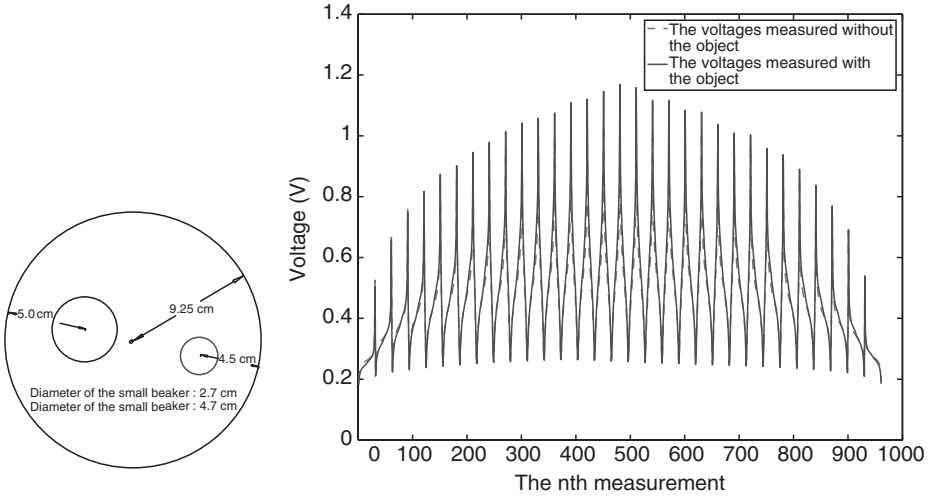

FIGURE 12.10
Left: The setup of Case 2 with two nonconducting circular objects (beakers). Right: The measured voltage with and without the objects in Case 2.

image shown in the left panel of Figure 12.11. The dotted circles in this figure indicate the ground truth of the objects. It is observed that the reconstructed image matches well with the ground truth, although the absolute values of the conductivity of the highly resistive objects are again not well recovered because of the extreme contrasts.

From the reconstructed conductivity image, we use the forward simulator to predict the secondary field data. This simulated result is then compared with the measured secondary field in the right panel of Figure 12.11. Again, we observe that these two sets of results have excellent agreement, indicating small data misfit from the reconstructed data.

12.6.3 Case 3: One Conductive and One Resistive Object Inside the Container

The third case, shown in the left panel of Figure 12.12, consists of two objects in the container. The bigger object is a conductive metal cylinder, while the smaller

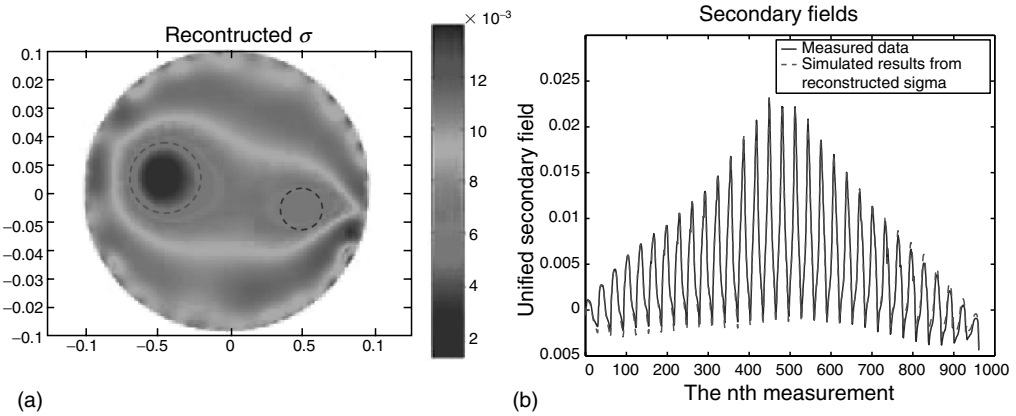

FIGURE 12.11 (See color insert following page 380.)
Left: Image reconstructed from the measured data in Case 2. The dashed circles indicate the ground truth. Right: Comparison of the secondary field between measurements and simulated by forward solver with the reconstructed σ in Case 2.

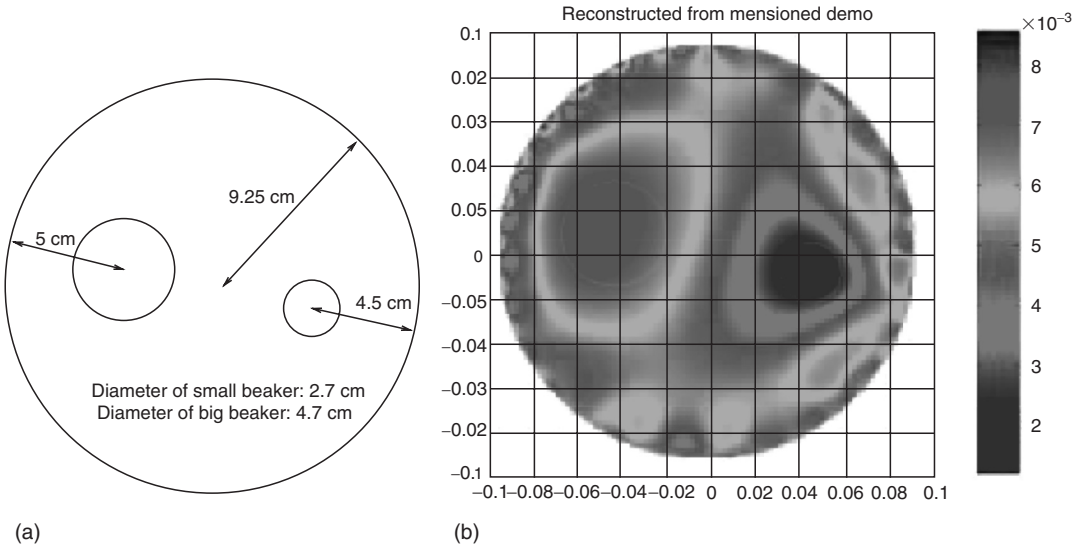

FIGURE 12.12 (See color insert following page 380.)
Left: The setup for Case 3 with one larger metal object and one smaller insulator object. Right: The reconstructed σ. The two circles denote the locations of the objects.

object is a resistive beaker (an insulator). This represents a more interesting case for reconstruction as the conductivity contrast is positive in one region and negative in another.

The reconstructed σ is shown in the right panel of Figure 12.12. The anomalies reconstructed match well with the original objects in location. However, the size of both objects has been somewhat overestimated. The conductivity value of the bigger object is indeed greater than the background, and the smaller object has conductivity values smaller than the background. These indeed match with the original setting that one object is a conductor and another is an insulator, although again the exact values of conductivity are not obtained because of the large contrasts. Nevertheless, the reconstructed images show high-quality reconstruction.

The CPU time for the above image reconstruction examples is less than 3 min on a Pentium IV computer. We emphasize that this speed is expected to be greatly reduced once the program is optimized. Furthermore, in clinical application, the image reconstruction will be performed offline, and thus the computation time of a few minutes is not a concern.

Observations—There are some artifacts in the areas close to the electrodes, perhaps caused by the surface resistance at the interface between the saline solution and the electrodes. However, the overall reconstructed images are excellent. The size and shape of the objects can be well predicted by the reconstructed images. Our future work is to extend the methodology reported here to a full 3-D EIT system. In such a system, we will further improve the sensitivity and resolution of the system by incorporating higher-precision multimeters and by placing a denser 3-D electrode array in the system. Furthermore, to match the higher sensitivity and resolution requirements, we will improve the accuracy of the forward and inverse solvers by incorporating higher-order and spectral methods. From the successful data acquisition and image reconstruction with our 2-D EIT system, it is believed that the 3-D EIT system is highly promising for breast cancer detection.

12.7 Summary and Conclusions

This chapter is a brief summary of MWI and electrical impedance tomography projects ongoing at Duke University. The modeled and measured results presented herein on artificial materials show the kinds of clear images one would fully expect to generate in the clinic using the same techniques. Other research groups are also developing improved MWI and impedance imaging systems, and some breast cancer images derived from clinical data have been published [14,44,45]. Because of 2-D artifacts or algorithm limitations, the earlier clinical images are not as clear as the ones that can be generated with the improved techniques now available. While improvements in current prototypes are encouraging, more work remains before MWI and EIT systems are integrated into clinical applications to produce the high-resolution breast cancer images that are now obtained in the laboratory.

Acknowledgment

We wish to thank the students and postdoctoral research associates involved in the work. Rebecca Willett, Adam Bryan, Erika Ward, Patrick Mathias, John Stang, and Rodger Dalton made significant contributions to the development of MWI hardware. Zhong Qing Zhang helped to develop the forward and inverse scattering algorithms for MWI. Jim Di Sarro, Jackie Hu, Guining Shi, Gang Ye, and Kyle McCarter made significant contributions to the development of electrical impedance tomography hardware. Kim Hwa Lim and Jun Ho Lee developed the forward and inverse solvers for electrical impedance tomography.

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Exhibit F: An Update on Physical and Biological Variables, Cancer and Safety Standards by Igor Belyaev, Dr.Sc., Cancer Research Institute Slovak Academy of Sciences, Slovak Republic

This review is divided into comments on two separate sections, one for extremely-low frequency (ELF) and the other for radiofrequency (RFR) studies. Comments are presented to address deficiencies in the Preliminary Opinion on EMF issued by the SCENIHR Committee. The comments are relevant to sections of the BioInitiative Working Group letter including brain tumors, oxidative damage, genomic instability, mitochrondrial damage, carcinogenic classifications, biological plausibility and methodological deficiencies.

Comments on ELF Sections

ELF Carcinogenicity

Page 131 of the SCENIHR provides misleading and flawed conclusions on ELF and neoplastic diseases. As a matter of fact, the increased risk of childhood leukemia with daily average exposure above 0.3 to 0.4 μT is as strong as never before. All available studies from Europe, America and Asia consistently show such correlation. It has been further supported by recent meta-analysis by Zhao et al. (Zhao, Liu et al. 2014). The statement of lack of mechanisms for ELF effects is wrong. Recent studies provided more evidence for such mechanisms even if they have not been comprehensively studied, see below. Considerations of ELF carcinogenicity in the SCENIHR report did not use standard methods such as the Bradford Hill criteria which do not require complete knowledge of mechanisms in case when epidemiological evidence is overwhelming as in case of childhood leukemia (Zhao, Liu et al. 2014).

Similar to effects of MW, the ELF effects depend on variety of parameters that should be taken into account and have not been considered by the SCENIHR report when comparing data from different studies.

Baldi et al analyzed the relationship between residential and occupational exposure to electromagnetic field and brain tumors in adults (Baldi, Coureau et al. 2010). A case-control study was carried out in southwestern France between May 1999 and April 2001. A total of 221 central nervous system tumors (105 gliomas, 67 meningiomas, 33 neurinomas and 16 others) and 442 individually age- and sex-matched controls selected from general population were included. Electromagnetic field exposure to ELF and radiofrequency separately was assessed in occupational settings through expert judgment based on complete job calendar, and at home by assessing the distance to power lines. Confounders such as education, use of home pesticide, residency in a rural area and occupational exposure to chemicals were taken into account. Separate analyses were performed for gliomas, meningiomas and acoustic neurinomas. A nonsignificant increase in risk was found for occupational exposure to electromagnetic fields [odds ratio (OR = 1.52, 0.92-2.51)]. This increase became significant for meningiomas, especially when considering ELF separately [OR = 3.02; 95 percent confidence interval (95% CI) =1.10-8.25]. The risk of meningioma was also higher in subjects living in the vicinity of power lines (<100 m), even if not significant (OR = 2.99, 95% CI 0.86-10.40). These data suggest that occupational or residential exposure to ELF may play a role in the occurrence of meningioma. The insignificance of data obtained in group RF+ELF is well explained by majority of RF data showing no significant relationship of RF exposure with increased risks of meningioma (Carlberg, Soderqvist et al. 2013).

ELF affects cell proliferation

In line with many previous studies, new studies unmentioned in the SCENIHR report provide further evidence that ELF can affect cell proliferation under specific conditions of exposure (Segatore, Setacci et al. 2012; Bae, Do et al. 2013; Jadidi, Safari et al. 2013). Bai et al. investigated ELF effects on proliferation of epidermal stem cells (ESC) (Bai, Zhang et al. 2012). The ESC obtained from human foreskin were grafted into type-I three-dimensional collagen sponge scaffolds, and then were exposed with EMF (frequency 50 Hz, intensity 5 mT) for 14 days, 30 min daily. The effects of EMF on growth and proliferation of ESC were analyzed with staining of hematoxylin and eosin (H&E) and 4',6-diamidino-2-phenylindole (DAPI) under microscope or scanning electron microscope. The data of DAPI staining for 2 d, 7 d, 10 d and 14 d were collected respectively to investigate the cells proliferation. EMF promoted ESC proliferation compared with controls.

Belyaev analyzed the effect of ELF-MF on chromatin conformation in E. coli GE499 cells using anomalous viscosity time dependence technique (AVTD) (Belyaev 2011). Possible genotoxic effects of the specific combination of static and ELF-MF, which has been proven to affect chromatin conformation, were investigated by a clonogenic assay, by assessing cell-growth kinetics, and by analysis of the SOS-response by means of inducible recA-lacZ fusion-gene products and the beta-galactosidase assay. The genotoxic agent nalidixic acid (NAL) was used as a positive control and in combination with ELF-MF. Nalidixic acid decreased AVTD and induced a cytotoxic effect. In contrast to NAL, ELF-MF fields increased AVTD, stimulated cell growth, and increased cloning efficiency. In line with many previous studies, these effects depended on the frequency within the range of 7-11Hz. While NAL induced an SOS-response, exposure to ELF-MF did not induce the recA-lacZ fusion-gene product. Exposure to ELF-MF did not modify the genotoxic effects of NAL either. All together, the data show that ELF-MF, under specific conditions of exposure, acted as a non-toxic but cell-growth stimulating agent.

Cid et al verified hypothesis that ELF MF effect on cancer progression could be mediated by MF-induced effects on the cellular response to melatonin (MEL), a potentially oncostatic neurohormone (Cid, Ubeda et al. 2012). HepG2 cells were exposed to intermittent 50 Hz, 10 microT MF, in the presence or absence of MEL at physiological (10 nM) or pharmacological doses (1 microM). The results indicated that the MF exerts significant cytoproliferative and dedifferentiating effects that can be prevented by 10 nM MEL. Conversely, MEL exerts cytostatic and differentiating effects on HepG2 that are abolished by simultaneous exposure to MF.

Dependence of ELF effects on number of physical and biological parameters

The SCENIHR report did not take into account dependence of ELF effects on number of physical and biological parameters when comparing the data from different studies. This is in significant contrast with generally accepted methodology which requires considering a number of such parameters which include cell type, frequency, intensity (Belyaev, Alipov et al. 1999; Belyaev and Alipov 2001; Shcheglov, Alipov et al. 2002) and which are similarly important for the MW effects (IARC 2013). Due to this fundamental flaw, incorrect comparisons of studies, which used completely different parameters were performed in the SCENIHR report. For example, negative study by (Buldak et al., 2012) was opposed to positive study (Luukkonen et al. 2011) on Page 164-165. Significant and decisive differences between these studies include exposure time (24 h in (Luukkonen et al. 2011) versus 16 min in (Buldak et al., 2012)), cell type (human neuroblastoma SHSY5Y cells (Luukkonen et al. 2011) versus AT478 murine carcinoma cells (Buldak et al., 2012)). Recent study by the same

authors confirmed and further extended evidence that prolonged exposure to ELF of human neuroblastoma SHSY5Y cells induce reactive oxygen species (ROS) and genomic instability (Luukkonen, Liimatainen et al. 2014).

Fijałkowski et al. analyzed effects of the rotating magnetic field (RMF, f = 1-50 Hz, RMF magnetic induction B = 22-34 mT, ptime of exposure t = 60 min, temperature of incubation 37 °C) on the growth rate, cell metabolic activity and ability to form biofilms by E. coli and S. aureus (Fijałkowski, Nawrotek et al. 2013). RMP exposure increased the growth dynamics, cell metabolic activities and percentage of biofilm-forming bacteria in both S. aureus and E. coli cultures. In line with many other studies, it was found that the RMF effects depended on frequencies and magnetic induction.

Sarimov et al have reported that magnetic field (MF) at 50 Hz within the peak amplitude range of 5-20 microT affected chromatin conformation in human lymphocytes from two healthy donors. These MF effects differed significantly between studied donors, and depended on magnetic flux density and initial condensation of chromatin. While the initial state of chromatin was rather stable in one donor during one calendar year of measurements, the initial condensation varied significantly in cells from another donor. Both this variation and the MF effect depended on temperature during exposure. Despite these variations, the general rule was that MF condensed the relaxed chromatin and relaxed the condensed chromatin. Thus, in this study individual effects of 50 Hz MF exposure at peak amplitudes within the range of 5-20 microT were observed in human lymphocytes in dependence on the initial state of chromatin and temperature.

ELF induced ROS and genomic instability

Induction ROS and is generally considered as a candidate mechanism for carcinogenicity for EMF (IARC 2013). Several recent studies unmentioned in the SCENIHR report provided further evidence for this mechanism in case of ELF exposure (Duan, Wang et al. 2013; Khaki, Khaki et al. 2013).

Duan et al. exposed mice to ELF-EMF at 50 Hz, 8 mT, 28 days (Duan, Wang et al. 2013). A water maze test indicated that ELF-EMF exposure deteriorated significantly learning and memory abilities as compared with the control group. Administration of lotus seedpod procyanidins (LSPCs) had remarkably improved learning and memory abilities in exposed animals compared with the ELF-EMF group. ELF-EMF exposure significantly increased malondialdehyde (MDA), reactive oxygen species (ROS), nitric oxide (NO) and nitric oxide synthase (NOS), while the activities of glutathione peroxidase (GPx), catalase (CAT) and superoxide dismutase (SOD) were decreased significantly. Along with improved learning and memory abilities in exposed animals, LSPCs administration effectively prevented oxidative damage caused by the ELF-EMF, most likely through the ability of LSPCs to scavenge oxygen free radicals and to stimulate antioxidant enzyme activity. The majority of experimental studies (9 out of 10 animal studies) show oxidative stress induced by ELF in brain (Consales, Merla et al. 2012).

Mechanisms for effects of weak ELF

While all mechanisms of ELF effects are not known with certainty, new important data emerged about these mechanisms which were neglected by the SCENIHR report. For ELF fields, these mechanisms involve magnetoreception of fields in the μT-range which is observed in many studied animals including lizards (Nishimura, Okano et al. 2010). It should be stressed that the lack of precise knowledge for this mechanism (radical pairs and magnetite are mainly

considered) does not preclude general acceptance of these phenomena. In analogy, and in accordance to the Bradford Hill criteria, lack of precise knowledge on mechanism for leukemogenesis of weak ELF ≥0.3 μT, which was consistently shown in children in multiple studies (Zhao, Liu et al. 2014) should not preclude classification of μT-range ELF as an IARC carcinogen group 1.

The SCENIHR report completely neglects variety of mechanisms based on ELF effects on ions (Halgamuge and Abeyrathne 2011; Foletti, Grimaldi et al. 2013). Despite physical differences in and incompleteness of these mechanisms all of them relate ELF effects with ion cyclotron resonance frequencies and their harmoniques/subharmoniques (Belyaev and Alipov 2001; Sarimov, Markova et al. 2005). Poniedzialek et al. analyzed ELF effects on reactive oxygen species (ROS) production in human neutrophils in peripheral blood in vitro (Poniedzialek, Rzymski et al. 2013). Two fluorescent dyes were used: 2′7′-dichlorofluorscein-diacetate and dihydrorhodamine. Phorbol 12-myristate 13-acetate (PMA), known as strong stimulator of the respiratory burst, was also used. Three different levels of magnetic induction have been analyzed: 10, 40 and 60 μT. The experiments demonstrated that only EMF tuned to the calcium ion cyclotron resonance frequency was able to affect ROS production in neutrophils. Statistical analysis showed that this effect depended on magnetic induction value of applied EMF.

ELF section omits significant number of ELF positive studies

Except for aforementioned studies, ELF section of the SCENIHR report omits significant number of other ELF positive studies. These include but not limited to (Mariucci, Villarini et al. 2010; Nishimura, Okano et al. 2010; Ravera, Bianco et al. 2010; Severini, Bosco et al. 2010; Ulku, Akdag et al. 2011; Bai, Zhang et al. 2012; Ince, Akdag et al. 2012; Martirosyan 2012; Portelli, Madapatha et al. 2012; Balassa, Varro et al. 2013; Gang, Parker et al. 2013; Iorio, Bennato et al. 2013; Kang, Hong et al. 2013; Khaki, Khaki et al. 2013; Li, Zhang et al. 2013; Martirosyan, Baghdasaryan et al. 2013; Panagopoulos, Karabarbounis et al. 2013; Shams Lahijani, Tehrani et al. 2013; Villarini, Ambrosini et al. 2013).

Mariucci et al exposed CD1 mice to ELF MF (50 Hz-1 mT) for 1 or 7 days (15 h/day) and sacrificed either at the end of exposure or after 24 h (Mariucci, Villarini et al. 2010). Mouse brains were dissected into cerebral cortex-striatum, hippocampus and cerebellum to evaluate primary DNA damage and hsp70 gene expression. An increase in primary DNA damage was detected in all cerebral areas of the exposed mice sacrificed at the end of exposure. This damage, evaluated by the comet assay, appeared to be repaired in mice sacrificed 24 h after a 7-day exposure. The results indicate that in vivo ELF-MF exposure induces transient brain DNA damage did not induce hsp70. Importantly, these results were further replicated by the same research group (Villarini, Ambrosini et al. 2013).

Ulku et al. investigated a set of elements in costa of rats chronically exposed to ELF-MF, 100 and 500 μT, 2 h/day during 10 months (Ulku, Akdag et al. 2011). The levels of elements were measured by using atomic absorption spectrophotometry (AAS) and ultraviolet (UV) spectrophotometry. Ca levels decreased in the ELF-500 exposure group in comparison to sham group ($p < 0.05$). Statistically significant decrease was found in Mg levels in the ELF-500 exposure group in comparison to sham and ELF-100 exposure groups ($p < 0.05$). Zn levels were found to be lower in the ELF-500 exposure group than those in the sham and ELF-100 exposure groups ($p < 0.05$). No significant differences were determined between groups in terms of the levels of P, Cu and Fe. Thus, long-term ELF-MF exposure could change the levels of some important elements such as Ca, Zn and Mg in rat bones.

Balassa et al. analyzed effects of a long-term ELF-MF (0.5 and 3 mT, 50 Hz) exposure on synaptic functions in the developing brain (Balassa, Varro et al. 2013). Rats were chronically exposed to MF during two critical periods of brain development, i.e. in utero during the second gestation week or as newborns for 7 days starting 3 days after birth, respectively. Excitability and plasticity of neocortical and hippocampal areas were tested on brain slices by analyzing extracellular evoked field potentials. The basic excitability of hippocampal slices (measured as amplitude of population spikes) was increased by both types of treatment (fetal 0.5 mT, newborn 3 mT). Neocortical slices seemed to be responsive mostly to the newborn treatment, the amplitude of excitatory postsynaptic potentials was increased. Fetal ELF-MF exposure significantly inhibited the paired-pulse depression (PPD) and there was a significant decrease in the efficacy of LTP (long-term potentiation induction) in neocortex, but not in hippocampus. On the other hand, neonatal treatment had no significant effect on plasticity phenomena. Results demonstrated that ELF-MF has significant effects on basic neuronal functions and synaptic plasticity in brain slice preparations originating from rats exposed either in fetal or in newborn period.

Gang et al. exposed planarian to either 140 or 400 nT peak amplitude-modulated 7 Hz magnetic fields for 6 min once per hour, 8 h per night for 5 days (Gang, Parker et al. 2013). The planarian exposed to either intensity magnetic field exhibited faster regeneration of photoreceptors and auricles compared to sham field and reference groups. The magnetic field exposure accommodated 50% of the variance during the faster growth days. Authors concluded that naturally-patterned, intermittently-presented weaker electromagnetic fields may produce enhanced regeneration rates in flat worms similar to those observed for 60 Hz, higher intensity fields.

Severini et al. exposed cohorts of Xenopus laevis laevis (Daudin) tadpoles during their immature period (approximately 60 days) to a 50 Hz magnetic field of $63.9 \leq B \leq 76.4$ microT rms (root mean square, average values) magnetic flux density (Severini, Bosco et al. 2010). Mean developmental rate of ELF-exposed cohorts was reduced with respect to controls (0.43 vs. 0.48 stages/day, $p < 0.001$) starting from early larval stages. Exposure increased the mean metamorphosis period of tadpoles by 2.4 days compared with the controls ($p < 0.001$). Maturation rates of exposed and control tadpoles changed during maturation period. Important mortality, alformations or teratogenic effects were not observed in exposed matured tadpoles. Authors concluded that a long-term exposure of X. laevis tadpoles to a relatively weak 50 Hz magnetic field causes a sub-lethal effect that slows down their larval developmental rate and delays their metamorphosis.

Panagopoulos et al studied the effect of 50-Hz alternating magnetic field on Drosophila melanogaster reproduction (Panagopoulos, Karabarbounis et al. 2013). Newly eclosed insects were separated into identical groups of ten males and ten females and exposed to three different intensities of the ELF magnetic field (1, 11, and 21 G) continuously during the first 5 days of their adult lives. The magnetic field decreased reproduction by up to 4.3%. The effect increased with increasing field intensities. The decline in reproductive capacity was found to be due to severe DNA damage (DNA fragmentation) and consequent cell death induction in the reproductive cells as determined by the TUNEL assay applied during early and mid-oogenesis (from germarium to stage 10) where physiological apoptosis does not occur. The increase in DNA damage was more significant than the corresponding decrease in reproductive capacity (up to ~7.5%). The TUNEL-positive signal denoting DNA fragmentation was observed exclusively at the two most sensitive developmental stages of

oogenesis: the early and mid-oogenesis checkpoints (i.e. region 2a/2b of the germarium and stages 7-8 just before the onset of vitellogenesis). The TUNEL-positive signal was observed in all three types of egg chamber cells, mainly in the nurse and follicle cells and also in the oocyte.

Kang et al. analyzed specific electromagnetic field conditions (frequency and magnetic flux density) which significantly regulate osteogenic differentiation of adipose-derived stem cells (ASCs) (Kang, Hong et al. 2013). Before inducing osteogenic differentiation, ASC stemness was determined and uniform electromagnetic field was created using the solenoid coil. Then, authors selected positive (30/45 Hz, 1mT) and negative (7.5 Hz, 1mT) osteogenic differentiation conditions by quantifying alkaline phosphate (ALP) mRNA expression. Osteogenic marker (runt-related transcription factor 2) expression was higher in the 30/45Hz condition and lower in the 7.5 Hz condition as compared with the nonexposed group. Both positive and negative regulation of ALP activity and mineralized nodule formation supported these responses. The data indicated that the ELF effects on osteogenic differentiation differ depending on the electromagnetic field conditions and thus provided evidence that ELF can control stem cell differentiation depending on frequency and intensity.

Iorio et al. investigated whether ELF-MF could affect myoblast migration (Iorio, Bennato et al. 2013). ELF-MF (1 mT; 50 Hz) resulted in a transient but significant increase of myoblast migration. This effect was associated with a marked increase of mu- and m-calpain activity followed by the concomitant variation in their subcellular localization. No significant changes in intracellular distribution and protein levels of calpastatin were detected. A significant decrease of myristoylated alanine-rich C-kinase substrate (MARCKS) expression and modifications of actin dynamics were reported. This study provided evidence for involvement of calpains in ELF-MF-mediated myoblast migration.

Page 129, line 26-27. This statement misleads the reader who is not expert in effects of weak EMF to judge results as nonreplicable. In fact, ELF effects similar to MW effects depend on cell type (Belyaev 2010) and this study just provides further support for this dependence. In addition, reference to (Focke, Schuermann et al. 2010) is missing in Reference list.

Page 130. Study of Girgert et al (Girgert, Hanf et al. 2010) is erroneously marked as Girgert et al 2009 and reference if not provided in the Reference list.

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Exhibit F: An Update on Physical and Biological Variables, Cancer and Safety Standards by Igor Belyaev, Dr.Sc., Cancer Research Institute Slovak Academy of Sciences, Slovak Republic

Comments on RFR Sections

Main conclusions on health effects from RFR fields

1. The positive and negative studies were selected by unclear criteria, which (i) are different from those generally accepted and used by IARC and (ii) resulted in omission of majority of positive findings and almost all laboratory studies which were performed using conditions of EMF exposure similar as general public is exposed (see text below and reference list).
2. The report shows fundamental flaw in assessment of mechanisms for non-thermal EMF effects.
3. Analysis of data seem to be biased in favor of negative studies and negative interpretations.

Flawed assessment of negative studies

The main fundamental flaw of the report is neglecting the mechanistic data on non-thermal (NT) effects of microwaves (MW). As reported in multiple studies, these effects depend on variety of biological and physical parameters including polarization, frequency, modulation and environmental EMF (see (Belyaev 2010) and (IARC 2013). The *in vitro* and *in vivo* studies included in the preliminary Opinion are largely negative studies only. Moreover, negative studies cannot be directly compared to positive studies if the exposure was performed under different conditions as it almost always done. Thus, obtained so far data of negative studies cannot be extrapolated to all real cell phone signals. The negative studies cannot neither dismiss positive studies, which were performed under other conditions, nor provide evidence for safety of majority of signals used for mobile communication. The reported" inconsistency" of *in vitro* and *in vivo* data (see for example page 120) and "conflicting results" (see for example page 121) has at least one simple explanation because the studies were performed under different conditions. Thus, results of most studies cannot be directly compared and conclusion by the SCENIHR report on inconsistency. Conflicting results instead reflect the level of superficial analysis. Another fundamental flaw deals with neglecting many studies showing dependence of the NT MW effects on exposure duration or dose (defined in radiation physics as multiplication of SAR on exposure duration), see (Belyaev 2010). In addition to laboratory studies, when brain caner risk was epidemiologically examined as a function of dose received in different time windows before diagnosis, increasing trend was observed with increasing RFR dose, for exposures 7 years or more in the past (Cardis, Armstrong et al. 2011). This study provided straightforward evidence for one of most important Bradford Hill criteria - dependence on dose.

Another important parameter is intermittence of exposure which involves interaction with adaptation mechanisms and accumulative effects of NT MW. Chavdoula et al. used a 6 min daily exposure of dipteran flies, Drosophila melanogaster, to GSM-900 MHz mobile phone electromagnetic radiation (EMR), to compare the effects between continuous and four different intermittent exposures of 6 min total duration on the insect's reproductive capacity as well as on the induction of apoptosis (Chavdoula, Panagopoulos et al. 2010). It was found that intermittent exposure, similar to continuous exposure, decreases the reproductive capacity and alters the actin-cytoskeleton network of the egg chambers, another known aspect of cell death, and that this effect is due to DNA fragmentation. Intermittent exposures with l0-min intervals between exposure sessions proved to be nearly equally effective as continuous exposure of the same total duration, however, longer intervals between the exposures seemed

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to allow the organism the time required to recover and partly overcome the described effects of the GSM exposure.

The preliminary Opinion bases it's conclusions mostly on SAR value, which is a main parameter for thermal MW effects but has much less value for NT MW to which general public is exposed to (Belyaev 2010; Panagopoulos, Johansson et al. 2013).

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RFR epidemiologic evidence for carcinogenicity

The SCENIHR preliminary Opinion has conclusions on brain cancer that are heavily based on the Danish subscriber cohort study of mobile phone subscribers. However this study has not assessed exposure, has been heavily criticized an thus far is inconclusive. This study is not informative even according to the requirement of this SCENIHR reports : " *The minimum requirement for exposure assessment for an epidemiological study to be informative is to include reasonably accurate individual exposure characterization over a relevant period of time capturing all major sources of exposure for the pertinent part of the body"* (page 10). The preliminary Opinion is internally inconsistent with this requirement as the authors have based their review largely on epidemiological studies, where individual exposure was not accurately accessed. These studies include those coauthored by Dr Schüz who is one of the authors for this SCENIHR report. For example, the UK Million women study (Benson et al 2013) included only two simple questions regarding usage of mobile phone which cannot estimate individual exposure in any reasonable degree. Following the general bias of this report in favor of negative finding, the authors forgot to state that this study found statistically significant increase of acoustic neuroma for long term users vs never users (10+ years: RR = 2.46, 95% CI = 1.07–5.64, $P = 0.03$), the risk increasing with duration of use (trend among users, $P = 0.03$).

Another example is the underestimation of importance of the positive findings of de Vocht et al (2013) on global link of mobile phone usage and brain cancer. "*The study is not informative for causal inference, as popular use of mobile phones can also reflect standard of living, which is also associated with, for example, availability of diagnostic services"*. The SCENIHR's preliminary Opinion did not mention that this statement is relevant to most negative studies and especially to the Danish subscriber cohort study upon which this preliminary Opinion heavily relies. In contrast, the meta-analyses of studies which included only data on ipsilateral tumors in subjects using mobile phones for at least 10 years, show large and statistically significant increases in risk of ipsilateral brain gliomas and acoustic neuromas (Levis, Minicuci et al. 2011). The risk of head tumors was nearly doubled and was induced by long-term mobile phone use.

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Consideration of the data on childhood cancers in relation to base stations is also biased in favor of weighting negative studies. While limitation of positive study by (Li et al. 2012) is provided, no limitations of negative study by (Elliott et al. 2010) is considered in contrast to about one-page description of such limitations provided by the authors (Elliott et al. 2010). In addition, the report did not provide the main positive result of the (Li et al. 2012) study which has shown increased (brain+leukemia) incidence related to base stations.

Brain cancer time trend analysis

The SCENIHR report provides biased consideration of available information. It should be noted that histology analysis and localization of tumors in respect to irradiation from mobile phone is of key importance for this analysis.

At the time of IARC meeting in 2011 the following data were available and included into the IARC monograph (IARC 2013):

USA

According to data collected by the Surveillance, Epidemiology, and End Results (SEER) Program, age- and sex-specific trends and overall temporal trends in rates of incidence of brain cancer in the USA were flat or downward between 1992 and 2006, with the exception of women aged 20–29 years (Inskip *et al.*, 2010). In this age group, a statistically significant increasing trend was driven by the rising incidence in tumors of the frontal lobe. [It is the temporal lobe that is most heavily exposed to radiation when using a mobile phone at the ear (Cardis *et al.*, 2008).] Incidence of brain cancer in USA "could be consistent with the modest excess risks in the Interphone study" (Little, Rajaraman et al. 2012).

UK

Overall rates of incidence of cancer of the brain in males or females, or in any specific age group were not increased in England between 1998 and 2007 (de Vocht, Burstyn et al. 2011). For men and women, the incidence of tumors (primarily glioma) was increased ($p<0.01$) in the temporal lobe that is most heavily exposed to radiation when using a mobile phone at the ear (Cardis, Deltour et al. 2008). The incidence increased also in frontal lobe for men ($p < 0.01$) and in the frontal lobe for women, although not statistically significant ($p = 0.07$). The incidence decreased in other parts of the brain. In a subsequent paper, the same authors reported separate time trends for cancers of the temporal lobe in the periods 1979–99 and 2000–08 (de Vocht, Burstyn et al. 2011). For men, a linear regression of age-adjusted rates showed an overall annual increase in 2000 –2008 of 3.3% (95% CI, 1.1–5.4), whereas it was lower 2.0% (95% CI, 1.4–2.6) for 1979–1999. For women, a linear regression of age-adjusted rates showed an overall annual increase in 2000 –2008 of 2.8% (95% CI, 0.9–4.8), whereas it was lower 1.4% (95% CI, 0.7–2.2) for 1979–1999. This change may be suggestive of increased rates for brain cancers of the temporal lobe in the recent years. [The linear regression used for this analysis was not an appropriate method and therefore the 95% confidence intervals reported may not be reliable.] p.190

After the IARC meeting in 2011 the following data were available

USA

Zada et al. studied incidence trends of primary malignant brain tumors in the Los Angeles area during 1992-2006 (Zada, Bond et al. 2012). Incidence data for histologically-confirmed brain tumors were obtained from the Los Angeles County Cancer Surveillance Program (LAC), the California Cancer Registry (CCR), and the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program for 1992 to 2006. Annual percentage change (APC) was calculated for microscopically confirmed histological subtypes and anatomic sub sites. The overall incidence of primary malignant brain tumors decreased over the time period with the exception of glioblastoma multiforme (GBM) (astrocytoma grade IV). The annual age adjusted incidence rate of that tumor type increased statistically significant in the frontal lobe with APC +2.4 % to +3.0 % ($p < 0.001$) and temporal lobe APC +1.3 % to +2.3 % ($p < 0.027$) across all registries. In the California Cancer Registry the incidence of glioblastoma multiforme increased also in cerebellum, APC +11.9 % ($p < 0.001$). In the parietal and occipital lobes or in overlapping lobes no statistically significant changes in incidence were seen. For lower grade astrocytoma decreases of annual age adjusted incidence rates were observed. The authors concluded that despite decreased incidences in other brain regions there was an increase in the incidence of glioblastoma multiforme in

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frontal and temporal lobes and cerebellum. These parts of the brain are characterized by highest absorbed dose of radiation from mobile phones (Cardis, Deltour et al. 2008; Deltour, Wiart et al. 2011).

China

Ding et al. (Ding and Wang 2011) investigated time trends in the incidence of brain and nervous tumor in urban Shanghai, from 1983 to 2007, applying joinpoint regression models to analyze the annual incidence rates. From 1983 to 2007, the age-adjusted incidence rate of brain and nervous tumors increased gradually by 1.2% per year (95% confidence interval [CI] = 0.4% to 1.9%) among men and 2.8% per year (95% CI =2.1 to 3.4) among women. While the authors concluded that this study did not support an association between cellular telephone use and increased risk of brain and nervous tumors, the conclusion was made on assumption about *latency periods shorter 5-10 years.* Authors themselves recognize that this conclusion is not valid for longer latency periods, which are indeed predictable for gliomas and acoustic neuromas. Thus, authors do not take into account that radiation induced glioma (RIG) studies would reasonably not show so soon, given significantly higher latency periods. Common conclusions reached across diverse cases on RIG is that mean latency time was in the order of many years *(range: 9–17 years)* (Prasad and Haas-Kogan 2009). Thus, while the incidence rate has been shown to be increased in urban Shanghai, the conclusion of the authors on lack of association with mobile phones is flawed.

Australia

A multicenter study was performed to determine the brain cancer incidence in Australia (the state of New South Wales (NSW) and the Australian Capital Territory (ACT)) with age-, sex-, and benign-versus-malignant histology-specific analyses (Dobes, Shadbolt et al. 2011). One hundred percent of tumors were histologically confirmed. Data were weighted for patient outflow and *data completeness.* Incidence rates were age standardized and trends analyzed using joinpoint analysis. An overall significant increase in primary malignant brain tumors was observed over the study period from 2000 to 2008 (APC, 3.9; 95%CI, 2.4–5.4). Overall increasing trend in malignant tumors was consistent for both males (APC, 2.3; 95% CI, 0.4–4.2) and females (APC, 2.3; 95% CI, 0.3– 4.3). This increase appears to be largely due to an increase in malignant tumor incidence in the >/=65-year age group. The same authors reported an analysis of incidence by tumor subtype (Dobes, Khurana et al. 2011). A significant increasing incidence in glioblastoma multiforme (GBM) was observed in the study period (annual percentage change [APC], 2.5; 95% confidence interval [CI], 0.4-4.6, n = 2275), particularly after 2006. In GBM patients in the >/=65-year group, a significantly increasing incidence for men and women combined (APC, 3.0; 95% CI, 0.5-5.6) and men only (APC, 2.9; 95% CI, 0.1-5.8) was seen. Rising trends in incidence were also seen for meningioma in the total male population (APC, 5.3; 95% CI, 2.6-8.1, n = 515) and males aged 20-64 years (APC, 6.3; 95% CI, 3.8-8.8). Significantly decreasing incidence trends were observed for Schwannoma for the total study population (APC, -3.5; 95% CI, -7.2 to -0.2, n = 492), significant in women (APC, -5.3; 95% CI, -9.9 to -0.5) but not men.

Korea

Recent data from Korea has shown increase in brain cancer incidence (Jung, Won et al. 2013). Tumors of the brain and nervous system increased APC 1.0% per year for men and 0.5% per year for women during 1999 - 2010. The rate of increase was statistically significant for men ($p < 0.05\%$), while was not statistically significant for women. It should be noted that key parameters for the NT MW effects include sex and age (Belyaev 2010; IARC 2013). For both sexes, combined statistically significant rate of increase was 0.8% annually.

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Nordic national cancer registers

In Denmark, the Danish cancer register has reported increase in brain cancer incidence of 40% in men, and by 29% in women during 2001-2010. (http://www.sst.dk/publ/Publ2011/DAF/Cancer/Cancerregisteret2010.pdf)

Finland

In Finland, age-adjusted (world) brain cancer incidence rates per 100,000 person-years has not changed significantly since 1997 (http://www.kreftregisteret.no/no/Registrene/Kreftstatistikk/). Age-adjusted (world) incidence rates per 100 000 person-years by primary site and five-year period was in females 12,0 in 1992-96, 13,6 in 1997-01, 14,2 in 2002-06, 13,7 in 2007-11 (http://stats.cancerregistry.fi/stats/eng/veng0006i0.html) Age-adjusted (world) incidence rates per 100,000 person-years by primary site and five-year period was in males 10,7 in 1992-96, 10,6 in 1997-01, 11,7 in 2002-06, 11,2 in 2007-11. (http://stats.cancerregistry.fi/stats/eng/veng0005i0.html)

Norway

In Norway, age-adjusted (world) brain cancer incidence rates per 100 000 person-years has grown since 1997 (http://www.kreftregisteret.no/no/Registrene/Kreftstatistikk/). Age-adjusted (world) incidence rates per 100,000 person-years by primary site and five-year period was in females 10.6 in 1992-96, 13.3 in 1997-01, 17.3 in 2002-06, and 16.4 in 2007-11. Age-adjusted (world) incidence rates per 100,000 person-years by primary site and five-year period was in males 10.7 in 1992-96, 12.2 in 1997-01, 14.1 in 2002-06, and 14.2 in 2007-11.

Sweden

In Sweden, no statistically significant changes in brain cancer incidence per 100,000 person was shown in Cancer Register (Socialstyrelsens Cancerregister) during 1996 -2011. (http://www.socialstyrelsen.se/statistik/statistikdatabas/cancer). There is a scientifically reasonable suspicion that underreporting of brain cancers masks the brain cancer incidence in Sweden (Barlow, Westergren et al. 2009).

All Nordic countries. NORDCAN

Nordic cancer register (NORDCAN) shows increases in brain cancer incidence. NORDCAN project presents the incidence, mortality, prevalence and survival statistics from 41 major cancers in the Nordic countries (http://www-dep.iarc.fr/NORDCAN/english/frame.asp). In Denmark, a statistically significant increase in incidence rate per year for brain and central nervous system tumors (combined) was seen during 2001-2011 both in men, *annual percentage change (APC)*, 3.77, [95% CI 2.90; 4.64] and in women 3.68, [95% CI 2.29; 5.10]. While no statistically significant changes are observed in incidence rate per year for brain and central nervous system tumors during last 10 years in other Nordic countries (Finland, Iceland, Norway, and Sweden), a statistically significant increase is seen during last 10 years in men 1.02, 95%CI [0.40;1.65] and women, 1.05, 95%CI [0.35;1.74] in all Nordic countries combined.

Quality and completeness of cancer registers

The SCENIHR preliminary Opinion reaches an indefensible and highly controversial conclusion on brain cancer: *"That renders all studies reporting increased risks of such magnitude implausible. The reason for the increases are methodological artefacts"*. First, the time trends for brain cancer incidence is positive according to at least some data shown

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above. Second, it generally accepted that if two pieces of data do not fit each other both pieces should be scientifically analyzed. As a matter of fact, the utility of Cancer registries depends heavily on their quality including the *completeness* with which patients eligible for registration are ascertained (Bray and Parkin 2009; Parkin and Bray 2009). The *completeness* of cancer registry data – the extent to which all of the incident cancers occurring in the population are included in the registry database – is an extremely important attribute of a cancer registry (Parkin and Bray 2009). However, registries rarely report their completeness because it is difficult to measure (Bullard, Coleman et al. 2000).

Incompleteness was found in the Swedish Cancer Register (Barlow, Westergren et al. 2009). Underreporting of brain cancers including gliomas in Swedish Cancer Register was about 3.7% of the cases reported in 1998 (Barlow, Westergren et al. 2009).
It was estimated, that the Thames Cancer Registry (UK) attains 92.1% completeness 5 years after diagnosis for all cancers (Bullard, Coleman et al. 2000). Recent data have confirmed relatively low completeness of the Thames Cancer Registry with estimates ranging from around 78% (female melanoma) to 95% (female stomach cancer) (Robinson, Sankila et al. 2007). The Finnish data appeared to be more complete, with estimates ranging from around 96% completeness for prostate cancer to 100% for ovarian cancer (Robinson, Sankila et al. 2007).

The best characterized is the Cancer Register of Norway (CRN) (Larsen, Smastuen et al. 2009). A total of 93.8% of the cancer cases registered in the period 2001–2005 were morphologically verified. The proportion of DCO (death certificate only) cases 2001–2005 was only 0.9%, and only 2.2% were registered with primary site unknown (PSU). The overall completeness for the period 2001–2005, estimated by the capture/recapture method, was 98.8%. The lowest completeness was estimated for pancreas (95.7%), multiple myeloma (95.5%), leukemia (94.6%) and central nervous system (93.8%). Authors recognize that cancers of the central nervous system did not meet the highest standards. Nevertheless, recent registration data from Norway are among the most complete among the European Registries (Larsen, Smastuen et al. 2009).

Recent study has indicated the US cancer registries data may be incomplete as related to cancer mortality (German, Fink et al. 2011). Confirmation rate was estimated as 93.4 (95% CI, 92.6–94.2) (per 100 deaths) = the number of individuals who died sometime in 2002–2004 and had been diagnosed with brain cancer sometime in 1993–2004 for whom the cancer site listed in the population-based cancer registry matched the site (underlying cause) on their death certificate, divided by the total number of these decedents (both matched and unmatched). Detection rate was estimated 93.7 (95% CI, 90.5–96.9) = the number of individuals diagnosed with brain cancer (ICD-10, the International Statistical Classification of Diseases and Related Health Problems, 10th Revision) sometime in 1993–1995 who died sometime in 1993–2004 for whom the cancer site listed in the population-based cancer registry matched the site (underlying cause) on their death certificate, divided by the total number of these decedents (both matched and unmatched).

Similar incompleteness has been reported by Meguerditchian et al for the National Cancer Data Base (NCDB) (Meguerditchian, Stewart et al. 2010). Claims for patients with breast cancer surgery from one payer in Western New York (WNY) were matched with NCDB for participating hospitals for 2001-2003 using available identifiers (reporting hospital, gender, birth date, ZIP code). Four hundred seventy patients with health insurance provided by IHA with a breast procedure and a diagnosis code for breast cancer between January 1, 2001 and

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January 1, 2003 at the participating institutions were identified by ICD-9 and CPT codes. These patients were matched to all breast cancers reported to the NCDB from the CoC-approved hospitals during the same period and in the same geographic area. The final match rate between the two datasets was 93.4% (430 patients). Forty cases identified by IHA remained unmatched to the registries.

The time trends for *incompleteness* of the Cancer Registers is not known. Finally, Cancer Register's data should be questioned if no consistence is observed between them and epidemiological data on mobile phone usage.

Conclusion on brain cancer time trend data and mobile phones

Cancer incidence data are derived from cancer registries and quality of these data dependent on quality and completeness of cancer registers. Completeness and quality of most cancer registries are not comprehensively characterized and vary between cancer registers. At least some cancer registries including better described Nordic Cancer Register show increased time trends in brain cancer incidence, especially in those parts of brain which are mostly exposed to radiation from mobile phones. Taking into account the IARC statement regarding the role of incidence data in phone risk assessment, the incidence data do not contradict to the increased cancer risk seen in epidemiological studies at latencies more than 10-25 years (Carlberg, Soderqvist et al. 2013; Hardell and Carlberg 2013; Hardell, Carlberg et al. 2013; Hardell, Carlberg et al. 2013). The IARC Working Group further noted that these descriptive analyses would be null if an excess in cancer risk from mobile-phone use became manifest only decades after phone use began, or if an increase affected only a small proportion of the cases by location.

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On page 68 the SCENIHR report states: "it appears the evidence for glioma became weaker". This conclusion is in evident contradiction with available data. Recent publications including those omitted in the SCENHIR report and mentioned in these comments make this evidence much stronger then during the last IARC meeting in 2011 and demands IARC classification "carcinogen, group 1" for EMF exposures from mobile phones.

In vivo studies

Similar to other parts of this report, the conclusions from *In vivo* studies, p 68- , are fundamentally flawed because they are not based on mechanistic studies and consideration of important physical and biological parameters (IARC 2013).

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As a matter of fact, only negligible amount of real signals (frequency, modulation, polarizaton) were tested in mentioned *in vivo* studies. Thus, the statement, p 68, "*Overall, it was concluded that RFR fields such as those emitted by mobile phones were not carcinogenic in laboratory rodents*" may be relevant only to these limited number of tested signals. Similarly the statement: *" Overall, because a considerable number of well-performed studies using a wide variety of animal models have been mostly negative in outcome, the animal studies are considered to provide strong evidence for the absence of an effect*" deals with only minority of real signals and cannot be used as an argument against overwhelming evidence for increased cancer risks following from epidemiological studies, which involved all possible signals. What is even more important, most positive studies involved exposure to the more realistic exposure that includes combined signals from real mobile phones. These are the most relevant for health risk assessment, but were omitted in the SCENIHR report (see below).

It is fundamentally flawed to question results of epidemiological studies obtained with exposure to all signals from mobile phones by *in vivo* or *in vitro* negative studies obtained with negligible number of mobile phone-like signals.

Genotoxic RFR effects, p. 70

These studies were omitted from review in the preliminary Opinion and should be incorporated. Positive studies on RFR/mobile phone genotoxicity include but are not limited to (Guler, Tomruk et al. 2010; Cam and Seyhan 2012; Guler, Tomruk et al. 2012; Karaca, Durmaz et al. 2012; Sekeroglu, Akar et al. 2012; Atasoy, Gunal et al. 2013; Atli Şekeroğlu, Akar et al. 2013; Hanci, Odaci et al. 2013; Liu, Duan et al. 2013; Liu, Gao et al. 2013; Pesnya and Romanovsky 2013).

Considering Belyaev's group studies (Belyaev, Markova et al. 2009; Markova, Malmgren et al. 2010) the SCENIHR preliminary opinion stated, page 72, that effects at 905 MHz were inconsistent. It should be noted that this "inconsistency" was actually individual variability, which nature has recently been established to be dependant on individual state of chromatin at time of exposure (Sarimov, Alipov et al. 2011). One of the main results following from the Belyaev's group studies including those unmentioned neither in this nor in previous SCENIHR report (Sarimov, Malmgren et al. 2004; Belyaev, Hillert et al. 2005; Markova, Hillert et al. 2005) is strong dependence of effects from mobile phones on carrier frequency/frequency channel. Effects at 905 MHz/GSM channel 74 on DNA repair foci were consistently lower compared to effects at 915 MHz/GSM channel 124 regardless cell type, human lymphocytes, fibroblasts or stem cells. In addition, the data indicated stronger effects of exposure to RF from UMTS mobile phone at frequency at 1947.4 MHz, middle channel. Importantly, human stem cells (not "steam cells" as spelled in the SCENIHR preliminary opinion on page 72, line 16) were most sensitive to MW exposure providing a mechanistic link to carcinogenesis. This is because stem cells are the generally accepted cellular target for origination of different types of tumors and leukemia. These data provided evidence that different frequency channels of different types of mobile communications should be separately tested for health effects and that primary human stem cells are an key cellular focus for in vitro EMF studies dealing with carcinogenesis.

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Mechanisms for non-thermal MW effects below ICNIRP safety levels

It is generally accepted now that MW induce effects under non-thermal intensities which are generally called non-thermal effects. The SCENIHR preliminary opinion states that: *"(I)n view of the lack of verification of any proposed non-thermal interaction mechanism, established knowledge does not suggest effects accumulating with time".*

First, this statement is in contradiction with generally accepted Bradford Hill criteria: *"Plausibility: It will be helpful if the causation we suspect is biologically plausible. But this is a feature I am convinced we cannot demand. What is biologically plausible depends upon the biological knowledge of the day. '*. . . no biological knowledge to support (or to refute) Pott's observation in the 18th century of the excess of cancer in chimney sweeps. It was lack of biological knowledge in the 19th that led a prize essayist writing on the value and the fallacy of statistics to conclude, amongst other "absurd" associations, that "*it could be no more ridiculous for the stranger who passed the night in the steerage of an emigrant ship to ascribe the typhus, which he there contracted, to the vermin with which bodies of the sick might be infected*". And coming to nearer times, in the 20th century there was no biological knowledge to support the evidence against rubella.' ..... the association we observe may be one new to science or medicine and we must not dismiss it too light-heartedly as just too odd. As

Sherlock Holmes advised Dr Watson, *'when you have eliminated the impossible, whatever remains, however improbable, must be the truth*.' "(Hill 1965).

Second, there are a number of studies showing accumulation of effects with time (Belyaev 2010).

Third, the majority of scientists consider NT MW effects within the frame of mechanisms using quantum mechanics and physics of nonlinear systems in biological non-equilibrium systems, which are relevant for mechanisms of NT MW in biological systems (Belyaev 2010). It is generally accepted that more then one physical theory may describe the same phenomena (compare for example Debye model of phonons in a box and Einstein model of quantum harmonic oscillators for solids). Thus, the demand of a generally accepted mechanism is not scientifically justified and represents methodological flaw. Most representative so far international IARC expert panel has concluded: "*Although it has been argued that RF radiation cannot induce physiological effects at exposure intensities that do not cause an increase in tissue temperature, it is likely that not all mechanisms of interaction between weak RF-EMF (with the various signal modulations used in wireless communications) and biological structures have been discovered or fully characterized*", see page 104 (IARC 2013). Thus, the IARC Working Group does not reject physical mechanisms for mobile phone exposure and recognizes that either new mechanisms may come or already known mechanisms may be better characterized to explain the non-thermal effects.
Among other mechanisms, radical pairs mechanisms is widely accepted. In many recent reports unmentioned by the SCENIHR preliminary opinion it has been shown that ROS may be involved in radical pair reactions, thus, radical pairs may be considered one of the mechanisms of transduction able to initiate cell oxidative stress (Georgiou 2010; Apollonio, Liberti et al. 2013; Bodera, Stankiewicz et al. 2013; Burlaka, Tsybulin et al. 2013). Furthermore, many of the changes observed in RF-exposed cells were prevented by (pre)treatment with antioxidants (IARC 2013). In addition, recent review has summarized studies on EMFs exposure and oxidative stress in brain (Consales, Merla et al. 2012). While the data from different studies should be compared with care in view of variation in physical and biological parameters, most part of collected data have shown effects of ELF and RF EMF on oxidative stress in brain (Consales, Merla et al. 2012). IARC monograph states: "*even small effects on radical concentration could potentially affect multiple biological functions*", page 103 (IARC 2013).

One of the main arguments against NT MW effects, so called kT-paradox, has further been challenged by consideration of biological processes far from thermodynamic equilibrium (Cifra, Fields et al. 2011). Subculture structures such as molecular motors operate, in general, under conditions far from thermodynamic equilibrium and, therefore, the formalism of non-equilibrium thermodynamics, which was generally used in critics of mechanisms for NT MW effects, for coupled mechano-chemical processes is not applicable (Chowdhury 2013). Therefore, one has to use the more sophisticated toolbox of stochastic processes and nonequilibrium statistical mechanics for theoretical treatment of molecular motors.
Theoretical studies by Srobar in development of fundamental theory by H. Fröhlich have not been considered neither in this nor in previous SCENIHR Opinion on EMF (Srobar 2009; Srobar 2009).

Effects of RFR exposure on oxidative stress, p 177

This chapter provides a biased record of very minor part of oxidative stress studies without definition how these studies have been chosen for analysis. Recent positive studies on

RF/mobile phone oxidative stress and genotoxicity have not been included (Haghani, Shabani et al. 2013) (Tomruk, Guler et al. 2010; Esmekaya, Ozer et al. 2011; Kumar, Behari et al. 2012) (Lu, Huang et al. 2012) (Tkalec, Stambuk et al. 2013) (Deshmukh, Banerjee et al. 2013) (Shahin, Singh et al. 2013) (Eser, Songur et al. 2013) (Burlaka, Tsybulin et al. 2013) (Esmekaya, Aytekin et al. 2011) (Avci, Akar et al. 2012) (Ceyhan, Akkaya et al. 2012) (Sokolovic, Djordjevic et al. 2013) (Oksay, Naziroglu et al. 2012) (Sisodia, Rifat et al. 2013) (Liu, Duan et al. 2013) (Jelodar, Akbari et al. 2013) (Liu, Gao et al. 2013) (Ghanbari, Mortazavi et al. 2013) (Guler, Tomruk et al. 2010; Guler, Tomruk et al. 2012) (Imge, Kilicoglu et al. 2010) (Jelodar, Akbari et al. 2013) (Liu, Duan et al. 2013) (Naziroglu, Cig et al. 2012) (Ni, Yu et al. 2013) (Ozgur, Gler et al. 2010) (Park, Seo et al. 2013)

Replication studies

The most representative so far international IARC panel have included in the RF monograph, pages 101-102: "*The reproducibility of reported effects may be influenced by exposure characteristics (including SAR or power density, duration of exposure, carrier frequency, type of modulation, polarization, continuous versus intermittent exposures, pulsed-field variables, and background electromagnetic environment), biological parameters (including cell type, growth phase, cell density, sex, and age) and environmental conditions (including culture medium, aeration, and antioxidant levels)*" (IARC 2013). IARC admits also that some of the discrepancies between EMF replication studies could be due to differences in species, page 416 (IARC 2013). And at the page 104: "*Biological systems are complex and factors such as metabolic activity, growth phase, cell density, and antioxidant level might alter the potential effects of RF radiation*". Physical factors that affect interpretation of study results are considered in the IARC monograph in more detail on pages 385-387 (IARC 2013).

The SCENIHR preliminary Opinion requires "*replication studies in a strict sense*" for positive findings (page 101). Furthermore, those studies which consistently showed positive findings were criticized for deviations in protocols (p 101, lines 41-49). No such criticism was applied to studies which failed to "replicate" original positive finding (for example page 102, lines 39-49) even if the key parameters of experiments were or might be different between original studies and "replications". At many occasions, the SCENIHR preliminary Opinion states that replication of positive findings is essential before weight is given to positive results. However, the SCENIHR preliminary Opinion has never applied the same criteria to negative studies even if statistical power was not evaluated in most of them and thus the value of possibly missed effects is not known. As a matter of fact, not one of the negative studies has been replicated "*in a strict sense*" and not one of positive studies has been "unreplicated"/dismissed in "*in a strict sense*". Application of double standards for assessment of positive and negative studies is methodologically flawed and makes the SCENIHR preliminary Opinion internally inconsistent.

The SCENIHR report missed successful replications of positive studies (Grigoriev, Grigoriev et al. 2010; Havas and Marrongelle 2013).

In addition to aforementioned omitted studies reporting positive effects, this preliminary Opinion omitted many other recent positive studies which include but not limited to:

(Fragopoulou, Samara et al. 2012) (Karaca, Durmaz et al. 2012) (Dasdag, Akdag et al. 2012) (Celikozlu, Ozyurt et al. 2012) (Sharma, Sisodia et al. 2013) (Lv, Chen et al. 2014) (Jin, Zong et al. 2012) (Trivino Pardo, Grimaldi et al. 2012) (Aboul Ezz, Khadrawy et al. 2013) (Kesari, Kumar et al. 2011) (Redmayne, Smith et al. 2013) (Deshmukh, Banerjee et al. 2013; Deshmukh, Megha et al. 2013) (Aboul Ezz, Khadrawy et al. 2013) (Cam and Seyhan 2012)

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(Cervellati, Valacchi et al. 2013) (Finnie, Cai et al. 2010) (Jorge-Mora, Misa-Agustino et al. 2011) (Kwon, Vorobyev et al. 2011) (Panagopoulos, Chavdoula et al. 2010; Panagopoulos and Margaritis 2010; Panagopoulos and Margaritis 2010) (Shckorbatov, Pasiuga et al. 2010) (Suhhova, Bachmann et al. 2013) (Vishnu, Nithyaja et al. 2011) (Sun, Shen et al. 2013) (Tomruk, Guler et al. 2010) (Wu, Wang et al. 2012) (Xu, Chen et al. 2013)

Negative studies were preferentially included into the report even if the same group published both positive and negative studies analyzing different endpoints. An example is the group of Lopez-Martin, which has published negative study on apoptosis in adult male Sprague-Dawley rats exposed for 1 hour to 900 MHz. This negative study was included to the SCENIHR report on page 157. However, the same group has published study revealing that similar exposure at 900 MHz and intensities lower then those from mobile phones induces c-fos proto-oncogene and glial fibrillary acid protein (GFAP) marker in brain of exposed male Sprague-Dawley rats (Carballo-Quintas, Martinez-Silva et al. 2011). This positive study has not been included in the SCENIHR report.

Omission of positive studies showing detrimental effects of RFR exposure and their possible mechanisms especially negatively affects conclusions of the SCENIHR report. An example is data from by Deshmukh et al., which show effects of RFR on cognitive function, DNA damage and oxidative stress in rats exposed under the same conditions (Deshmukh, Banerjee et al. 2013; Deshmukh, Megha et al. 2013).

Exclusion of positive studies questions the conclusions of the SCENIHR report on RFR health effects because some of them describe critical effects which were not considered by the SCENIHR report. Example is study by Aboul Ezz (Aboul Ezz, Khadrawy et al. 2013) which investigated the effect of RFR (frequency 1800 MHz, specific absorption rate 0.843 W/kg, power density 0.02 mW/cm2, modulated at 217 Hz) on the concentrations of dopamine (DA), norepinephrine (NE) and serotonin (5-HT) in the hippocampus, hypothalamus, midbrain and medulla oblongata of adult rats. Adult rats were exposed daily to EMR and sacrificed after 1, 2 and 4 months of daily RFR exposure and 1 month after 4 months of daily RFR exposure. RFR exposure induced significant changes in DA, NE and 5-HT in all studied areas of adult rat brain. The authors concluded that exposure of adult rats to RFR may cause disturbances in monoamine neurotransmitters and this may underlie many of the adverse effects reported after RFR including memory, learning, and stress. In a recent German study, 24 out of 60 participants were exposed to MW from a base station (cell tower) at a power density of < 60 $\mu W/m^2$, 20 participants to 60 - 100 $\mu W/m^2$, and 16 participants to more than 100 $\mu W/m^2$ (Buchner and Eger 2011). The values of the stress hormones adrenaline and noradrenalin increased significantly during the first 6 months after exposure to the GSM base station; the values of the precursor substance dopamine substantially decreased in this time period. The subject's initial endocrine state was not restored even after 1.5 years. Due to the non-regulable chronic difficulties of the stress balance, the phenylethylamine levels dropped until the end of the investigation period. These effects show a dose response relationship.

Provocation studies, p. 108

In view of complex dependence of NT MEW effects on physiological state of the object, individual sensitivity, physical parameters of exposure, duration and time after exposure the provocation studies should not be considered as informative regarding exposure to all real mobile communication systems including cellphones because only minor part of these parameters (frequency, modulation, duration of exposure et cetera) have been analyzed.

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Conclusions on symptoms. p. 115

Similar to other conclusions on RFR health effects, conclusions on symptoms on page 115 do not take into account dependence of RFR effects on physical parameters such as frequency and modulation. In contrast to this flawed approach by the SCENIHR report, in recent study Redmayne et al. evaluated associations between New Zealand early-adolescents' subjective well-being and self-reported use of, or exposure to diffrent types of wireless phones and internet technology (Redmayne, Smith et al. 2013). In this cross-sectional survey, participants completed questionnaires in class about their cellphone and cordless phone use, their self-reported well-being, and possible confounding information such as whether they had had influenza recently or had a television in the bedroom. Parental questionnaires provided data on whether they had WiFi at home and cordless phone ownership and model. Data were analysed with Ordinal Logistic Regression adjusting for common confounders. Odds ratios (OR) and 95% confidence intervals were calculated. The number and duration of cellphone and cordless phone calls were associated with increased risk of headaches (>6 cellphone calls over 10 minutes weekly, adjusted OR 2.4, CI 1.2-4.8; >15 minutes cordless use daily adjusted OR 1.74, CI 1.1-2.9)). Using a wired cellphone headset was associated with tinnitus (adjusted OR 1.8, CI 1.0-3.3), while wireless headsets were associated with headache (adjusted OR 2.2, CI 1.1-4.5), feeling down/depressed (adjusted OR 2.0, CI 1.1-3.8), and waking in the night (adjusted OR 2.4, CI 1.2-4.8). Several cordless phone frequencies bands were related to tinnitus, feeling down/depressed and sleepiness at school, while the last of these was also related to modulation. The only significant negative regression was less likely Waking nightly for those with Wi-Fi at home (adjusted OR 0.7, CI 0.4-0.99). Being woken at night by a cellphone was strongly related to tiredness at school (OR 3.49, CI 1.97-6.2).
There were more statistically significant associations (36%) than could be expected by chance (5%). Several were dose-dependent relationships. The obtained data were in line with previous findings of others and suggested limiting use of cellphones and cordless phones to less than 15 minutes daily, and employing a speaker-phone device for longer daily use.

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Methodological flaw in assessment

In contrast to generally accepted methodology used by IARC, this SCENIHR report subjectively divides studies into informative and non-informative (page 83-84). As a result the same studies SCENIHR report assess differently as compared to IARC : *" For in vivo studies our assessment of evidence is weaker than IARC, based on the same studies as used in the IARC evaluation".* While the SCENIHR report requires statistical power for negative studies (page 17), the majority of negative studies which the preliminary Opinion relies upon did not analyze statistical power and were not able to determine at what level of sensitivity the RFR effects might be missed. It is not stated in the SCENIHR preliminary Opinion how many experts evaluated each study and whether experts were allowed to evaluate own studies. The SCENIHR report inconsistently uses criteria for replication studies and verification of results. Strict following to generally accepted key biological and physical parameters the conditions is demanded at some occasions of the SCENIHR report. On the other hand, the effects of gender and biological efficiency of low SAR values is used to question validity of results (lines 3-4, page 103). Effects of low SARs and gender were described in many papers (Belyaev 2010; IARC 2013) and thus cannot be used as argument against NT MW effects.

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Exclusion of studies with exposure to real mobile phones, which are most relevant for assessment of health effects from mobile telephony p. 117

On Page 117 the SCENIHR report states that studies with exposure to real mobile phones "*are of no use for health risk assessment, as the exposures would have been highly complex and very variable, especially if the animals were unrestrained and free to move in their*

cages". This is fundamentally flawed statement which results in excluding mostly important for health risk assessment studies and thus masking health risks from mobile communication. As a matter of fact, the studies with real mobile phones, given the EMF field was measured from the phone, represent most valuable type of studies for assessment of risks from mobile telephony. The reasons were recently analyzed in review by Belyaev that has not been included in the SCENIHR report (Belyaev 2010). In brief, real signals contain multiple (hundreds and even thousands, in dependence on type of mobile communication) components, such as carrier frequencies or frequency bands, different types of modulations. It is generally accepted that all these parameters are important for effects of MW (IARC 2013). Exposure to mobile phone may reproduce the majority of real signals during the same exposure session and thus provide the best possibility to asses detrimental effects from mobile telephony. Another type of exposure, to which the SCENIHR report has chosen to rely upon, is exposure to one fixed frequency and fixed modulation which reproduces one from thousands possible signals. While one RFR frequency/frequency band/modulation can induce detrimental effect, another one can be inactive (Belyaev 2010). In addition, mobile phones emit not only MW but also ELF fields, which have also been shown to produce detrimental effects (www.bioititive.org) and to interfere with MW effects (Belyaev 2010; Sun, Shen et al. 2013). Importantly, most of aforementioned studies with mobile phones as source of EMF exposure and omitted by the SCENIHR report show detrimental effects and most importantly indicate mechanism of these effects based on induction of ROS.

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Data obtained with selected frequency/frequency band/modulation provides possibility to asses only this specific signal and may be important for consideration of biophysical mechanisms for NT MW effects. However, these studies are evidently less important for health risk assessment by the reasons provided above.

Recommendations

The main issue of further research is to promote studies on biophysical mechanisms that will provide a mechanistic basis for risk assessment. Such parameters as frequency, modulation, polarization should be given priority for mechanistic studies so that physical and biological variables that influence study outcome can be taken into account.

For risks assessment in laboratory studies, the complexity and interplay of variables from real systems of mobile communication should also be taken into account. In other words, to assess health risks from any type of mobile communication, all specific frequency channels and all specific modulations should be investigated in combinations as at real exposures.

Recent studies indicated that financial interests may affect the outcome of EMF laboratory studies (Huss, Egger et al. 2007; Huss, Egger et al. 2008). Also recent review reports that the negative results produced by studies funded by the cell-phone companies are affected by many biases and flaws, giving rise to a systematic underestimate of the risk (Levis, Minicuci et al. 2011). On the contrary, studies producing positive results - without errors and financial conditioning - indicate a cause/effect relationship supported by biological plausibility (Levis, Minicuci et al. 2011). In view if these facts, it is recommended to take into account the source of funding in evaluation of the results.

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https://needtoknow.news/2020/10/cdc-study-admits-covid-virus-infects-only-poisoned-monkey-cells-not-humans/

CDC Study Admits COVID "Virus" Infects Only Poisoned Monkey Cells, Not Humans!

October 26, 2020 Dr. Tom Cowan 6

Unicorn, Dr. Tom Cowan's website

SARS-CoV-2 is the name of the virus that is claimed to cause the disease Covid-19. Dr. Tom Cowan published an astonishing analysis of a study from the CDC that admits that the SARS-CoV-2 "virus" has not been properly isolated or purified, which means that they cannot prove that a novel, never-been-seen-before virus, even exists. Instead of isolating the virus, the scientists only looked at 37 out of the approximately 30,000 of the base pairs that are claimed to be the genome of the intact virus. The 37 segments were put into a computer program that filled in the rest of the base pairs, which Dr. Cowan says is scientific fraud.

The virologists introduced solutions they say contain the virus into a variety of tissue cultures, including three that contained human cells. None of the human cells became infected, and is, therefore, harmless to humans. The only tissue cultures that did become infected were monkey kidney cells that were treated with two potent drugs that are toxic to kidneys.

This week, my colleague and friend Sally Fallon Morell brought to my attention an amazing article put out by the CDC. The link to the article is here, and it was published in June 2020. The purpose of the article was for a group of about 20 virologists to describe the state of the science of the isolation, purification and biological characteristics of the new SARS-CoV-2 virus, and to share this information with other scientists for their own research. A thorough and careful reading of this important paper reveals some shocking findings.

First, in the section titled "Whole Genome Sequencing," we find that rather than having isolated the virus and sequencing the genome from end to end, they found 37 base pairs from unpurified samples using PCR probes This means they actually looked at 37 out of the approximately 30,000 of the base pairs that are claimed to be the genome of the intact virus. They then took these 37 segments and put them into a computer program, which filled in the rest of the base pairs.

To me, this computer-generation step constitutes scientific fraud. Here is an equivalency: A group of researchers claim to have found a unicorn because they found a piece of a hoof, a hair from a tail, and a snippet of a horn. They then add that information into a computer and program it to re-create the unicorn, and they then claim this computer re-creation is the real unicorn. Of course, they had never actually seen a unicorn so could not possibly have examined its genetic makeup to compare their samples with the actual unicorn's hair, hooves and horn.

The researchers claim they decided which is the real genome of SARS-CoV-2 by "consensus," sort of like a vote. Again, different computer programs will come up with different versions of the imaginary "unicorn," so they come together as a group and decide which is the real imaginary unicorn.

The real blockbuster finding in this study comes later, a finding so shocking that I had to read it many times before I could believe what I was reading. Let me quote the passage intact:

"Therefore, we examined the capacity of SARS-CoV-2 to infect and replicate in several common primate and human cell lines, including human adenocarcinoma cells (A549), human liver cells (HUH 7.0), and human embryonic kidney cells (HEK-293T). In addition to Vero E6 and Vero CCL81 cells. … Each cell line was inoculated at high multiplicity of infection and examined 24h post-infection. No CPE was observed in any of the cell lines except in Vero cells, which grew to greater than 10 to the 7^{th} power at 24 h post-infection. In contrast, HUH 7.0 and 293T showed only modest viral replication, and A549 cells were incompatible with SARS CoV-2 infection."

What does this language actually mean, and why is it the most shocking statement of all from the virology community? When virologists attempt to prove infection, they have three possible "hosts" or models on which they can test. The first is humans. Exposure to humans is generally not done for ethical reasons and has never been done with SARS-CoV-2 or any coronavirus. The second possible host is animals. Forgetting for a moment that they never actually use purified virus when exposing animals, they do use solutions that they claim contain the virus. Exposure to animals has been done once with SARS-CoV-2, in an experiment that used mice. The researchers found that none of the wild (normal) mice got sick. In a group of genetically modified mice, a statistically insignificant number lost some fur. They experienced nothing like the illness called Covid 19.

The third method virologists use to prove infection and pathogenicity — the method they most rely on — is inoculation of solutions they say contain the virus onto a variety of tissue cultures. As I have pointed out many times, such inoculation has never been shown to kill (lyse) the tissue, unless the tissue is first starved and poisoned.

The shocking thing about the above quote is that using their own methods, the virologists found that solutions containing SARS-CoV-2 — even in high amounts — were NOT, I repeat NOT, infective to any of the three human tissue cultures they tested. In plain English, this means they proved, on their terms, that this "new coronavirus" is not infectious to human beings. It is ONLY infective to monkey kidney cells, and only then when you add two potent drugs (gentamicin and amphotericin), known to be toxic to kidneys, to the mix.

My friends, read this again and again. These virologists, published by the CDC, performed a clear proof, on their terms, showing that the SARS-CoV- 2 virus is harmless to human beings. That is the only possible conclusion, but, unfortunately, this result is not even mentioned in their conclusion. They simply say they can provide virus stocks cultured only on monkey Vero cells, thanks for coming.

Read full article here…

http://microwavenews.com/news-center/ntp-cancer-results

Cell Phone Radiation Boosts Cancer Rates in Animals;
$25 Million NTP Study Finds Brain Tumors

U.S. Government Expected To Advise Public of Health Risk

May 25, 2016

The cell phone cancer controversy will never be the same again.

The U.S. National Toxicology Program (NTP) is expected to issue a public announcement that cell phone radiation presents a cancer risk for humans. The move comes soon after its recently completed study showed statistically significant increases in cancer among rats that had been exposed to GSM or CDMA signals for two-years.

Discussions are currently underway among federal agencies on how to inform the public about the new findings. NTP senior managers believe that these results should be released as soon as possible because just about everyone is exposed to wireless radiation all the time and therefore everyone is potentially at risk.

The new results contradict the conventional wisdom, advanced by doctors, biologists, physicists, epidemiologists, engineers, journalists and government officials, among other pundits, that such effects are impossible. This view is based, in part, on the lack of an established mechanism for RF radiation from cell phones to induce cancer. For instance, earlier this week (May 22), a medical doctor in Michigan wrote an opinion piece for the *Wall Street Journal* stating that, "There is no known mechanism by which mobile phones might cause brain tumors." He went on to argue that there is no need to warn the public about health risks.

The NTP findings show that as the intensity of the radiation increased, so did the incidence of cancer among the rats. "There was a significant dose-response relationship," a reliable source, who has been briefed on the results, told *Microwave News.* No effect was seen among mice. The source asked that his/her name not be used since the NTP has not yet made a formal announcement. The rats were exposed to three different exposure levels (1.5, 3 and 6 W/Kg, whole body exposures) and two different types of cell phone radiation, GSM and CDMA.

An Amazing Coincidence?

Importantly, the exposed rats were found to have higher rates of two types of cancers: glioma, a tumor of the glial cells in the brain, and malignant schwannoma of the heart, a very rare tumor. None of the unexposed control rats developed either type of tumor.

A number of epidemiological studies have linked cell phones to both gliomas and to Schwann cell tumors. The Interphone study, for instance, found an association between the use of cell phones and gliomas.

The sheath that wraps around cranial nerves —such as the one that connects the inner ear to the brain— is made of Schwann cells. Tumors of those cells are called acoustic neuromas. That is, an acoustic neuroma is a type of schwannoma. At least four different epidemiological studies have found an association between the use of cell phones and acoustic neuromas.

Ron Melnick, who led the team that designed the NTP study and who is now retired, confirmed the general outline of the results detailed by the confidential source. "The NTP tested the hypothesis that cell phone radiation could not cause health effects and that hypothesis has now been disproved," he said in a telephone interview. "The experiment has been done and, after extensive reviews, the consensus is that there was a carcinogenic effect."

"These data redefine the cell phone radiation controversy," Melnick said. The safety of cell phones has been debated for more than 20 years, especially after the International Agency for Research on Cancer (IARC) classified RF radiation as a possible human carcinogen in 2011.

"This is a major public health concern because the cells which became cancerous in the rats were the same types of cells as those that have been reported to develop into tumors in cell phone epidemiological studies," Melnick added. "For this to be a chance coincidence would be truly amazing."

The NTP radiation project, which has been underway for more than a decade, is the most expensive ever undertaken by the toxicology program. More than $25 million has been spent so far.

Another interesting coincidence is that the Ramazzini study of rats in Bologna exposed to extremely low frequency (50 Hz) EMFs also developed a significant increase in malignant schwannoma of the heart.

NTP Stands By the Study Results

Because of the importance of these results to public health, the NTP alerted the highest levels of the National Institutes of Health (NIH), where resistance prompted further reviews. No serious flaws in the data or the conduct of the studies were identified.

Senior managers including Linda Birnbaum, the director of the National Institute of Environmental Health Sciences (NIEHS) who also serves as the director of the NTP, and John Bucher, the associate director of the NTP, who is in charge of the cell phone study, are standing by the study findings. They see the need to release the results as a public health imperative, according to the source.

Chris Portier, who once held Bucher's job, agrees that the NTP is doing the right thing. "I would be adamant that we should share the data with the public as soon as possible," he said in an interview. The cell phone study was initiated while Portier was serving as the associate director of the NTP. He is now retired, though he continues to work as a consultant.

After extended discussions, the two federal agencies responsible for regulating exposures to cell phone radiation, the Food and Drug Administration (FDA) and the Federal Communications Commission (FCC), were briefed on the results last week. It is not clear how these regulatory agencies plan to respond.

All the various agencies are now in the process of planning the release of the NTP findings. Neither Birnbaum nor Bucher responded to a request for comment on how this will be done.

Unexpected Findings

Few outsiders are yet aware of the NTP results. When *Microwave News* told some of those who have been tracking the study for years what had been found, all expressed surprise.

Indeed, in an interview published years ago, NTP's Bucher said that he expected the results to show no association between RF radiation and cancer.

“Everyone expected this study to be negative,” said a senior government radiation official, who asked that his name not be used. “Assuming that the exposures were carried out in a way that heating effects can be ruled out, then those who say that such effects found are impossible are wrong,” the official said. (The study was designed to ensure that the body temperature of the exposed rats increased less than 1ºC.)

“This is a game changer, there is no question,” said David Carpenter, the director of the Institute for Health and the Environment at the University of Albany. “It confirms what we have been seeing for many years —though now we have evidence in animals as well as in humans.” Carpenter went on to add, “The NTP has the credibility of the federal government. It will be very difficult for the naysayers to deny the association any longer.” Carpenter’s institute is a collaborating center of the World Health Organization (WHO).

John Boice, the president of the National Council on Radiation Protection and Measurements (NCRP), is one of the leading skeptics. “For most of us, the issue of brain cancer and cell phones is resolved. There is no risk. There is no biological mechanism and no animal study or cellular study that finds reproducible evidence of an effect,” Boice told a reporter for Medscape Medical News earlier this month.

This view is so deeply held that in the summer of 2014, the NCRP pressured the Centers for Disease Control (CDC) to delete precautionary advice from a fact sheet on cell phones.

Boice was discounting last year’s report from Germany by Alex Lerchl confirming an earlier animal study showing that cell phone radiation can promote tumors in mice that were induced by toxic chemicals. The NTP experiments did not use any agent to initiate cancer cells in the animals.

With respect to mechanisms, just a couple of months ago, Frank Barnes and Ben Greenebaum, two senior members of the RF research community, announced that they could explain how low levels of RF radiation could alter the growth rates of cancer cells.

Later…
See also our follow-up articles:

— NTP: RF Breaks DNA

— Setting the Record Straight on NTP Cell Phone Cancer Study

— News Media Nix NTP Phone Cancer Study; “Don’t Believe the Hype”
Are More People Getting Brain Tumors?
GBMs, the Most Virulent Type, Are Rising

— Brain Tumors More Likely in Male than Female Rats
Historical Controls Show the Difference

NTP RF Animal Project: Timeline

1999 FDA nominates RF from wireless devices for testing by NTP

2001 NTP decides to sponsor RF–cancer studies

2003 NTP solicits proposals for RF–cancer experiments

2004 NTP issues second request for proposals

2005 NTP signs contract with IITRI in Chicago to carry out exposures

2007 Exposure systems made by IT'IS installed at IITRI

2009 The lead investigator Ron Melnick retires, Michael Wyde takes over

2014-15 Exposures of two-year studies completed

2016 Results in hand

Further reading:

— Institute of Environmental Health Secrets: NIEHS Mum on $25 million RF Animal Project

— NCRP Pressured CDC To Remove Cell Phone Safety Advice

— RF Cancer Promotion: Animal Study Makes Waves

— CDC Calls for Caution on Cell Phones, Then Gets Cold Feet

— Something Is Rotten in Denmark: Danish Cancer Society Plays Games with Tumor Rates

— It May Not Be Impossible After All

— Power-Frequency EMFs Promote Cancer in Massive Animal Study

— Will NIEHS Ever "Get" EMFs?

RF animal studies,
NTP,
NIEHS,
NIH,
John Bucher,
Linda Birnbaum,
Ron Melnick,
Christopher Portier,
John Boice,
Alexander Lerchl,
Frank Barnes,
Ben Greenebaum,
cancer,
glioma,
acoustic neuroma,
schwannoma,
brain cell phones,

https://www.rfsafe.com/studyproof-cell-phone-radiation-exacerbates-disease-inflammation-etiologic-factor/

Study: Proof Cell Phone Radiation Exacerbates Disease In Which Inflammation Is An Etiologic Factor

Millions of people around the world are becoming increasingly sensitive to radio frequency radiation; often manifesting itself as pain and mild inflammation (Latin, īnflammō, "I ignite, set alight") brought on through the complex biological response of vascular tissues as a result of harmful man-made stimuli — such as stressed or damaged cells from exposure to microwave radiation produced by cell phones.

Cell phone users sensitive to radiation exposure have long complained of headaches and a burning sensation directly where a phone is used nearest to the body. Through their own pain and suffering, many of these cell phone users have made the connection between cell phone usage and the body's natural defenses against toxicants.

In a new study published September 2014, in the International Braz J Urol, researchers wanted to understand the impact of electromagnetic waves from cell phones on mammalian tissue.

The researchers conclusion : *"Intensive use of mobile phones has negative impact on bladder tissue as well as the other organs. Keeping a minimum level of mobile phone use makes it easy to be kept under control of diseases in which inflammation is an etiologic factor"*

The scientists from the Department of Urology, Haydarpasa Numune Training and Research Hospital, Istanbul, Turkey sought answers to understand the health implications arising from technological developments that provide a lot of conveniences in our lives. This issue is one of the risks that arise along with these conveniences. In this study researchers demonstrated that electromagnetic waves from cell phones have a severe inflammatory effect on bladder tissue with reason to believe other organ tissues are affected as well.

The study abstract is available here
http://www.ncbi.nlm.nih.gov/pubmed/25251956?dopt=Abstract

MATERIALS AND METHODS:

Twenty-one adult male albino rats were divided into three equal groups. Group 1 was exposed to electromagnetic wave for 8 hours per day for 20 days and then their bladders were taken off immediately. Group 2 was firstly exposed to electromagnetic wave for 8 hours per day for 20 days then secondly another for 20 days without exposition to electromagnetic wave and then their bladders were taken off. Group 3 was the control group and they were not exposed to electromagnetic wave.

RESULTS:

Under microscopic examination of bladder tissue, in the first group severe inflammatory cell infiltration was seen in lamina propria and muscle layer in contrast to intact urothelium. In the second group mild inflammatory cell infiltration was seen in lamina propria and muscle layer. The mean scores for the three groups were 5.5 ± 2.5, 0.8 ± 1.3 and 1.2 ± 1.5 respectively. Mean score of group 1 was statistically higher than others (p = 0.001).

Diseases and Their Relationship with Inflammation

Disease	Mechanism
Allergy	4 Immune Mediated Types + Sensitivities, all of which cause inflammation
Alzheimer's	Chronic inflammation destroys brain cells
Anemia	Inflammatory cytokines attack erythropoietin production
Ankylosing Spondylitis	Inflammatory cytokines induce autoimmune reactions against joint surfaces
Asthma	Inflammatory cytokines induce autoimmune reactions against airway lining
Autism	Inflammatory cytokines induce autoimmune reactions in the brain arresting right hemisphere development
Arthritis	Inflammatory cytokines destroy joint cartilage and synovial fluid
Carpal Tunnel Syndrome	Chronic inflammation causes excessive muscle tension shortening tendons in the forearm and wrist compressing the nerves.
Celiac	Chronic immune mediated inflammation damages intestinal lining
Crohn's Disease	Chronic immune mediated inflammation damages intestinal lining
Congestive heart failure	Chronic inflammation contributes to heart muscle wasting
Eczema	Chronic inflammation of the gut and liver with poor detoxification and often antibodies against Transglutaminase-3.
Fibromyalgia	Inflamed connective tissue often food allergy related and exacerbated by secondary nutritional and neurological imbalances.
Fibrosis	Inflammatory cytokines attack traumatized tissue
Gall Bladder Disease	Inflammation of the bile duct or excess cholesterol produced in response to gut inflammation
GERD	Inflammation of the esophagus and digestive tract nearly always food sensitivity and pH driven
Guillain-Barre	Autoimmune attack of the nervous system often triggered by autoimmune response to external stressors such as vaccinations.
Hashimoto's Thyroiditis	Autoimmune reaction originating in the gut triggered by antibodies against thyroid enzymes and proteins
Heart attack	Chronic inflammation contributes to coronary atherosclerosis
Kidney failure	Inflammatory cytokines restrict circulation and damage nephrons and tubules in the kidneys
Lupus	Inflammatory cytokines induce an autoimmune attack against connective

	tissue
Multiple Sclerosis	Inflammatory cytokines induce autoimmune reactions against myelin
Neuropathy	Inflammatory cytokines induce autoimmune reactions against myelin and vascular and connective tissues which irritate nerves.
Pancreatitis	Inflammatory cytokines induce pancreatic cell injury
Psoriasis	Chronic inflammation of the gut and liver with poor detoxification
Polymyalgia Rheumatica	Inflammatory cytokines induce autoimmune reactions against muscles and connective tissue
Rheumatoid Arthritis	Inflammatory cytokines induce autoimmune reactions against joints
Scleroderma	Inflammatory cytokines induce an autoimmune attack against connective tissue
Stroke	Chronic inflammation promoted thromboembolic events
Surgical complications	Inflammatory cytokines (often pre-dating the surgery) slow or prevent healing

http://articles.mercola.com/sites/articles/archive/2013/09/21/cell-phone-wifi-radiation.aspx

Children's Health Expert Panel: Cell Phones & Wi-Fi— Are Children, Fetuses and Fertility at Risk?

September 21, 2013 | 289,926 views

2.5K

By Dr. Mercola

"It may take some sort of catastrophe to get people's attention," said Frank Clegg, former president of Microsoft Canada and founder of Canadians 4 Safe Technology, referring to the increasing saturation of Wi-Fi technologies on the public at large, and especially, children.

Leading experts from top universities recently convened at a program organized by ElectromagneticHealth.org in Connecticut to discuss the reality that such a catastrophe is already brewing and, as the panel warned, is now already negatively impacting children, fetuses and fertility. But the majority of parents are not connecting the dots by linking symptoms in their children to the radiation.

During the discussion "Cell Phones & Wi-Fi – Are Children, Fetuses and Fertility at Risk?," a wide range of scientific evidence was presented that RF/MW electromagnetic radiation has indisputable biological and health effects, including at non-thermal levels, with chronic exposures generally associated with greater harm. This is the kind of radiation emitted not only by cell phones but also by:

Wi-Fi routers	Baby monitors	Bluetooth earpieces
Towers	Antennas	Smart boards
Smart meters	Cordless phones	Other wireless devices

'Our Grandchildren and Children Are Being Used as Lab Rats…'

This quote, from Devra Davis, PhD, MPH, president of Environmental Health Trust, sums up perhaps the most alarming EMF issue to date. The fact is, we know that exposure to this 'unnatural bath of radiation' damages DNA and impairs natural cellular repair processes, a phenomenon that may lead to cancer. Yet we are proceeding with this large-scale, uncontrolled experiment anyway.

Because children are still developing, they have rapid cellular replication and growth rates that make them especially vulnerable to DNA damage. They also have a longer lifetime exposure to this new pervasive radiation than any previous generation.

As the expert panel stated, research shows that radiation from cell phones and Wi-Fi has *already* been shown to cause diminished reaction time in children, decreased motor function, increased distraction, hyperactivity and inability to focus on complex and long-term tasks.

In one controlled study, researchers from Yale University positioned a cell phone above a cage of pregnant mice. The phone was transmitting an uninterrupted active call for the entire 17 days of gestation.

When the exposed offspring were later tested, they showed signs of ADHD, and reduced transmissions in the prefrontal cortex of the brain.[1] It's widely known that children, due to their thinner skulls, smaller brains, softer brain tissue and far more rapidly dividing cells, are far more susceptible to damage from cell phone use than adults. This study clearly showed brain patterns are altered, with life long repercussions from brief prenatal exposures to microwave radiation.

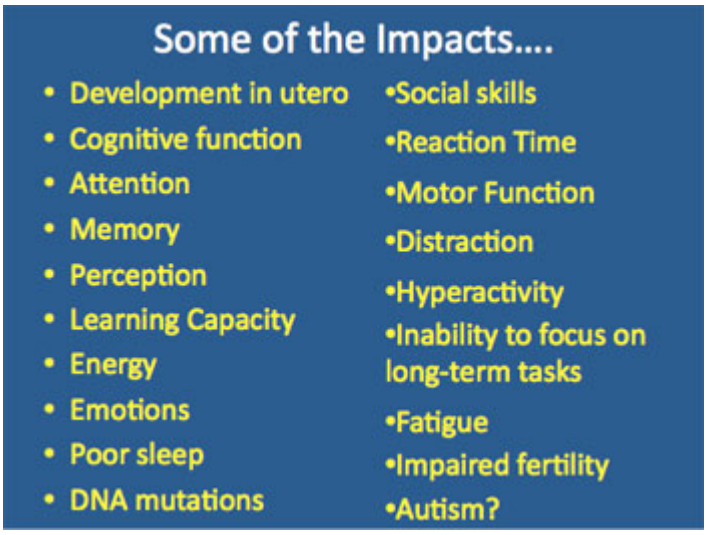
Dr. Taylor indicated that there was a dose-response relationship found, and that disruption to the electrical signaling between neurons resulted in permanent changes in the way the brain is patterned that will carry forward into adulthood. The electrical signaling plays a major role in how the brain develops, which determines a lot of who we are as adults, he said, including "how we think and how we behave."

"This is the first experimental evidence that fetal exposure to radiofrequency radiation from cellular telephones does in fact affect adult behavior…" said Hugh Taylor, Professor and Chairman, Department of Obstetrics, Gynecology and Reproductive Sciences, Yale University.

Camilla Rees, MBA of ElectromagneticHealth.org,[2] said Dr. Taylor encouraged the audience to appreciate that while we don't think of ourselves as being on the cell phone 24 hours a day, the cell phone is still emitting radiation 24/7 and impacting us if it is turned on and near us, day or night.

"It's not talking on the phone that matters, it's any time the phone is turned on," he said. Every 900 milliseconds, whether you are using the phone or not, your cell phone has a spike in radiation because it is looking for a signal from the tower…"

She summarized key impacts on children from cell phone and WiFi radiation drawn from the BioInitiative Report, the Mobilewise (UK) report on cell phone effects on children, Russian research overseen by the Chairman of the Russian National Committee on Non-Ionizing Radiation Protection, and the Yale report, "*Cell Phones: Technology, Exposures, Health Effects*."



Reference to the latest BioInitiative Report's (2012) section on possible EMF links to autism written by Harvard Professor Dr. Martha Herbert, who runs the Transcend Research Lab at Mass General, was also made. Dr. Herbert has said,

"EMF/RFR from wifi and cell towers can exert a disorganizing effect on the ability to learn and remember, and can also be destabilizing to immune and metabolic function. This will make it harder for some children to learn, particularly those who are already having problems in the first place."

"Powerful industrial entities have a vested interest in leading the public to believe that EMF/RFR, which we cannot see, taste or touch, is harmless, but this is not true."

Several panelists mentioned the new condition "Digital Dementia," increasingly being reported globally, where children are exhibiting signs of deterioration in cognitive abilities from overuse of internet technologies, thought to result from imbalanced development of the brain. The lesser cognitive function will also result from the RF/MW exposures, but researchers who are focused on 'overuse' have not been as aware of this factor.

More research is necessary here to ferret out how much of the behavioral and brain effects of technology overuse are coming from the RF/MW, or brain changing aspects use of the technology itself, and the resulting lesser human interaction and lower quality relationships.

An excellent new book by Raffi Cavoukian, renowned singer, children's champion and supporter of a commercial-free childhood, "#LightWebDarkWeb," takes a deep philisophical look at society's unquestioning embrace of these technologies for children. It covers the health, privacy, safety, security, social, societal, mental health and addiction issues from children's use of social media and modern communications technologies. Raffi says we need to "act quickly to subdue the perils of InfoTech's shadow," and "to move the risk-benefit ratio in favor of the LightWeb."

In light of the growing evidence for harm to children and fetuses, Dr. Davis explained:[3]

"The cell phone standards we use today for the 6.5 billion cell phones in the world were set 17 years ago and have never been updated, despite the fact that the users and uses of cell phones are very different now. And they've never been tested for their safety around children… We're in the midst of a huge experiment on ourselves and on our children…

A whole generation of people has been unaware of the risks of wireless radiation, and have not been taking precautions. This is why public health officials are so concerned. There is already evidence that exposure to radiofrequency radiation in excess leads to disease. And exposures have grown dramatically in the last few years. ***Our grandchildren and children are "being used as lab rats in an experiment with no controls****… that's what we are doing with cell phone and wireless radiation with our children today."*

Frank Clegg, formerly CEO of Microsoft Canada, also commented on the adequacy of safety guidelines: Clegg said he is disappointed with industry, and regrets the lack of responsibility demonstrated by the technology sector in turning a blind eye to the biological realities of this radiation.

Nine Types of Cancer are Linked to Cell Phone Use

It was back in 2011 that the International Agency for Research on Cancer (IARC), a committee of 27 scientists from 14 different countries working on behalf of the World Health Organization (WHO), concluded that exposure to cell phone radiation is a "possible carcinogen" and classified it into the 2B category -- the same category as the pesticide DDT, lead, gasoline engine exhaust, burning coal and dry cleaning chemicals, just to name a few. The children's health expert panel explained that, as of 2013, there are *nine* types of cancer linked to cell phone use, including:

Glioma (brain cancer) Acoustic Neuroma (tumor on acoustic Meningioma (tumor of the

	nerve)	meninges)
Salivary Gland Cancer (parotid gland in cheek)	Eye Cancer	Testicular Cancer
Leukemia	Thyroid Cancer	Breast Cancer

The science connecting cell phone and Wi-Fi radiation is among the strongest there is, and children, again, are slated to bear the brunt of what could become a new epidemic of cell-phone and Wi-Fi-induced cancers. The panel reported:

"The latency period between cell phone use and brain cancer is thought to be 20 to 30 years. Brain cancer rates are double for people who've been using cell phones for 10 years or more, appearing on the side of the head where they hold their phones, and risks are 5x greater for children using cell phones under the age of 20 than those over the age of 50."

Fertility and Sperm Count May Be at Risk

Infertility rates have been on the rise in the US, and today's children may be even worse off than their parents if current trends continue. Several of the panel members focused on this issue, including studies that have found cell phone radiation can affect men's sperm count and the quality and motility of their sperm. One such study, published in *PLoS One,*[4] found:

"RF-EMR [radiofrequency electromagnetic radiation] in both the power density and frequency range of mobile phones enhances mitochondrial reactive oxygen species generation by human spermatozoa, decreasing the motility and vitality of these cells while stimulating DNA base adduct formation and, ultimately DNA fragmentation. These findings have clear implications for the safety of extensive mobile phone use by males of reproductive age, potentially affecting both their fertility and the health and wellbeing of their offspring."

The panel further reported:[5]

*"There is a **direct relationship between duration of cell phone use and sperm count decline.** Sperm count is reduced by half in men who carry cell phones in their pants pockets for four hours per day. The motility of the sperm is also impaired. The testicular barrier, that protects sperm, is the most sensitive of tissues in the body, and is 100x more absorbent. Besides sperm count and function, the **mitochondrial DNA of sperm are damaged 3x more if exposed to cell phone radiation**.*

...DNA mutations have been linked more to damage on the male side in research from Iceland, the assumption being that male sperm is more vulnerable than female eggs, which are more protected. Mutations increase with the age of the father, and more autism and schizophrenia increase with the age of the father."

EMF-Free Zones Should Be Available for Pregnant Women and Children

The weight of the evidence clearly supports the need for Wi-Fi-free or low-Wi-Fi areas where pregnant women or those hoping to conceive, children and others sensitive to EMFs, can be protected, according to the panel.

The European Council has already taken the exemplary step of recommending that mobile phones and wireless networks get banned in classrooms and schools, according to Dr. Davis, and the Turkish government is launching a campaign to educate pregnant women and young men of reproductive age about the safety risks of cell phone radiation. Rajasthan India has banned cell towers on or near schools. The Israeli Health Ministry has issued a report

recommending against Wi-Fi in schools, on the basis that not enough is known about its chronic exposure. It has been shown, however, that increasing numbers of people think and learn better in locations that are free of cell phones, wireless devices and other forms of EMFs.

The Israeli Supreme Court in July ordered the Israeli government to investigate how many Israeli students are suffering from electrosensitivity in response to a brief claiming that it is unreasonable to expose children to WIFI when it is proven to cause sickness. The Government must submit the result of its investigation, supported with a sworn affidavit, to the court by November 16, 2013. Israel Minister of Health Rabi Yaakov Litzman wrote to the Minister of Education saying:

"I do fear that there will come a day that we will all cry because the irreversible damage that we, in our own hands cause the future generation."

The panel noted that 'extreme caution' is advised for pregnant women and women hoping to conceive:[6]

"Prenatal exposure results in fewer cells in the hippocampus of the brain, the area we need for thinking, reasoning, judgment and significantly impairs the development of neurons in the brain… Some of the most profound effects in children from in utero EMF exposure are emotional and behavioral."

Around the world, many countries are already adopting the Precautionary Principle regarding cell phone use, and this is also what the panel recommended. Russian officials have issued the recommendation that all children under the age of 18 should avoid using cell phones entirely. The UK, Israel, Belgium, Germany, India, France and Finland also urge citizens to err on the side of caution with respect to their children's use of cell phones. Panel member Martin Blank, PhD said:

"The precautionary principle is in order here – certain precautions should be taken as a result of the risk that's been identified. That's the reason we have seat belts in cars… not because every car is going to crash, but because we want to minimize the damage when they do."

Safety Recommendations for Cell Phone and Wi-Fi Use

The cell phone industry is one of the fastest growing and strongest global industries in the world today and is even stronger than the pharmaceutical industry. As a multi-trillion dollar industry that funds media around the world they are capable of making sizable political donations and persistent lobbying efforts that dictate government policies, and that also influence science carried out at universities and prominent cancer institutes.

So while cell phone dangers will one day likely be as well known as tobacco dangers, there's going to be a window when people are extremely vulnerable. And that window is right now. Children are especially vulnerable to damage from cell phone radiation, and should not use them at all (or only for very limited amounts). Men and women who want to have healthy children need to take special precautions to protect their reproductive organs and should not keep phones in their front pockets or close to their abdomens.

In the US, public warnings are not yet commonplace, but it's still important to protect yourself – and your children. There is plenty of science showing harm to warrant taking action now

The panel advised:[7]

• **Children should not play with radiating cell phones.** Young children should not use cell phones except in an emergency. While you can put the phone in 'airplane mode,' which disconnects it from Wi-Fi and the Internet, the cell phone still emits magnetic fields from the battery, which have also been shown to have equally important biological consequences.

In no cases should children sleep with cell phones.

Extreme caution was advised for pregnant women or women hoping to conceive due to the profound long-term impact of environmental factors.

• **Limit or eliminate Wi-Fi exposures. If you have a WI-Fi router make sure your** router is a low power version, not in a high-use area and keep it turned off as much as possible. Consider putting it on a timer so it is only available during certain hours, and never during sleeping hours.

• **Schools should not have Wi-Fi.** Cabled/wired connections do not pose the same risks. If there is Wi-Fi, again, it should be limited to the time when the Wi-Fi is specifically needed and not be operating at other times. Ideally, classrooms and school libraries and gyms should be WiFi-free.

◦ **Resume using landline phones whenever possible.** Get rid of your portable phone and use your landline. At the very least, don't keep your cell phone in your bedroom while you sleep. Be aware even landline phones emit magnetic fields from the speaker, and sensitive people can sometimes feel them, especially on long calls and particularly when using trim phones. Old-fashioned desk phone earpieces offer a greater distance between the speaker and your ear that can make a meaningful difference.

◦ **Keep your cell phone away from your body.** Avoid keeping it in your pocket or on your belt. If you're pregnant, keep your cell phone away from your belly. Keep your phone at the other end of the room or on the seat of the car. Use texting more than talking. A cell phone case for the iPhone is available that filters out a significant portion of radiation (but by no means all the power and frequencies and other biologically disruptive signal characteristics also remain). There are several options for shielded cell phone cases and holsters at www.EMFSafetyStore.com.

◦ **Use a wired earpiece or headphones with cell phones.** Like with landline phones, some people are impacted by the magnetic fields from the speaker in the ear buds, so choose a model with the greatest distance from your ear, or use air tube technology with no electronics near your ear.

◦ **Use caution using your cell phone in your car.** Signals bounce around inside your vehicle, and your head is the antenna.

◦ **Opt-out of new utility meters called 'smart meters.'** Prevent smart meters from being installed in your home whenever possible.

◦ **Avoid using wireless baby monitors,** as they all operate on microwave frequency. Look for the old wired monitors.

◦ **Know your exposures.** You or your community can purchase an RF meter for about $500 to measure the RF in homes, schools, churches, etc. See www.EMFSafetyStore.com.

◦ **Support labeling laws** that require cell phone manufacturers to list radiation levels in an obvious place on the packaging and at the retailer.

http://www.electricsense.com/8822/cell-phones-cause-cancer-fact/

44 Reasons To Believe Cell Phones Can Cause Cancer

Posted by Lloyd Burrell on November 10, 2014 under Cell phone radiation |

Cell phones can cause cancer. Here's why.

Cell phones emit microwave radio-frequency radiation. Fact.

This radiation has the ability to penetrate our bodies. Fact.

Our governments do virtually nothing to protect us from these dangers. Fact.

And yet there is strong evidence, multiple peer reviewed studies, to indicate that cell phones cause cancer and other diseases.

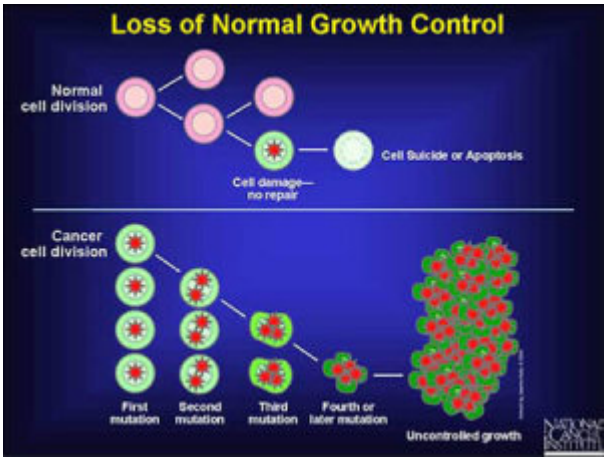
Take a look for yourself at these facts.

But first let's just consider what cancer is.

Cancer And DNA

The National Cancer Institute says,

"Cancer is a term used for diseases in which abnormal cells divide without control and are able to invade other tissues…..all cancers begin in cells……cells grow and divide in a controlled way to produce more cells as they are needed to keep the body healthy. When cells become old or damaged, they die and are replaced with new cells. However, sometimes this orderly process goes wrong. The genetic material (DNA) of a cell can become damaged or changed, producing mutations that affect normal cell growth and division. When this happens, cells do not die when they should and new cells form when the body does not need them."



National Cancer Institute Image – click to enlarge

So cancer typically involves abnormal cell division and DNA damage and in some cases cells may form a mass of tissue called a tumor.

Types Of Brain Tumor

In the studies done to date cell phone radiation exposures are principally linked to two types of brain tumor, gliomas and acoustic neuromas.

Gliomas, a type of tumor that starts in the brain or spine are typically malignant. Gliomas are particularly deadly. Most people survive only 1 to 3 years after diagnosis.

Acoustic neuromas though non-malignant (low-grade cancer), are in many cases life threatening given that they are an intracranial tumor.

Free Download: thousands of studies link cell phone radiation exposures to many different types of cancer. That's why I've put together this summary '*Cell Phones Can Cause Cancer – 10 Good Reasons*' **click here** to download.

Cell Phones Can Cause Cancer – 44 Reasons

Here are 44 reasons why cell phones can cause cancer.

1. Cellular Damage: Telecoms giant T-Mobile in Germany commissioned an independent study to review all relevant research on the health risks from wireless telecommunications. It was concluded that,

"*On the cellular level, a multitude of studies found the type of damage from high frequency electromagnetic fields which is important for cancer initiation and cancer promotion.*"

Brain Tumors And Brain Cancers

2. Significantly Increased Risk of Glioma: Gliomas are becoming increasingly common. The $25 million Interphone Study found that:

"regular use of a cell phone by adults can significantly increase the risk of gliomas by 40% with 1640 hours or more of use (this is about one half hour per day over ten years)."

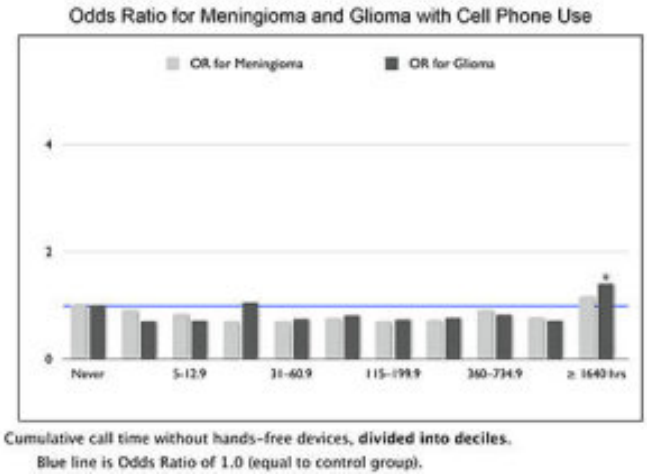


Image – Paul Dart MD (click to enlarge)

Source: Table 2 INTERPHONE Study Group. Brain tumour risk in relation to mobile telephone use: results of the INTERPHONE international case-control study. Int J Epidemiol (2010); 39(3):675-694.

3. Tumor Risk on Cell Phone Side of Head: Again from the Interphone Study – currently the big daddy of cell phone radiation studies it being the largest and longest study on the link between cell phones and brain tumors – it also found, *"tumors were more likely to occur on the side of the head most used for calling"*.

4. Harmful Association Between Cell Phone Radiation and Tumors: A review of 23 epidemiological studies by 7 scientists on the link between cell phones and cancer concluded, "*harmful association*". One of the reports authors commenting the study results said, *"although as a whole the data varied, among the 10*

higher quality studies, we found a harmful association between phone use and tumor risk. The lower quality studies, which failed to meet scientific best practices, were primarily industry funded."

5. Increased Risk For Glioma and Acoustic Neuroma: the studies performed by the Hardell Research Group are widely regarded as being amongst the best. This recent study finds, *"A consistent pattern of increased risk for glioma and acoustic neuroma associated with use of wireless phones."* These findings are consistent with their earlier studies.

6. Temporal Lobe & Glioma Risk: A recent French study found evidence of an increased risk of glioma and temporal lobe tumors. The study found that, "r*isks were higher for gliomas, temporal tumours, occupational and urban mobile phone use.* ". According to EMF watchdog Powerwatch this is an important paper, *"that confirms existing studies and which should help move the IARC RF evaluation strongly towards a Group 2A – 'probable human carcinogen'*".

7. Increased Risk of Acoustic Neuroma in Long-Term Users of Cell Phones: A recent study on 790,000 middle aged women in the UK found that, "*women who used cell phones for ten or more years were two-and- a-half times more likely to develop an acoustic neuroma. Their risk of acoustic neuroma increased with the number of years they used cell phones.*"

8. Increased Risk of Acoustic Neuroma: Research conducted by Lonn suggests, *"an increased risk of acoustic neuroma associated with mobile phone use of at least 10 years' duration."*

9. Brain Tumor Risk is Higher on 'Cell Phone' Side of Head: A research paper that reviewed 11 studies found, "*a link between prolonged cell phone usage and the development of an ipsilateral* [same side of head as cell phone] *brain tumor".*

10. Meningioma: This Swedish study looked at adult brain tumor cases diagnosed over a two year period. Although the study concluded that, "*no conclusive evidence of an association between use of mobile and cordless phones and meningioma was found*". The studies authors did say, "*an indication of increased risk was seen in the group with highest cumulative use*".

11. Malignant Brain Tumors: Recent work by Hardell looked at long-term use of mobile and cordless phones. In conclusion it was found that, "*this study confirmed previous results of an association between mobile and cordless phone use and malignant brain tumours. These findings provide support for the hypothesis that RF-EMFs play a role both in the initiation and promotion stages of carcinogenesis*".

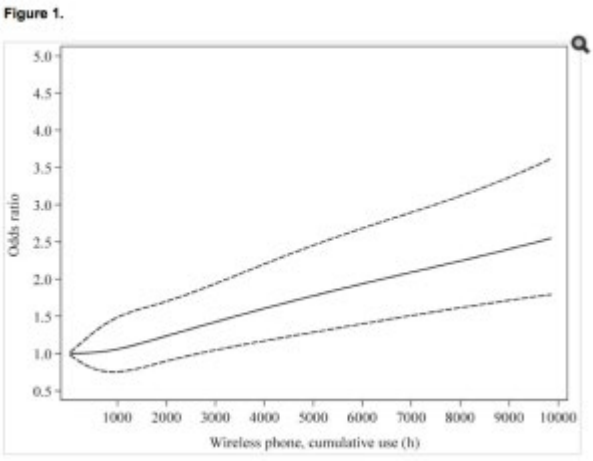


Image: Hardell Research Group – click to enlarge

Other Cancers And Tumors

12. Cancer of the Pituitary Gland: The pituitary gland, considered by many to be the "master gland" of the body, is a pea sized organ located in the middle of the base of the brain that produces hormones that play a major role in regulating vital body functions and general well-being. This study (already referenced above) also found that,

"*the risk of cancer of the pituitary gland more was more than twice as high among women who used a cell phone for less than five years as compared to never users*".

13. Thyroid Cancer: The thyroid gland is situated in the neck. Using a cell phone against your ear exposes your thyroid to cell phone radiation. A recent Israeli study observing that, "*the incidence of thyroid cancer has been on the rise in Israel for more than a decade which matches the rise in the use of cellphones*" collected human thyroid cells from healthy patients and subjected them to radiation. The study found, "*evidence of changes in thyroid cells in response to electromagnetic radiation*".

14. Melanoma Risk: Melanoma is a cancer that starts in a certain type of skin cell. A Swedish study found "*a very clear association between increasing use of mobile phones and increasing rates of head melanoma* [ ] *in Nordic countries*".

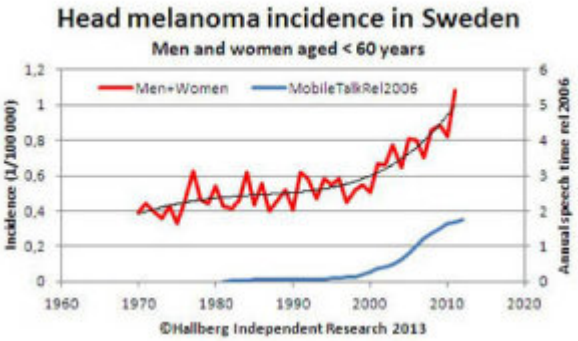


Image: Örjan Hallberg (click to enlarge)

15. Stem Cell Cancer: In a controversial US study on 29 cases of neuroepithelial tumors, cell phone users accounted for 11 of them. These initial results indicated a near tripling in the risk of neuroepithelial tumors through cell phone use. The published results were revised to reflect a doubling of risk and then reported as not 'statistically significant'.

16. Oral Cancer: An Israeli study on 460 cases of parotid gland tumors found, "*based on the largest number of benign PGT patients reported to date, our results suggest an association between cellular phone use and PGTs* [parotid gland tumors]." The parotid is the salivary gland near the cheek where many users hold their cell phone.

17. Parotid Malignant Tumors: Another Israeli study analyzed deaths as recorded on the National Cancer Registry over a 36 year period found, "*the total number of parotid gland cancers in Israel increased 4-fold from 1970 to 2006 , whereas other major salivary gland cancers remained stable*".

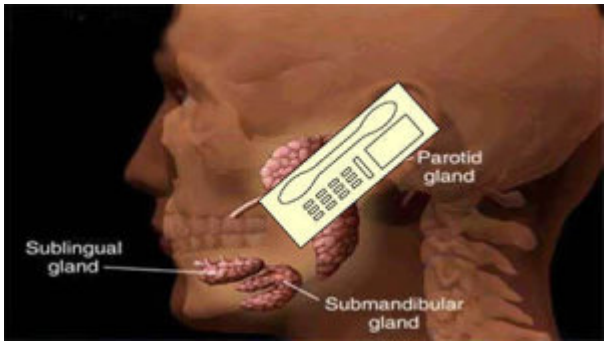
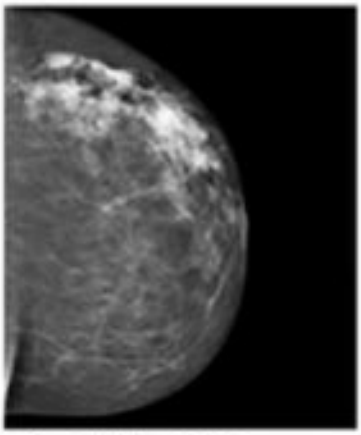


Image: Environmental Health Trust (click to enlarge)

18. Leukaemia: A comprehensive review of over a dozen studies including studies on exposures from cell tower radiation, TV and Radio broadcast towers concluded, "*cancer, especially brain tumour and leukaemia, but all other cancers also*".

19. Lymph Node Cancer: In an Australian study one hundred mice were exposed to RF radiation for two 30-minute periods per day for up to 18 months. The authors called the increased incidence of lymphoma "*highly significant*". They added that "*it is very unlikely that the faster onset of cancer was due to chance*".

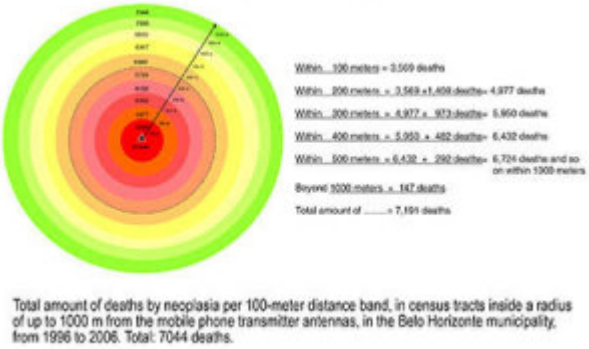
20. Multifocal Breast Cancer: American researchers studied four young women with breast cancer. They found that, "*all patients regularly carried their smartphones directly against their breasts in their brassieres for up to 10 hours a day, for several years, and developed tumors in areas of their breasts immediately underlying the phones*".



Representative imaging of patient in Case 1. Left mammogram showing clustered calcification corresponding to multiple sites of disease in craniocaudal (a) and mediolateral-oblique (b) projections. MRI showing extensive nonmass enhancement in the lateral hemisphere of the left breast in segmental distribution (c).

21. Eye Cancer: A German Study has established a link between uveal melanoma and cell phone radiation and similar exposures. The study "*found an elevated risk for exposure to radiofrequency-transmitting devices*". Another study found ocular symptoms and sensations in long term users of mobile phones.

22. Diverse Cancerous Tumors: A Brazilian Study established a direct link between various cancer deaths such as tumors in the prostate, breast, lung, kidneys and liver in Brazil's third largest city, and cell phone tower radiation exposures. The study found that, "*more than 81 percent of people who die in Belo Horizonte by specific types of cancer live less than 500 meters away from the 300 identified cell phone antennas in the city*".



Total amount of deaths by neoplasia per 100-meter distance band, in census tracts inside a radius of up to 1000 m from the mobile phone transmitter antennas, in the Belo Horizonte municipality, from 1996 to 2006. Total: 7044 deaths.

Click to enlarge

Source.
This same study also lists more than a dozen other research papers that have found a link between different cancers and cell phone/cell tower radiation exposures.

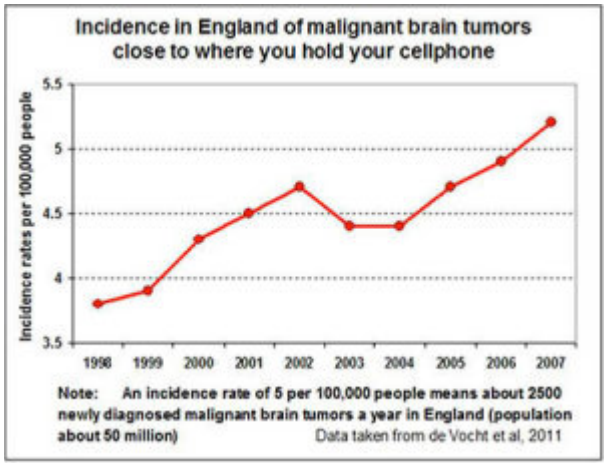
Cell Phone Subscriptions And Brain Tumors

23. Cell Phone Subscription Link to Brain Tumors: A U.S. study analyzed the number of cell phone subscriptions and brain tumors in nineteen US states, they concluded,

"*the very linear relationship between cell phone usage and brain tumor incidence is disturbing and certainly needs further epidemiological evaluation.*"

24. Brain Cancer Incidence Increases Over Time (U.S): another U.S. study of brain cancer incidence trends in relation to cell phone use in the United States found, "*there was a statistically significant increasing trend between 1992 and 2006 among females but not among males.The recent trend in 20–29-year-old women was driven by a rising incidence of frontal lobe cancers*".

25. Brain Cancer Incidence Increases Over Time (Europe): Studies carried out in Norway, Finland and the U.K. have identified a similar trend of an increase in the incidence of brain cancer over time. In the UK study the incidence of malignant brain tumors close to where you hold your phone was highlighted.



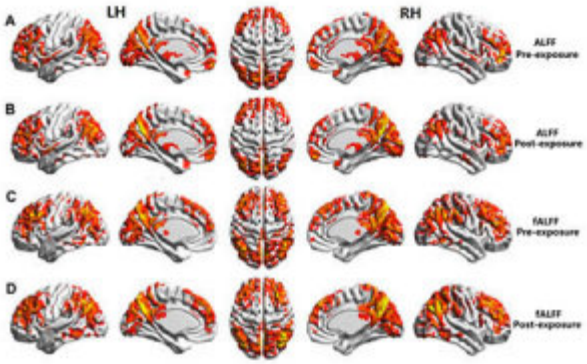
Source: Mobile Phone Use and Cancer Risk – Research on a Group 2B Carcinogen. Joel M. Moskowitz Ph.D.

Other Effects On the Brain

26. Blood-Brain Barrier (BBB) Permeability: The BBB is a membrane which prevents toxic materials from the blood from entering the brain. It was first discovered in 1975 that RF radiation causes the BBB to leak, since then at least a dozen laboratories around the world have corroborated this effect. There's no consensus on the link between BBB damage and cancer but some studies elude to this.

27. Brain Cell Loss: A Turkish study on adult female rats that were exposed to a 900 MHz electromagnetic field found that, "*EMF exposure caused a significant decrease of the…….cell number…… additionally, cell loss can be seen……*". In their conclusions the researchers drew parallels between these exposures and teenagers' brains that are exposed to cell phone radiation.

28. Brain Activity: Researchers in China exposed 18 participants to RF radiation (LTE) for 30 minutes which was well within international (ICNIRP) cell phone legal limits. They concluded that, "*30min LTE RF-EMF exposure modulated the spontaneous low frequency fluctuations in some brain regions.*"



29. Brain Blood Flow Affected: This Finnish brain imaging study found that "*that the EMF emitted by a commercial mobile phone affects rCBF* [regional cerebral blood flow] *in humans*". This suggests that cell phone radiation affects neuronal activity.

30. Texting Affects Memory: An Australian study on young adolescents found *"students who reported making or receiving more voice or SMS calls per week, and in particular more of both, demonstrated shorter response times on learning tasks, but less accurate working memory"*.

DNA Damage

One way cancer and other diseases are believed to develop is when the DNA (genetic information) in a cell becomes damaged. This damage mutates the DNA. There are many studies linking cell phone radiation exposures to different types of DNA damage. This is explains how cell phones can cause cancer.

31. Single and Double-Strand DNA Breaks: In pioneering work a University of Washington team found DNA single strand breaks from RF radiation exposures on rats in an initial study. A subsequent study found single and double-strand DNA breaks.

32. Various Genetic Effects: An Austrian study analyzed the results of 101 different published articles on the effects of radio frequency EMFs on DNA. The study concluded that, "*there is ample evidence that RF-EMF can alter the genetic material of exposed cells*".

33. Increased Rates of Micronuclei: Micronuclei proliferation indicates a type of DNA damage strongly associated with cancer.A Brazilian study found that, "*electromagnetic field irradiation* [low level cell phone type exposures] *during pregnancy leads to an increase in erythrocytes micronuclei incidence in rat offspring*". Several studies have found increased rates of micronuclei in the body following exposures to RF radiation.

34. Heat Shock Proteins (HSPs) Production Decreased: A U.S. study exposed chick embryo's to RF radiation. They concluded that, "*this EMF-induced decrease in HSP70 levels and resulting decline in cytoprotection suggests a mechanism by which daily exposure (such as might be experienced by mobile phone users) could enhance the probability of cancer and other diseases*".

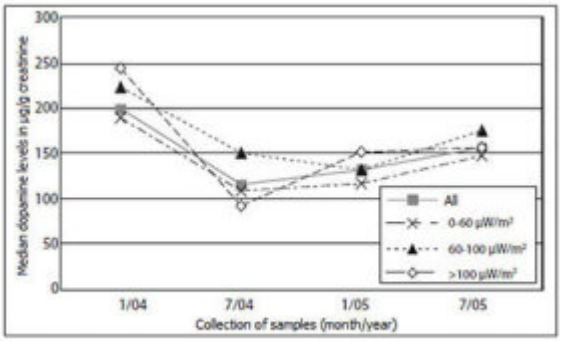
35. Oxidative DNA Damage: the Guler study in Turkey exposed female and male infant rabbits to 1800 MHz radio frequency radiation and found, *"GSM-like RF radiation may induce biochemical changes by increasing free radical attacks to structural biomolecules."* Free radical damage is associated with the development of cancer.

36. DNA Strand Breaks: this Austrian study exposed human and rat cells to mobile phone radiation and found, *"DNA single- and double-strand breaks"*.

37. Changes in Gene Expression: the Belyaev study found that, exposing the *"rat brain to 915 MHz GSM microwaves induces changes in gene expression"*. Other studies suggest that, *"subtle changes of gene expression associated with* [disease]".

38. Genotoxic Effects: the Schwarz study exposed human cells to 1,950 MHz UMTS. It concluded that *"UMTS exposure may cause genetic alterations in some but not in all human cells in vitro."*

39. Neurotransmitters Impacted: this Bavarian study followed 60 people over one and a half years following the installation of a new cell phone base station in their village. The study concluded that, "*the effects showed a dose-response relationship*", that it had "*occurred well below current limits for technical RF radiation exposures*" and that these effects have "*great relevance for health and [are] well known to damage human health in the long run*". In other words the more people were exposed to cell phone type radiation the bigger the impact on their health.



Median dopamine levels for different GSM power density levels

40. Chromosome Damage: a Belgian study reviewed 16 expert gene monitoring studies from around the world. In 13 of the 16 independent studies performed worldwide it was found that, "*RF-exposed individuals have increased frequencies of genetic damage (e.g., chromosomal aberrations)*".

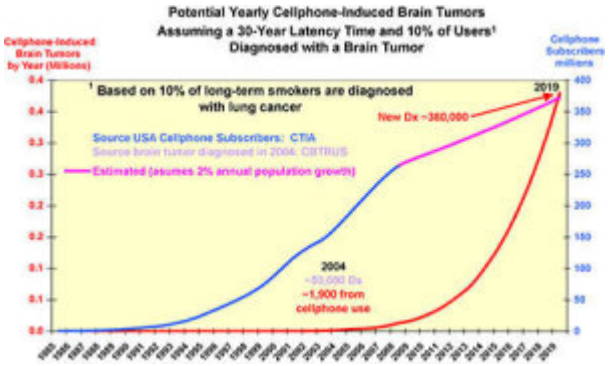
41. Central Nervous System: US based researcher Dr. Henry Lai comments that there are several studies which show that repeated RF exposure at relatively low power caused morphological changes in the central nervous system, "*changes in morphology, especially cell death, could have an important implication on health. Injury-induced cell proliferation has been hypothesized as a cause of cancer.*"

Reading Between The Lines

The studies don't tell all of the story. Here are some other things you need to know.

42. Latency Period Before Diagnosis: To put this in the words of researcher Dr. Martin Blank "*cancers do not form overnight*". *In almost all cases cancerous tumors take many years to form and metastasize"* Dr. Martin Blank: Overpowered. This would suggest that we might be sitting on a cell phone radiation cancer time bomb.

43. Cell Phone Radiation Cancer Time Bomb: To give a sense to what this latency period could mean in terms of the incidence of brain tumors in the years to come, researcher Lloyd Morgan produced this alarming graphic showing that brain tumor cases could reach epidemic proportions within the next decade:



44. Flawed Research: Not all of the research points to a link between cell phone radiation and cancer. But then that's hardly surprising given the lengths some researchers go to, to skew the results. This research paper also lays bare the phenomenon of study bias. This can take many different shapes and forms; insufficient latency time, incorrect definition of "regular" cellphone user, cell phones radiating higher power levels in rural areas not investigated, exposure to other transmitting sources not considered, exclusion of brain tumor cases due to death or illness, etc.

Flawed Conclusions

The argument that gets bandied around by the naysayers is, *"if cell phones cause cancer how come the cancer stats, and particularly brain cancer stats, don't reflect that?"* Part of the answer is due to the latency period and flawed research but a closer look at the research is even more revealing.

Analyzing data from the Netherlands of a study conducted over the 21 year period from 1989-2010, Dr. Louis Slesin of Microwave News notes, *"while the total incidence of all types of brain tumors in the Netherlands rose at the rate of only about 0.7% per year, the increase in glioblastoma multiforme (GBM) was about 3.1% per year".*

That's to say the incidence of the most aggressive and deadly type of brain tumors, GBMs, more than doubled. But because over the same period the rate of all the other types of brain tumors went down the higher incidence of GBMs is being masked by the lower rates of the other types of brain cancer.

Dr. Slesin notes that, *"a similar trend is occurring in the U.S., according to a team from the University of Southern California Medical School in Los Angeles…….anecdotal evidence from Denmark also supports a rising incidence of GBMs".*

The Tip Of The Iceberg

There is lot of interest surrounding the link between cell phone radiation and cancer. But cancer is only the tip of the iceberg.

Microwave radio-frequency radiation exposures of the type emitted by cell phones are also **linked to many other diseases** and potentially **life threatening illnesses**, including:

- sperm damage & male infertility
- miscarriages
- vaginal discharge
- vascular system disease
- tinnitus
- childhood cancer
- sleep problems
- depression
- irritability
- memory loss
- concentration difficulties

- headaches
- dizziness and fatigue
- suicidal tendencies
- arrhythmia
- heart attacks
- bone marrow interference
- altered calcium level in cells
- ADHD
- reduction in night-time melatonin
- suppression of the immune system
- arthritis
- rheumatism
- skin symptoms
- lymphatic diseases
- autism
- hearing problems

Make no mistake, cell phones can cause cancer.

This post was updated June 2016.

Chronic Fatigue Syndrome - Is prolonged exposure to environmental level powerline frequency electromagnetic fields a co-factor to consider in treatment?

D. Maisch, B. Rapley, R.E. Rowland, J. Podd*

ABSTRACT

This paper outlines a brief description of the illness commonly known as Chronic Fatigue Syndrome (CFS) which is becoming increasingly common in modern westernised countries. While CFS has become somewhat of a 'catch-all' of medical symptoms, it is still commonly diagnosed by exclusion of other diseases rather than a specific, unique symptomatology.

One feature of the disorders commonly termed CFS is a depressed immune system. This paper attempts to link the impaired immune function associated with CFS to possible chronic low-level exposure to extremely low frequency (ELF) electromagnetic fields (EMFs). The evidence includes both *in vivo* and *in vitro* studies in both human and animal systems. In particular, the recent link between ELF EMFs, melatonin and the immune system are outlined.

The authors conclude that, although the link between ELF EMFs and cellular dysfunction are far from proven, sufficient evidence exists to suggest a causal link. Lack of full scientific certainty should not be used as a reason for postponing prudent avoidance of ELF EMFs, particularly in cases where CFS has already been diagnosed.

KEY WORDS

Chronic Fatigue Syndrome; CFS; electromagnetic fields; EMF; 50 - 60 Hz; melatonin; prudent avoidance.

INTRODUCTION

With any illness characterised by chronic fatigue, such as CFS, Chronic Fatigue (CF) and Immune Dysfunction Syndrome (CFIDS), Chronic Epstein-Barr Virus (CEBV), Myalgic Encephalomyelitis (ME), and Multiple Chemical Sensitivity (MCS), the important outcome is a severely dysfunctional immune system.

Evidence that these conditions involve an immunological disorder is accumulating rapidly. Within the past few years various abnormalities have been found in the immune system of CFS patients, for example. These include alterations in the activity and cell surface structure of two important types of white blood cells: natural killer cells and T-lymphocytes. In some patients, subtle changes have been found in the levels of neuroendocrine hormones in the brain. Evidence indicates that CFS is associated with, if not directly caused by, a persistent, low-level impairment of the immune system.

Irrespective of the 'trigger' of the condition, whether it be viral, an environmental factor, a genetic predisposition, stress, or a combination of these factors, any additional contributing factors which may also detrimentally affect the immune system should be identified, investigated and eliminated (or reduced) as part of the treatment.

In this regard, a co-factor may be considered anything that may cause hormone disruption and biological changes at a cellular level, thus interfering with immune system function. This co-factor may not have initiated the condition, but exposure to it may further stress an already affected immune system. As long as such a situation exists, any treatment is unlikely to have any lasting effect.

Existing evidence indicates that exposure to environmental level 50 - 60 Hz EMFs may be an immune system stressor with the potential to cause hormone disruption and changes at a cellular level. Therefore, EMF exposure should be evaluated as a potential risk factor for people suffering from disorders with the common feature of unexplained chronic fatigue.

CHRONIC FATIGUE SYNDROME (CFS)

CFS is a general label used to describe a debilitating illness, the cause of which is still unknown. CFS is also referred to as CFIDS (Chronic Fatigue and Immune Dysfunction Syndrome), CEBV (Chronic Epstein-Barr Virus), ME (Myalgic Encephalomyelitis), as well as several other designations. It is a complex illness which has been intensively studied for the past 40 years without firm conclusions as to its cause. Diagnosis is done largely by exclusion of other possible diseases.

Clinical CFS is characterised by incapacitating fatigue (experienced as exhaustion and extremely poor stamina) of at least 6 months' duration, neurological problems and a constellation of symptoms which can resemble other disorders, including: mononucleosis, multiple sclerosis, fibromyalgia, aids-related complex (ARC), Lyme disease, post-polio syndrome and autoimmune diseases such as lupus. These symptoms tend to wax and wane but are often severely debilitating and may last for many months or years. All segments of the population (including children) are at risk, but women under the age of 45 seem to be the most susceptible. As with most diseases, CFS affects people differently. Not everybody reaches the severe end of the CFS spectrum[1].

There is a difference between CF and CFS. CF is a fairly widespread symptom in the community, whereas CFS is an unexplained debilitating fatigue of at least 6 months duration which severely reduces the level of activity. CFS is considerably less common.

In addition to persistent and extreme fatigue, usually with an abrupt onset accompanied by an 'infectious-like' illness, other CFS symptoms that have been identified include the following: substantial impairment in short-term memory and concentration; depression; sore throat; tender lymph nodes; muscle pain; multi-joint pain without joint swelling or redness; unusual headaches; unrefreshing sleep; cognitive function problems (such as spatial disorientation and impairment of speech and/or reasoning); visual disturbances (blurring, sensitivity to light, eye pain); chills and night sweats; dizziness and balance problems; sensitivity to heat and cold; irregular heartbeat; abdominal pain; diarrhoea; irritable bowel; low temperature; numbness or a burning sensation in the face or extremities; dryness of the mouth and eyes (Sicca syndrome); hearing disorders; menstrual problems including PMS and endometriosis; hypersensitivity of the skin; chest pains; rashes; allergies and sensitivities to odours (including chemicals and medications); weight changes without changes in diet; hair loss; lightheadedness; fainting; muscle twitching and seizures[2].

Research suggests that CFS results from a dysfunction of the immune system, involving a disruption of fundamental Central Nervous System (CNS) mechanisms, such as the sleep-wake cycle and the hypothalamic-pituitary-adrenal axis[3]. One study found that more than a quarter of CFS patients had abnormal brain scans, and subtle changes have been found in the levels of neuroendocrine hormones[4]. Other research has found electrolyte disturbances which sometimes included permanent changes in cell membranes' ability to pass electrolytes, permanent biochemical changes in mitochondrial function and disturbances of insulin and T3-thyroid hormone functions[5].

In 1989, Hickie, Lloyd and Wakefield, at the Prince Henry Hospital in Sydney, published results which show a significant reduction in the absolute number of peripheral blood lymphocytes in the total T-cell population and in two T-cell subsets, as well as a significant reduction in T-cell function. They also found reduced immunoglobulin (antibody) levels[6]. In a later paper, further alterations in peripheral blood T lymphocytes and impaired natural killer cell cytotoxicity were reported[7].

Based on physical and laboratory findings, many scientists believe that viruses are associated with CFS and may be directly involved in causing the syndrome. Several viruses have been studied to determine what, if any, part they play. These include enteroviruses, herpes viruses (especially human herpes virus-6, or hhv-6) and newly-discovered retroviruses[8].

Originally it was thought that the EBV, a herpes virus that causes mononucleosis, was the cause of this syndrome. However, researchers now believe that EBV activation (when it exists) is a result of or a complication of CFS rather than its cause[9]. To date, no virus has been conclusively shown to be an essential element of CFS.

There is one school of thought that holds that CFS is essentially a psychological disorder. This is because several of the symptoms seen in CFS patients are also seen in psychiatric illnesses, notably depression and anxiety disorders. Estimates of 28% - 50% have been claimed for the occurrence of depression in CFS sufferers, while 15% - 25% is the comparable rate in the general community. Depression sometimes appears before the onset of CFS. This suggests that depression might be a cause and not a consequence of the syndrome, or that depression may be the first manifestation of the illness in some patients. Sleep disorders which usually accompany depression would also exacerbate CFS, possibly through the disruption of melatonin activity. The overlap in symptoms between CFS and depression unfortunately blurs the distinction between a possible psychological or physical cause. However, in view of evidence that depression itself sometimes has a physical cause and responds best to physical treatments, there is some evidence that in CFS sufferers, depression may be a result of an active viral infection or an immunological disorder[10]. It is also possible that many CFS sufferers become depressed as a consequence of the limitations placed on them by their illness[11].

Research efforts are directed toward identifying and isolating the fundamental agent(s) responsible for triggering immune system disruption in persons with CFS. There are on-going studies of immunological, neurological, endocrinological and metabolic abnormalities and risk factors such as genetic predisposition, age, sex, prior illness, other viruses, environmental factors and stress. It may eventually be found that CFS is multi-factorial in origin with no single factor identifiable as the cause.

One factor that may play a role in CFS, is prolonged exposure to low level 50-60 Hz EMFs. We now turn our attention to examining the known biological effects of low level ELF EMFs, particularly those concerning impairment of the immune system.

POWERLINE FREQUENCY MAGNETIC FIELDS AND THE IMMUNE SYSTEM

As an indicator of the possibility that exposure to low level 50 - 60 Hz EMFs may play a role in chronic fatigue/immune system dysfunction, we must look for evidence that human exposure to these fields may cause changes at a cellular level, such as hormone disruption and calcium ion efflux[12], which may have the potential to adversely impact on the immune system.

NCRP DRAFT REPORT GUIDELINES (1995)

The biological effects of EMFs were examined in great detail by an expert committee of the USA National Council on Radiation Protection and Measurements (NCRP), a Congressionally chartered organisation which was contracted by the Environmental Protection Agency (EPA) in 1983 to conduct a review of the biological effects of ELF EMFs.

Work was discontinued in 1986, due to funding cuts at the EPA, but resumed in 1991. In early 1995 the draft of the 800-page NCRP report was leaked to the New York-based publication *Microwave News*, which published the report's findings in August 1995. The final report was supposed to be publicly available in early 1996, but has received such intense industry opposition to its findings that its final outcome remains uncertain.

The Committee's membership was described by chairman Dr. Ross Adey as "carefully selected to cover the great majority of societal interests on this scientific problem, including power industry engineers, epidemiologists, public health specialists as well as molecular and cellular biologists"[13]. The draft report generally endorses a 2 mG (0.2 mcT) exposure limit, having immediate implications for new day care centres, schools and playgrounds, and for new transmission lines near existing housing.

A somewhat more flexible policy would be applied to new housing and offices. For existing facilities, the committee recommended a more gradual approach with stronger restrictions phased in over time if the evidence of a health risk continues to grow.

The NCRP Committee states that, "In key areas of bioelectromagnetic research, findings are sufficiently consistent and form a sufficiently coherent picture to suggest plausible connections between ELF EMF exposures and disruption of normal biological processes, in ways meriting detailed examination of potential implications in human health."[14]

From studies on humans the committee cites evidence for a link between EMFs and: 1) childhood and adult cancer, including leukaemia and brain cancer; 2) teratological effects and other reproductive anomalies; 3) neuroendocrine and autonomic responses which, separately or collectively, may have pathophysiological implications; 4) neurochemical, physiological, behavioural and chronobiological responses with implications for development of the nervous system.

From laboratory studies the committee notes that EMFs: 1) affect cell growth regulation in animal and tissue models in a manner consistent with tumour formation; 2) increase tumour incidence and decrease tumour latencies in animals; 3) alter gene transcriptional processes, the natural defence response of T-lymphocytes and other cellular processes related to the development and control of cancers; 4) affect neuroendocrine and psychosexual responses.

In relation to the effect of low level EMFs on the pineal hormone, melatonin, the Committee concluded that:

"There has been a strong focus on ELF field actions in the pineal gland, relating to effects on synthesis and secretion of the pineal hormone melatonin, and on a broad series of regulatory functions mediated by this hormone. Melatonin plays a key role in controlling the 24-hour daily biological rhythm. Disturbance of the normal diurnal melatonin rhythm is associated with altered oestrogen receptor formation in the breast, a line of experimental evidence now under study, or possible links between ELF field exposure and human breast cancer. . . Further, melatonin has general properties as a free radical scavenger, with the possibility of a preventative role in oxidative stress, recognized as a basic factor in a broad spectrum of human degenerative disorders, including coronary artery disease, Parkinson's and Alzheimer's diseases, and aging."[15]

According to the Committee, problematic sources of ELF EMFs include local electrical distribution systems as well as high voltage power transmission systems. Particular appliances, including electric blankets and video display units also rate highly as problem sources along with "various occupational environments". The Committee states that the evidence points to human health hazards in everyday exposures to EMFs, particularly magnetic fields exceeding 2 mG (0.2 mcT) and electric fields at intensities in the range 10-100 V/m (volts per metre).

"..there is an implication that a significant proportion of the world's population may be subjected to a low level of risk, but a risk factor with significant societal consequences, by reason of its pervasive nature and the serious consequences for affected individuals."[16]

MAGNETIC FIELD EXPOSURE AT THE CELLULAR LEVEL

The inter-relationships between various cellular processes are far too complex for a thorough discussion here. However, the scientific evidence accumulated to date from cell biology, biochemistry and bioelectromagnetics gives an excellent understanding of these processes and how EMFs may possibly interact with these processes. It is important to note that laboratory findings are not necessarily fully applicable to real life situations. Cell-level experiments are intended to detect and characterise an effect in a system simpler than a multi-celled organism. As such, in vitro experimental results are not affected by endogenous homeostatic [repair] mechanisms encountered in the whole organism and thus may be more sensitive to applied fields[17].

The hormone, melatonin, and the neurotransmitters, serotonin and dopamine, are neurochemical messengers that aid in central nervous system transmission, or in the case of hormones, travel throughout the body to effect cellular changes. There are believed to be more than 100 transmitters and hormones that allow a complex interaction among the CNS, the endocrine system, and the immune system.

The cell membrane, where transmitters and hormones bind or cross into the cytoplasm, is the likely site of any interaction with external man-made EMFs. There are receptor sites both on the cell membrane and inside the cell to which these chemical messengers bind, starting a cascade of chemical events that may eventually alter the cell's behaviour in one of many ways.

An apt description of the cellular communication process was given by Dr W. Ross Adey, the former Associate Chief of Staff for Research and Development at the Pettis Memorial VA Medical Centre at Loma Linda, California, and NCRP committee chairman:

"It is generally agreed that the first detection of ELF and ELF-modulated RF/microwave fields occurs on the membranes that enclose all cells. These complex cell membranes act as detectors, amplifiers, and couplers of weak surface electrical and chemical signals to the cell's interior. Cells also communicate with neighbours by outward signals, faintly 'whispering together' electrically and chemically, through signals that are also sensitive to imposed EMFs."[18]

It is not necessary for external EMFs to penetrate into the cell interior in order to cause changes inside the cell, as reported by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) in 1996:

"By influencing signal transduction pathways, which in turn can regulate cell proliferation, cell differentiation, and even transformation to a cancer phenotype, ELF-EMFs can potentially be involved in a host of disease processes without ever penetrating the cell membrane in any significant manner."[19]

In summary, EMFs can bring about fundamental changes in both electrical and chemical signalling in the CNS. One chemical messenger that has been shown to be particularly susceptible to the influence of weak ELF EMFs is melatonin.

MELATONIN

Both human and animal circadian rhythms are synchronised with the natural day/night cycle. The major control gland over this natural cycle is the pineal gland which secretes the neurohormone, melatonin. In mammals, light falling on the eye's retina during the day, produces signals which are biochemically amplified to stimulate the pineal gland to reduce its melatonin output. At night the absence of light allows the pineal gland to produce melatonin. Melatonin directly enters the bloodstream, through which it has access to every cell in the body, passing directly to receptors in the nucleus[20].

In the cell nucleus, melatonin plays a role in regulating gene expression. The ability of melatonin to enter all cells is essential for one of its other important functions, which is to act as a scavenger of highly toxic oxygen-based free radicals. The production of these free radicals is a consequence of the utilisation of oxygen by all aerobic organisms. About 1% - 2% of inspired oxygen ends up as toxic free radicals, a by-product of the respiration cycle. These oxygen radicals can damage macromolecules such as DNA, proteins and lipids. This damage is referred to as oxidative stress[21].

Because of its ability to eliminate free radicals, melatonin is regarded as an efficient cell protection and oncostatic agent. At night the increasing level of melatonin helps eliminate the build up of free radicals, thereby allowing DNA synthesis and cell division to occur with a far lower chance of damage. Melatonin also inhibits the release of oestrogen, prolonged exposure to which may increase the risk of breast cancer[22].

According to Brzezinski, melatonin may enhance the immune system and counteract stress-induced immunosuppression by augmenting the immune response[23].

THE MELATONIN HYPOTHESIS

In 1987 Stephens et al. suggested that EMFs reduce melatonin production by the pineal gland and that melatonin suppresses the development of breast cancer[24]. They proposed that EMFs may operate as a co-factor in the development of some cases of this type of cancer. Since then, results from five in vitro studies, conducted in three major laboratories, using human breast cancer cell cultures, have shown that low-level powerline frequency magnetic fields in the order of 12 mG (1.2 mcT) can block melatonin's ability to suppress breast cancer cells[25]. This is known as the melatonin hypothesis. In addition, several human exposure studies have found lowered levels of melatonin in people exposed to EMFs. (Section 2.3)

At the Second World Congress for Electricity and Magnetism in Biology and Medicine, held in Bologna, Italy, in June of 1997, the program bulletin states that:

"A number of experimental studies have been conducted to test the [melatonin] hypothesis. Although the literature is still evolving and consensus is being built, it is fair to say, a) there exists credible scientific support for the hypothesis and, importantly, b) this support encompasses *in vitro*, *in vivo*, and epidemiological research. The melatonin hypothesis, thus, currently represents one of the more well-documented/tested interactions in the field of bioelectromagnetics."[26]

In 1988, Liburdy reported that "The melatonin hypothesis invokes a general mechanism that has relevance to all hormone-dependent tissue responsive to oestrogen and/or prolactin, such as human mammary epithelial tissue, ovarian tissue and prostate tissue"[27].

A further study found that office-place EMF exposure was apparently related not only to a decrease in melatonin levels but also to an increase in the level of the stress hormone adrenocorticotropic hormone (ACTH)[28]. The implications for CFS are obvious, for chronically high levels of ACTH are known to suppress immune function.

While the evidence for a link between ELF EMFs and melatonin is strong, other chemicals are known to be affected too. One of these is calcium ions, which are critical for the proper functioning of all cells.

CALCIUM IONS, PROTEIN KINASES AND ORNITHINE DECARBOXYLASE

In their comprehensive review of the effects of EMFs on molecules and cells, Goodman et al. note that the EMF effect on calcium flux has been the subject of intense scrutiny because of the important physiological role of calcium and its relationship to membrane changes. The results are equivocal, but most *in vitro* experiments performed on human tissues show enhanced calcium flux in response to radio-frequency and ELF fields. Liburdy and his colleagues in particular have examined the effectiveness of the magnetic or electric field component in altering calcium flux and their combined data strongly supports the conclusion that the electric field component is responsible for altered calcium flux. They suggest that the electric field operates by inducing an opening of the calcium channel in the membrane rather than by increasing calcium mobilisation from the endoplasmic reticulum[29].

The possible connection between EMFs, calcium ions and immune system function was summarised by Cherry:

"ELF and RF/MW, modulated at ELF frequencies, change the oscillation frequency and amplitude [of calcium ion signalling] and change the influx and efflux of calcium ions in and around the cell membrane. The changing oscillation frequency and amplitude is related to the immune response of the cell and shows that the oscillating applied field produces an antibody-like reaction as though the cell has been attacked. The influx and efflux changes relate to the signal transduction pathway in which calcium ions participate. This is one of the biochemical pathways which regulate cell behaviour. This is altered by the applied oscillating electromagnetic field. Since signal transduction controls cell division, cell differentiation and cell proliferation, this EMR-induced alteration to signal transduction has the strong potential to participate

in tumour formation or promotion. Alteration of T-lymphocytes and other immune system factors suggests that EMR exposure causes immunosuppression, partially through induced calcium ion efflux."[30]

Changes in cellular calcium flow are known to stimulate a group of enzymes called protein kinases, which play an important role in regulating several cellular functions. Two recent studies found evidence that inside cells, EMFs can activate certain signalling pathways; for example, protein kinase activity has been associated with cancer. Specifically these research groups discovered that the products of a particular class of oncogenes, Src tyrosine kinases, are rapidly activated by EMF exposure. The functions of other key cellular elements facilitating the cancer-promoting function of these tyrosine kinases also seem to be amplified five- to ten-fold. In addition, the results of these studies demonstrate that EMFs may alter biochemical events in the immune system that determine our susceptibility to infections[31].

It has been reported by Uckun that EMFs can disrupt the "growth regulatory balance" in cancer cells[32]. Uckun also reports similar EMF-induced activity in a different, but related, enzyme system where it was found that cells exposed for 5 to 15 minutes to EMFs similar in strength to those found in electric razors (1000 mG / 100 mcT) caused a 5- to 10-fold increase in the activity of a gene associated with the formation of leukemia[33]. Referring to this research, Adey states that, "This is another piece of evidence, which we first began to see in the 1980s, pointing to the importance of protein kinases as a key intracellular communication system that is sensitive to both ELF and modulated RF fields"[34]. The possibility exists that the immune system is compromised by external EMFs which may alter chemical messengers, resulting in erroneous instructions being sent to internal cellular regulation systems.

Uckun found that elevated activation of the enzyme tyrosine kinase by EMFs may represent the initial manifestation of EMFs' biological influence, leading to a cascade of biological events. He also reported the activation of a second tyrosine kinase, known as BTK, "Because you don't have any hormone production without activation of tyrosine, the new findings may also explain provocative hormonal perturbations linked to EMF exposures"[35].

Another important enzyme involved with cell growth is ornithine decarboxylase (ODC), which is required for DNA replication. ODC is always present during cell growth and plays a critical role in cell transformation, but increased levels are considered a marker for the type of cell activity connected with cancer growth. Research by Litovitz et al. into ODC activity has shown that at the applied frequencies of 55 and 65 Hz, there is a significant (two fold) increase in ODC activity in L929 cells exposed to a magnetic field of 100 mG (10 mcT). The authors conclude that "modification of its [ODC] enhancement by an applied field is of general interest for questions of EMF exposure. We suggest, however, that the coherence phenomenon noted in these experiments is likely of more widespread consequence, and that other biological responses with demonstrated EMF sensitivity will display comparable coherence dependence."[36]

The evidence we have so far reviewed would suggest a link between EMFs and calcium levels, melatonin levels, protein kinase and ODC activity. Thus it is not unreasonable to conclude that CFS, which may be an indicator of metabolic disruption, is partly a manifestation of exposure to low level EMFs.

HUMAN EXPERIMENTAL FIELD STUDIES AND HORMONE DISRUPTION

In the previous section we note the possible link between EMFs and melatonin flux. A preliminary study in 1997 of 60 workers at a Finnish garment factory found "a highly significant effect" of EMFs in reducing nocturnal melatonin levels. Magnetic field (MF) measurements were taken for the two types of machines used in the factory and operators were assigned to high or low exposure groups, based on the type of machine they were using, with average exposures either above or below 10 mG (1.0 mcT). Non industrial workers who were not exposed to MFs were the controls. This study found strong effects of magnetic field exposure on night-time levels of melatonin. No difference was found in melatonin levels on week nights and Sunday nights, indicating "that the possible suppression caused by magnetic field exposure is chronic, with little recovery during the weekend"[37].

A 1996 study of 192 electric utility workers by Reif and Burch found that some EMF exposures are associated with low levels of melatonin. They found a significant association between MF exposures and lower daytime melatonin levels on the second and third of three days of measurement[38]. The lack of an

effect on the first day (following a weekend or equivalent) may indicate a cumulative effect of exposure Some studies have suggested that EMF effects on melatonin may depend on whether the field is continuous or intermittent. Reif and Burch found that magnetic fields in the home that were "temporally coherent" (less intermittent) had a very significant association with lower melatonin levels at night. They concluded that the intensity and temporal characteristics of MFs may both play a role in the suppression of melatonin[39].

Visual display units (VDUs) have also been implicated as a significant source of MF radiation. According to Arnetz and Berg, office workers who used VDUs had a significant reduction in circulating levels of melatonin over the course of a working day. No such change was found during days at the office with no VDU use. Levels of the stress hormone, ACTH, increased during the working day and this showed a strong correlation with workers' subjective assessment of mental strain, but in contrast, mental strain did not significantly correlate with melatonin levels[40].

Davis (Fred Hutchinson Cancer Centre in Seattle Washington), found that low-level MFs can reduce the nocturnal release of melatonin in women. While the effect was small, it occurred at milliGauss levels and followed a dose-response trend. Davis called the findings "intriguing" given the "very low level of exposure" which reflects "real-world" conditions, but cautioned that the biological significance of the results is not known at this time. Davis stated, "This is the first time we are seeing evidence that relatively small changes in magnetic fields at night can be associated with decreases in melatonin levels that night among humans living in a normal environment"[41]. Davis argues that melatonin inhibits the production of other hormones such as oestrogen. Thus, a drop in melatonin has the potential to cause other hormones to surge[42].

As with the laboratory research these human field exposure studies indicate a possible link between EMFs and hormone disruption which may be a co-factor in the development of CFS. The link has not been firmly established, but further investigation is certainly warranted.

DEPRESSION AND EMF EXPOSURE

Research in the United States and Britain has found clinical depression to be the major factor in suicides in both countries. There are many types of depression, from seasonal depression (Seasonal Affective Disorder), which normally occurs in the winter months, to low level chronic depression that may linger for months or years. Among the symptoms of clinical depression are weight loss, early waking, diminished sex drive and a general feeling of hopelessness. On the contrary, some people have what is called atypical depression, which is characterised by weight gain and spending much of the day asleep.

In 1978, Perry published the findings of an EMF survey which examined the addresses of some 600 suicides reported in the Birmingham U.K. area and found that in homes where the magnetic field was above 1 mG (0.1 mcT) the relative risk of depressive illness was elevated[43]. Perry and Pearl conducted a study of 43 high-rise blocks with over 3,000 housing units (a total of approximately 6,000 occupants). The aim of the research was to determine whether there was any correlation between occupants' level of depression and their proximity to EMFs. Participants suffering from certain types of heart disease and from depression were more likely to be living near the main electrical supply cables in the apartment blocks. Magnetic field strengths measured in all 43 blocks with a single rising cable showed significantly higher magnetic field exposures in the apartments 'near' the cable. These fields averaged 3.15 mG (0.315 mcT) nearest the cable and 1.61 mG (0.16 mcT) in the 'distant' apartments. A further finding was that, if only those blocks with under floor or storage electric heating were considered, the proportion of cases of depression in occupants living in apartments categorised as 'near' the rising cable rose to 82%[44].

Changes in serotonin levels are known to be associated with depression. For example, lowered levels of this chemical in the brain have been linked to an increase in suicide frequency[45]. Wolpaw examined the brain functions of monkeys exposed to 60 Hz magnetic fields. He measured the levels of neurohormones in the spinal fluid of monkeys thus exposed for three weeks. It was found that the levels of serotonin and dopamine were significantly depressed immediately following exposure, and that only the dopamine returned to normal levels several months after[46].

Low night-time melatonin concentrations have been reported in patients with depression, and patients with Seasonal Affective Disorder have phase-delayed melatonin secretion[47].

Robert Becker, a leading researcher on EMF exposure and depression, summarises his own work, and that of others as follows:

"It seems that there may be two types of clinical depression: one which is produced by simple psychosocial factors, and one which is produced by some external factor which influences the production of these psychoactive chemicals by the pineal gland. In view of the known relationship between the pineal gland and magnetic fields, it is advisable that the search for the responsible factor include an evaluation of the effect of abnormal electromagnetic fields"[48].

OTHER RELEVANT RESEARCH FINDINGS

Since 1979, when, in a seminal paper, Wertheimer and Leeper first reported a correlation between exposure to power line MFs and childhood leukaemia, there have been well over 30 major epidemiological studies examining the EMF/cancer question. Few studies, however, have looked for evidence of association between environmental power-frequency magnetic field exposure and immune-related illnesses in humans.

In one notable study, Beale et al. examined eight immune-related and chronic illnesses (variables) in a group of 560 adults living near extra high voltage transmission lines in Auckland New Zealand. Using a cross-sectional design to examine the dose-response relationship between MF exposure of adults in their homes and prevalence of these illnesses, five of the eight health variables showed a linear dose-response relationship with exposure. After adjustment for possible confounding, significantly elevated odds ratios were obtained both for asthma and combined chronic illnesses at higher exposure levels. As reported in the paper abstract, "The results are consistent with a possible adverse effect of environmental magnetic field exposure on immune-related and other illnesses"[49].

Human peripheral blood lymphocyte activity may be affected by exposure to electric fields. For example, Coghill et al. (1998), exposed human peripheral blood lymphocytes in mu-metal- enclosed (EMF shielded) cultures to the donor's own endogenous electric field overnight and tested for viability by trypan blue exclusion. This showed a 70% viability. The controls (no endogenous electric field) and sham-exposed (same gold wire feed, but unattached to body) both showed about 50% viability. When they fed a 50 Hz electric field into the lymphocyte cultures (same power density, same period of exposure, same temperature, etc.), the viability fell to 40%. This study suggests that 50 Hz electric fields (not magnetic) adversely affect human peripheral blood lymphocytes[50]. A decrease in human peripheral blood lymphocytes could be implicated in the development of CFS.

A 1998 study by Bonhomme-Faivre et al. found "evidence that chronic human exposure to environmental low frequency EMFs ... can cause neurovegetative, haematological and immunological disorders". Specifically, they found that a group of workers who were exposed to MFs ranging from 0.9 mG (0.09 mcT) to 66 mG (6.6 mcT) had significantly lower lymphocyte counts than a similar control group not exposed to these levels. The exposed group also reported significantly more occurrence of subjective conditions - mental and physical fatigue, depression, melancholy, irritability, fainting and diminished libido - than did the control group. Of particular interest with this study were two workers who had exposures from 3 mG to 66 mG (0.3 mcT to 6.6 mcT) and worked full-time above transformers. Both were found to have depressed lymphocyte levels which quickly returned to normal when they stopped working in that area[51].

Finally it can be noted that not all researchers agree that environmental-level 50 - 60 Hz EMFs are causally related to hormone disruption and changes at the cellular level. This group supports the assumption that the small electric fields and currents induced in the body's tissues from external EMFs are smaller in magnitude than both internally-produced fields and even the thermal noise of liquid phase solutions. This assumption has been challenged by Gandhi, who has found evidence that the fields induced in the human body by power lines and appliances, essentially all strong artificial EMF sources, are much larger than the fields generated naturally inside the body. Gandhi used a computer model to calculate the electric and magnetic fields in the 41 - 70 Hertz frequency band from internal and external

sources. He found that even the largest natural fields generated by the heart are hundreds of times smaller than those induced by standing under a high-voltage line or by using a hair dryer. Ghandi stated, "My assumption was that what is already in the body is pretty substantial, but that turns out to be incorrect, . . . It is time for people to reject false assumptions"[52].

The work of Ghandi and others has led the current authors to examine mechanisms which might offer some explanation of how weak environmental EMFs might affect living systems. One possible mechanism which is now gaining popular support among biologists is stochastic resonance[53]. This novel application of stochastic resonance theory to biological systems is currently being explored in the authors' laboratories.

CONCLUSIONS

With the illness loosely termed Chronic Fatigue Syndrome, regardless of the cause, or causes, the primary outcome is an immune system which is markedly compromised. Considering this, it is advisable for medical practitioners working with CFS patients to advise them to avoid situations which may place an additional stress on their immune systems.

Current scientific evidence indicates that prolonged exposure to EMFs, at levels that can be encountered in the environment, may affect immune system function by affecting biological processes in ways similar to that seen with CFS. Considering the increasing incidence of CFS in the community, it is the opinion of the authors that medical practitioners should advise patients about the prudent avoidance of EMFs. It is usually a relatively simple matter to locate sources of EMF and generally to avoid them.

The lack of full scientific certainty should not be used as a reason for postponing measures to prevent exposure to any potentially harmful source. If measures generally reducing EMF exposure can be taken at reasonable expense and with reasonable consequences in all other respects, every effort should be made to reduce exposure to the lowest possible level.

GLOSSARY

Bioelectromagnetics:

An emerging science which focuses on how living organisms interact with electromagnetic fields (EMFs)

Electromagnetic Field (EMF):

Form of energy which consists of two oscillating forces (said to be at right angles to each other), an electric component and a magnetic component. Examples of electromagnetic energy include: powerline fields, radio waves; light; x-rays; gamma rays.

Electric Field:

Region of space in which forces are exerted between electrically charged particles (e.g. electrons). Wherever there is a voltage potential there is an associated electric field.

Extremely Low Frequency (ELF):

Electromagnetic energy where the frequency of oscillation of the energy lies in the region of 1 - 300 Hertz (Hz).

Epidemiology:

The study of disease in the population, defining its incidence and prevalence, examining the role of external influences such as infection, diet or toxic substances and examining appropriate preventative or curative measures.

Gauss (G):

CGS unit of magnetic field density [flux density], (equal to 1 Maxwell per cm-2). Named after the German mathematician Karl Friedrich Gauss (1777-1855). Commonly replaced by the newer unit Tesla. For ELF magnetic field levels commonly encountered in the urban environment, the unit of **milliGauss** (**mG**) is normally used. 1 mG equals 0.1 microTesla (mcT).

Hertz (Hz):

Unit of frequency indicating the number of cycles per second. Named after the German physicist who discovered radio waves, Heinrich Hertz (1857-1894).

in vitro:

Literally 'in glass'. Refers to experiments on cells and tissues which are performed in a test tube or petri dish.

in vivo:

Literally 'in life'. Refers to experiments that take place with or in living organisms.

Magnetic Field (MF):

The area of force which exists around a moving charge, e.g. an electron. Electrons flowing through a conductor (e.g. wire) produce a force in the area surrounding the conductor referred to as a magnetic field.

RF/MW:

Radio Frequency / MicroWave. That part of the electromagnetic spectrum with a frequency in the range 100 kilohertz (kHz) to 300 gigahertz (GHz).

Tesla (T):

MKS unit of magnetic field density [flux density], (equal to 1 Weber per m-2). Alternatively, the magnetic induction for which the maximum force it produces on a current of unit strength is 1 newton. Named after the Croatian-American physicist and electrical engineer, Nikola Tesla (1856-1943), who pioneered alternating current and invented the a.c. induction motor and Tesla coil. For ELF magnetic field levels commonly encountered in the urban environment, the unit of **microTesla** (**mcT**) is normally used.

CAVEAT

The authors wish to express the strong view that they do not support nor condone the use of any devices which claim to cleanse or protect the body from EMFs and have not been scientifically proven to do so.

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CHD Files Response Brief in Landmark Case Against FCC on 5G and Wireless Health Impacts

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News provided by **Children's Health Defense** Oct 20, 2020, 17:30 ET

WASHINGTON, Oct. 20, 2020 /PRNewswire/ -- Children's Health Defense (CHD), chaired by Robert F. Kennedy, Jr., filed its response brief on Monday to the Federal Communications Commission in the U.S. Court of Appeals for the District of Columbia. The case against the FCC challenges the agency's refusal to review its 25-year-old obsolete wireless "health guidelines" and to adopt scientific, biologically based radio frequency emissions rules that adequately protect public health. The brief was filed jointly with Environmental Health Trust. CHD is represented by Robert F. Kennedy Jr. and Scott W. McCollough.

PRESS CONFERENCE: Wednesday, October 21, 3:00 p.m. EDT. **REGISTER HERE.**

CHD's brief is a response to the FCC Brief filed on September 22nd. CHD's principal brief was filed on August 14, 2020.

The FCC used unauthorized materials in its brief, misconstrued evidence brought by the petitioners and misrepresented other government agencies' positions.

Petitioner's response brief accuses the FCC of failing to "meaningfully assess the vast amount of reliable peer-reviewed scientific and medical evidence generated after 1996" indicating health risks from exposure at "currently-authorized levels" and claims the FCC's irresponsible refusal to confront the evidence have resulted in widespread sickness including in children. The petitioners assert that FCC's disdain for human suffering reflects a disturbingly distorted view of the public's interest.

The majority of independent experts, as represented by the BioInitiative and EMF Scientist appeal, don't agree with the FCC guidelines. The scientific consensus is that the radiation emitted by wireless sources such as cell phones, Wi-Fi and cell towers within FCC allowed levels was proven to harm humans and the environment. The brief also accused the FCC of failing to address potential impacts of new technologies like 5G.

The brief shows that the FCC and FDA dismissal of the National Toxicology Program (NTP) study is indefensible. The $30 million study found clear evidence of cancer and DNA damage. The FDA opinion that the results cannot be extrapolated to humans is contrary to FDA's own protocols and was rejected by numerous experts including NIEHS former director, Dr. Linda Birnbaum.

"CHD is committed to protecting children from toxic exposures. This case seeks justice for parents of kids who have suffered health impacts from wireless radiation," said Robert F. Kennedy, Jr. "We are committed to making our government accountable, and giving a voice to injured children."

MEDIA CONTACT: Rita Shreffler 202.599.1461

SOURCE Children's Health Defense

Related Links

http://www.childrenshealthdefense.org

http://www.chicagotribune.com/news/sns-bc-us--cold-war-human-testing-20171002-story.html

Cold War radiation testing in US widespread, author claims

JIM SALTERAssociated Press

Three members of Congress are demanding answers after a St. Louis scholar's new book revealed details of secret Cold War-era U.S. government testing in which countless unsuspecting people, including many children, pregnant women and minorities, were fed, sprayed or injected with radiation and other dangerous materials.

The health ramifications of the tests are unknown. Lisa Martino-Taylor, an associate professor of sociology at St. Louis Community College who wrote "Behind the Fog: How the U.S. Cold War Radiological Weapons Program Exposed Innocent Americans," acknowledged that tracing diseases like cancer to specific causes is difficult.

But three House Democrats who represent areas where testing occurred — William Lacy Clay of Missouri, Brad Sherman of California and Jim Cooper of Tennessee — said they were outraged by the revelations.

Martino-Taylor used Freedom of Information Act requests to obtain previously unreleased documents, including Army records. She also reviewed already public records and published articles. She told The Associated Press that she found that a small group of researchers, aided by leading academic institutions, worked to develop radiological weapons and later "combination weapons" using radioactive materials along with chemical or biological weapons.

Her book, published in August, was a follow-up to her 2012 dissertation, which found that the government conducted secret testing of zinc cadmium sulfide in a poor area of St. Louis in the 1950s and 1960s. The book focuses on the mid-1940s to the mid-1960s.

An Army spokeswoman declined to comment, but Martino-Taylor's 2012 report on testing in St. Louis was troubling enough to trigger an Army investigation. The investigation found no evidence that the St. Louis testing posed a health threat.

Martino-Taylor said the offensive radiological weapons program was a top priority for the government. Unknowing people in places throughout the U.S., as well as parts of England and Canada, were subjected to potentially deadly material through open-air spraying, ingestion and injection, Martino-Taylor said.

"They targeted the most vulnerable in society in most cases," Martino-Taylor said. "They targeted children. They targeted pregnant women in Nashville. People who were ill in hospitals. They targeted wards of the state. And they targeted minority populations."

The tests in Nashville in the late 1940s involved giving 820 poor and pregnant white women a mixture during their first pre-natal visit that included radioactive iron, Martino-Taylor said. The women were chosen without

their knowledge. Blood tests were performed to determine how much radioactive iron had been absorbed by the mother, and the babies' blood was tested at birth. Similar tests were performed in Chicago and San Francisco, Martino-Taylor said.

Cooper's office plans to seek more information from the Army Legislative Liaison, said spokesman Chris Carroll.

"We are asking for details on the Pentagon's role, along with any cooperation by research institutions and other organizations," Carroll said. "These revelations are shocking, disturbing and painful."

In California, investigators created a radiation field inside a building at North Hollywood High School during a weekend in the fall of 1961, Martino-Taylor said. Similar testing was performed at the University of California, Los Angeles and at a Los Angeles Police Department building.

Sherman said he wants a survey of people who graduated from the school around the time of the testing to see if there was a higher incidence of illness, including cancer. He also said he will seek more information from the Department of Energy.

"What an incredibly stupid, reckless thing to do," said Sherman, whose district includes North Hollywood High School.

Among those who recall the testing is Mary Helen Brindell, 73. She was playing baseball in a St. Louis street in the mid-1950s when a squadron of green planes flew so low overhead that she could see the face of the lead pilot. Suddenly, the children were covered in a fine powdery substance that stuck to skin moistened by summer sweat.

Brindell has suffered from breast, thyroid, skin and uterine cancers. Her sister died of a rare form of esophageal cancer.

"I just want an explanation from the government," Brindell said. "Why would you do that to people?"

Clay said he was angered that Americans were used as "guinea pigs" for research.

"I join with my colleagues to demand the whole truth about this testing and I will reach out to my Missouri Delegation friends on the House Armed Services Committee for their help as well," Clay said in a statement.

St. Louis leaders were told at the time that the government was testing a smoke screen that could shield the city from aerial observation in case of Soviet attack. Evidence now shows radioactive material, not just zinc cadmium sulfide, was part of that spraying, Martino-Taylor said.

Doris Spates, 62, was born in 1955 on the 11th floor of the Pruitt-Igoe low-income high-rise where the Army sprayed material from the roof. Her father died suddenly three months after her birth. Four of her 11 siblings died from cancer at relatively young ages. She survived cervical cancer and suffers from skin and breathing problems.

"It makes me angry," Spates said. "It is wrong to do something like that to people who don't have any knowledge of it."

According to Martino-Taylor, other testing in Chicago; Berkeley, California; Rochester, New York; and Oak Ridge, Tennessee, involved injecting people with plutonium-239.

She said her book shines a light on the team of mostly young scientists tasked with developing radiological weapons. They worked in a closed world with virtually no input from anyone "who could say, 'This isn't right,' or put some sort of moral compass on it," she said.

She hopes her book prompts more people to investigate.

"We haven't gotten any answers so far," Martino-Taylor said. "I think there's a lot more to find out."

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http://radiationdangers.com/5g-roll-out/corona-virus-fakery-and-the-link-to-5g-testing/

Corona Virus Fakery And The Link To 5G Testing

The following article was written by Annie Logical

Original Link Can Be Found Here

This information is so important that is must shared far and wide

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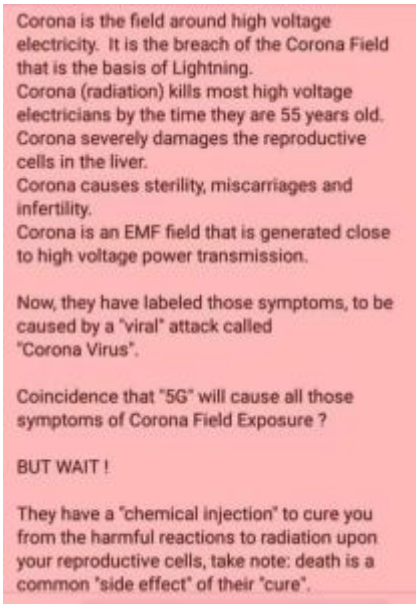

Back at the beginning of 2019, I predicted that there would be a link between 5G and a fake virus, hey presto! The area that is the epicentre of the so called virus is the same area that has reportedly been the province that 5G was rolled out with base stations.

https://www.allkpop.com/…/wuhan-was-the-province-where-5g…/…

Then we have the company Huawei offering to help combat the so called virus with their 5G base stations. I hope people wake up to this fraud that is being played out with Agenda 20/30 in mind, this is no joke.

The area in which the outbreak occurred in Wuhan has a lab.

The Wuhan National Biosafety Laboratory is the only lab in China designated for studying dangerous pathogens, which indicates a possible man made element. In other words, they can isolate cells and inject foreign cells into humans via vaccines. https://www.dailymail.co.uk/health/article-7922379/Chinas-lab-studying-SARS-Ebola-Wuhan-outbreaks-center.html?fbclid=IwAR0jIhPlQSsSYn2JkWCT9I_ThnwA4dqNOpBJNCjrJwtPdorOSX8bAIq0ti0

I documented a company called InOvio about eight years ago.

This same company have just been given 9 million dollars to come up with a vaccine for corona virus. They claim they were able to do so in two hours!

Local Biotech Company Developing Coronavirus Vaccine
The fact that they can claim to have a vaccine for a non existent virus in two hours proves that it is all fake.

Local Biotech Company Developing Coronavirus Vaccine

INOVIO

The pioneer of DNA vaccinations is a man called Dr Weiner. This is the same man involved in the Zika vaccine.

In 2000 Dr Kim and Dr Weiner began a company called InOvio, they first had a company called VGX.

Dr Joseph Kim, teamed up with his university lecturer called Professor Weiner, who is the leading DNA technology inventor, created a few companies one was called Inovio, in which the Professor was the chairman.

The DNA technology was first used on pigs, to make pigs breed at a younger age

.Dr Kim was funded by Merck for his education, he produced something called PCV2 which is Porcine Circovirus, they were working on a veterinary drug that would help pigs escape a wasting disease.

So this was evaluated by the Dept of Homeland Security and Plum Island animal research, this DNA plasma for pigs had approval in 2005, in 2009, the swine flu vaccines were filing for a patent.

In 2009 Dr Kim's company was filing with FDA to start trials on humans for the swine flu.
Dr Kim has many Merck Insiders on his board.
They created PCV1 and 2, which is Pig DNA.

Later on PVC1 and PCV2 were discovered in vaccines such as Gardasil, Rotatec and Rotarix.

A couple of years after they were given the patent for this pig DNA vaccine using PCV2 that same ingredient was found to be in Merck's Rotarix vaccine for diarrhoea and GSK vaccine Rotateq for diarrhoea.
Now how does pig virus magically turn up in a vaccine for diarrhoea?It doesn't! It gets put there. And what is unbelievable is that even though both vaccines were suspended and it transpired that all the vaccines for 2 years had been contaminated , the FDA suspended them for a few months then let them carry on.(The Information about the two drugs being suspended was found on the Medworm website and the article was written by Dr Kim).

Reports are now claiming that the coronavirus is linked to seafood after many people were reported to have contracted coronavirus from a seafood, 27 (66%) of 41 patients had been exposed to Huanan seafood market.

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30183-5/fulltext?fbclid=IwAR0Xe8TbDNKIeQzt9RyrJx3cBG_3K_lzvcO0VpEyGclmMXFxD44DwAzLcNg

It has long been established that seafood in the area is fed on pig waste.

https://abcnews.go.com/Business/consumers-eating-feces-tainted-shrimp-fish-seafood-asia/story?id=17491264&fbclid=IwAR1z3mxc7LXhEMnRj3pno5X3MStzO3IDuajsC7vdTNSSpultF3Uo7fjYVbY

In early 2013, some 16,000 dead pigs (including corpses infected by porcine circovirus) (which is really pig DNA)floated to Shanghai along the Huangpu river – a grisly sight that raised public concern about both unethical agricultural practices and water contamination.
https://www.theguardian.com/environment/2018/aug/31/eutrophication-algae-how-animal-waste-is-turning-chinas-lakes-green

China has concentrated its industry on pigs in the area too.
https://www.globalmeatnews.com/Article/2018/07/05/Wuhan-pig-farms-to-organise-China-s-pork-industry

Prof Weiner is not only the worlds DNA technology expert but he is also a special employee and adviser to the FDA.

This shows the depths to the corruption of this industry when an advisory to the supposed regulatory body is also a producer of vaccines that he advises on!

He has perfected a new method of giving these DNA vaccines via Electroporation which is a electro magnetic pulse that opens up the cells, injects foreign DNA and then it closes.

The system has been stated by Molecular Biologists to be unsafe as it could lead to death or cancer.They stated that only human antibody in genes is safe.

This is the same action that 5G technology uses in pulsed waves and the corona virus was reported to have started in an area in China that had rolled out 5G technology!

So we can see how geneticists using scientists are tampering with the building blocks of our existence and what is disturbing is that Prof Wiener is a HIV pioneer and we know that soon after the Polio vaccines were given to millions in Africa that HIV emerged.

They have perfected the art of injecting animal or bird DNA into human chromosomes which alters our DNA and causes things like haemorrhaging, fever, cancers and even death.

Weiner was highly involved in the Zika vaccine.

It appears that they used the genetically modified Mosquitoes which had been irradiated and have had their genes changed so they can't live to adulthood, they infect a mossy with gonad chomping parasite, which then affects a high proportion of insects and changes the sex of many, introducing anti biotic makes every male offspring transgender,they are making vaccines from these insect cell lines,this is what they are going to be using in the DNA vaccines, what if this was used with electroporation into human genes?

So here is a company heavily involved in experimenting on fake pandemics and fake viruses for many years, now been given the go ahead to produce the corona virus vaccine!

At this point, I would like to turn your attention to his partner, Dr Weiner.

An advisor to GSK, Pfizer and other Pharma giants, he is also a special employee and advisor to the FDA and the NIH grant review process.

No wonder then, how Inovio was given a 28 million dollar grant by the NIH to develop its genetically modified DNA based monoclonal antibodies and its new process of electroporation.

This is the process by which the very first genetically modified virus was used in this case, it was on pigs.

In 2006 VGX were providing HIV vaccines in Africa.

In 2008, VGX, which is also owned by Inovio, went into an arrangement to manufacture DNA plasmid for human use.

In 2009, Inovio filed a IND with FDA to start trials on humans with a DNA vaccine for H5N1.

Their lead drug for Swine flu was licensed in 2009.

In 2010, 8 different plasmids were produced in a study provided by the Defence threat Reduction Agency of the DoD.

In 2011 they were working with Homeland security on Foot and mouth disease.

New strains of foot and mouth disease began in 2012 in USA.

Under a research and development agreement, they were working with US Dept of homeland security and Plum Island Animal disease centre.

They were then given the go ahead to produce not only the Ebola vaccines but also the new novel method to administer them.

Conflicts of Interest

The Wistar Institute were given 9 million dollars to advance a coronavirus vaccine, the institute has Weiner as the executive vice president, who,s company will then make a profit from the vaccine.

THE METHOD

Electroporation

This is a pulsed electrical current applied to local tissue to allow the cell to have holes in it to allow just enough synthetic DNA to enter, then the pulse stops and the cell closes, the problem here is that according to studies, a manuscript in Molecular therapy with references from 74 separate articles written in 2004, concludes that the use of gene transfer using electroporation should only be used with human antibodies because problems could arise from cancer to death.

There is a brief explanation on how 'recombinant DNA technology' can influence "A HOST'S DNA" which is why this report was generated to begin with, as it looked into the 'then' Soviet Union's capabilities at that time. A link here shows that:https://gdsajj.wordpress.com/2009/11/

Recombinant DNA encompasses only one area of genetic engineering; namely, Biospecific biochemical and microbiological to alter,relatively controlled and reasonably predictable manner, the molecules that encode the genetic characteristics of an organism, and to introduce specifically selected new set of genetic Instructions.

The specific molecular manipulations that are made and the exact methods used to make them can vary widely from one recombinant DNA experiment to another. The basic process,usually involves the Initial isolation or synthesispecific set of chemically identical nucleic acid molecules (usually molecules are then bonded…?) specially prepared vector (carriers) that usually are plasmids. bacteriophages, or other virus-like infectious entities that can self-replicate in appropriate host cells. After the bonding has been completed, the modified can be inserted into bacteria or other cells that lave been prepared biochemically to accept them. If the vectors have been "constructed" appropriately, the piece of initially selected DNA can give the recipient new genetic instructions. For Instance, the host cell might be given the capability to synthesise an enzyme that it previously could not make.

It goes on to state that:

This science is exactly what you would need for a population reduction 'PROGRAM' using 'mandated' vaccine legislation! Poisoning the well i.e. GMO food could also work well with this science achieving population reduction quotas. Link shown. https://gdsajj.wordpress.com/2009/11/

FOI document https://www.cia.gov/library/readingroom/docs/DOC_0000969741.pdf

Beside the fact that Dr Kim has also served his five year tenure as a member of the Global Agenda Council of the World Economic Forum, which is clearly a huge advocate of a one world global government, attended by the world,s top 1000 corporations and involves a network of Government leaders.

We were informed via the mainstream media that the only way to test for Ebola was for those tests to be sent to UK/US labs, yet, a new piece of equipment had been produced that allowed those tests to be achieved in minutes, but, this appears to have been known and available since 2010, why has it been suppressed by the medical profession, it was part created by Wellcome, who are heavily involved in the medical agenda being played out.

I think the evidence gathered here brings a lot of scientific, military, bio-companies and government organisations into question on ethics and also on their real agenda.http://www.hartford-hwp.com/archives/45/298.html

Inovio reportedly made the vaccine in 2 hours!

So we can see how geneticists using scientists are tampering with the building blocks of our existence and what is disturbing is that Prof Wiener is a HIV pioneer and we know that soon after the Polio vaccines were given to millions in Africa that HIV emerged.

They have perfected the art of injecting animal or bird DNA into human chromosomes which alters our DNA and causes things like haemorrhaging, fever, cancers and even death.

Here's how this con job goes and although it repeats itself under different names, year after year (Corona, HIV, AIDS, SARS, Ebola, Zika, Mad cow etc etc) most of the uninformed public react as programmed, simply because fear is PROVEN to trigger a narrowing of the mind, a lowering of IQ, a stimulation of the child ego (that looks for an adult to save it) and a reflexive obedience toward perceived authority.
The con job goes like this.
Step 1) poison the population purposely to create disease that does not and would never occur naturally
Step 2) parlay the purposely created disease as being caused by something invisible, outside the realm of control or knowledge of the average person
Step 3) create a toxic vaccine or medication that was always intended to further poison the population into an early grave
Step 4) parlay the vaccine or medication poisoning as PROOF the disease, which never existed, is much worse than anticipated
Step 5) increase the initial poisoning, which is marketed as a fake disease, and also increase the vaccine and medication poisoning, to start piling the bodies into the stratosphere
Step 6) repeat as many times as possible upon an uninformed population because killing a population this way (the art of having people line up to kill themselves with poison……known as a "soft kill" method) is the only legal way to make sure such eugenic operations can be executed on mass and in plain sight.

How convenient

Prior to the coronavirus outbreak, 5G's potential for remote medical services was largely theoretical, as carriers and practitioners spoke of the future prospect of performing remote surgeries or offering diagnoses to patients in far-flung areas. The use of 5G communications to enhance practitioner safety in circumstances such as this, where a virus' transmission characteristics and other vectors remain unclear, is fairly new but

represents a highly practical test of the high-bandwidth wireless technology.https://venturebeat.com/2020/01/27/zte-5g-gear-lets-chinas-experts-remotely-diagnose-wuhan-coronavirus/

5G technology also uses the pulsed mechanism of electroporation and the outbreak is in the same area that 5G is introduced? DNA damaging vaccines will be introduced.

In Oct 2019 a Global Pandemic Exercise took place involving the US CDC and the Chinese CDC which focused on a Coronavirus from pigs. This was hosted by the Gates foundation. https://www.youtube.com/watch?v=Vm1-DnxRiPM&fbclid=IwAR1G1aQejmh9jSFZe2Cn7V3h1fMEPXDClrDwyzsyE6wVRloaRNuz5VExMAY&app=desktop

This was called Event 201

The event claims that a coronavirus is started with pigs and becomes a pandemic.

This patent was from a man they call the 'Godfather' of coronavirus, Ralph Baric, this is an extract from the 2002 patent. https://patents.justia.com/patent/7279327

Subjects which may be administered or treated by the viral particles or VLPs of the present invention may be any subject, generally vertebrates, for which the viral particles or VLPs are infectious, including but not limited to birds and mammals such as pigs, mice, cows, and humans).

STATEMENT OF FEDERAL SUPPORT

This invention was made possible with government support under grant numbers AI23946 and GM63228 from the National Institutes of Health. The United States government has certain rights to this invention.

FIELD OF THE INVENTION

The present invention relates to methods of producing recombinant nidovirus vectors, particularly coronavirus vectors, and expressing heterologous genes from said vectors.

BACKGROUND OF THE INVENTION

Transmissible gastroenteritis (TGE) is an economically important, acute enteric disease of swine, which is often 100% fatal in newborn piglets.

Here is the same patent holder, Baric claiming that the coronavirus is now being spread by people with no symptoms at all! After claims that a 10 yr old was tested positive with no symptoms.

"You may have mild disease spreaders that would be feeding sort of a community outbreak and they don't go to hospital because they don't feel that bad," said Ralph Baric, professor of microbiology and immunology at the Gillings School of Global Public Health at the University of North Carolina at Chapel Hill"

"That would be feeding sort of a community outbreak?"

https://www.ndtv.com/world-news/coronavirus-10-year-old-boy-raises-fears-coronavirus-could-spread-undetected-2171886

A debate amongst scientists about the lab created coronavirus also mentions Ralph Baric as being involved.

https://www.the-scientist.com/news-opinion/lab-made-coronavirus-triggers-debate-34502?archived_content=9BmGYHLCH6vLGNdd9YzYFAqV8S3Xw3L5

Baric also known to have filed a patent for a Zika vaccine!

https://www.dailytarheel.com/article/2019/02/zika-patent-0211

How convenient! Now they can create the pandemic and push the vaccine programme even if you are not showing any signs!

In the same article dated 30th January 2020 it states:

As more cases of the new coronavirus appear around the world, doctors and medical research teams are rushing to try to develop a vaccine or treatments that could prevent its spread

The coronavirus may be used as a vaccine for treating and/or preventing a disease, such as infectious bronchitis, in a subject in the form of a vaccine. https://patents.justia.com/patent/10130701

(patent 2015)

The virus is owned by Pirbright Institute (formerly the Institute for Animal Health) which is partially owned by the Gates foundation. One of the other owned is the African swine fever virus, which is listed as a "vaccine." This is all about the vaccines!

They are using the techniques they have developed to examine the neutralising antibody responses generated by candidate vaccines in research supported by Innovate UK who are the same agency who fund and support 5G in the UK!https://www.pirbright.ac.uk/our-science/livestock-viral-diseases/viral-glycoproteins

Innovate UK pushing the 5G agenda https://www.wired-gov.net/wg/news.nsf/articles/Developing+5G+networks+across+the+globe+apply+for+funding+25092019091000?open

Innovate UK ran a competition in 2018 with a £15 million share out to any small businesses that could produce vaccines for 'epidemic' potential'.https://apply-for-innovation-funding.service.gov.uk/competition/166/overview

The competition states that "Total project costs can be up to £2 million, including VAT. It must start by 1 September 2018 and can last up to 2 years."

JUST IN TIME FOR 2020!

In Dec 2018, a new 'not for profit' organisation was created with a £66m investment called Vaccine Manufacturing and Innovation Centre UK Ltd (VMIC). Costing 66 million and reportedly ready at the end of 2012.

This organisation was registered by Professor Adrian Hill of the University of Oxford Department of Healthcare Science.

In 2014 his group led the first clinical trial of an Ebola virus vaccine targeting the outbreak of Ebola in West Africa.

Hill is with the Jenner Institute which has partnered with Pirbright Institute.
https://www.abc.net.au/radionational/programs/bigideas/vaccines-for-ebola:-tackling-a-market-failure/7285468

So Pirbright Institute which has links to Gates and was also an animal research facility has ties to Dr Adrian Hill of the Jenner Institute. This is the man who was involved in Ebola vaccine studies!
Innovate UK who are the agency who are pushing the smart/5G agenda are also linked to Pirbright and fund trials.

But here is the thing!

A WEEK BEFORE the first reports of the Corona virus outbreak on 31st December 2019, this organisation created a new company called VMIC UK services Ltd.

Why would an English Institute have a patent which will be used for a supposed 'virus' in China? This is a patent number EP3172319B1 at Pirbright Institute in Surrey, England.(patent 2014)

The application is granted on the 20th November 2019 and the first case is claimed to occur on the 31st December 2019.

The coronavirus may be used as a vaccine for treating and/or preventing a disease, such as infectious bronchitis, in a subject'.

And the list of countries that are designated contracting states.

So why have all these countries recently as of November 20th 2019, all agreed to a contract for the coronavirus, (take into account the fact that the corona virus is built as a vaccine against bronchitis) and why has it been claimed in the media that the vaccine was created in two hours by InOvio?

Pirbright Institute has a list of stakeholders and shareholders who include veterinary vaccine manufacturers and other alphabet agencies including World Health Animal health. The director, Professor Bryan Charleston is also an animal practise professional.

It is clear that this vaccine was created in a lab in the UK some 6 years ago!

So does the patented corona company have links to vector technology?

Feb 2020 and Gilead have now declared that Ebola drugs have been used on Corona virus!

https://www.nytimes.com/reuters/2020/02/01/business/31reuters-health-china-gilead-sciences.html?fbclid=IwAR2QabUv6o6k0v1NWWHMrxPVEBX5CeboOBX8IlCsMNfs6KCawhT3XHztFlM

In an even bigger twist to this story, the Chinese reported in November 2019 that they were working on nanobots, the size of a so called virus!

How very coincidental that the 5G technology should be involved when the Chinese are experimenting on delivering nanobots?

The article goes on to state that they were :

Taking inspiration from self-driving cars, Li, now a post-doctorate at Stanford University, hopes autonomous movement might end up being a solution. "We could set the route to the precise site and the robots arrive there autonomously," he said.

https://www.scmp.com/tech/science-research/article/3036602/nanorobots-track-revolutionise-disease-treatment-making-1960s

Dr Zhou works at the Wuhan Institute of virology and is involved with genetically engineering immune pathways. https://theduran.com/is-this-the-man-behind-the-global-coronavirus-pandemic/?fbclid=IwAR1kW1mL6xbYVzE6D9Fnyrt6q03rqmBJ3ZS4_9CVNBIsRxrU-tl2oPk9xtM

The surname "corona" refers to in all cases developed laboratories and patented vaccine viruses. "Spontaneous mutations" are not patented.

CEPI Involvement

According to reports, Coalition for Epidemic Preparedness Innovations has granted Inovio, 9 million dollars to advance a vaccine for corona.

Previously, Inovio were advanced 56 million dollars to advance vaccines against Lassa fever and Middle East Respiratory Syndrome.

So who are CEPI?

They call themselves a 'global solution to a global problem' and the members are all of the usual culprits involved in past 'money making, fear induced false pandemics.'

CEPI is a Norwegian Association. The primary governing body is the Board, which has 12 voting members (four investors and eight independent members representing competencies including industry, global health, science, resource mobilisation, finance) and five observers.

They have four Board Committees: Executive and Investment, Compensation and Nomination, Audit and Risk, and Equitable Access, with members of our Board Committees are listed below. Other Board members or experts may be called upon as advisers or observers as needed.

Voting members include Peter Piot who was supposedly the man who discovered Ebola.

Even the story of Ebola and its initial discovery do not ring true.

Piot claims that he discovered Ebola in Yambuku and decided to name if after the nearest river some 60 miles away, yet Ebola was not the nearest river. Ebola was another lab created bioweapon and the US own the patent.

Other members include World bank, World Health Organisation and the Gates Foundation.

Very telling that it also has the Chinese Centre for Disease Control and Prevention and US Centre for Disease Control and Prevention as well as FDA, NIH and various pharmaceutical companies.

NOTE * Chinese CDC and US CDC both took part in the 'corona virus pandemic mock up' in October 2019 *

CEPI was founded in Davos by the governments of Norway and India, the Bill & Melinda Gates Foundation, the Wellcome Trust, and the World Economic Forum.

The CEO is the former director of BARDA (U.S. Biomedical Advanced Research and Development Authority (BARDA), part of the HHS Office.

During the Zika ' fear mongering scam' Takeda, (who are also members of CEPI) were given $19.8 million to cover the vaccine development through Phase 1, with potential funding of up to $312 million if ASPR/BARDA exercises all options to take the vaccine through Phase 3 trials.https://www.takeda.com/newsroom/newsreleases/2016/Takeda-to-develop-Zika-Vaccine-with-up-to-$312-million/

The director is an ex employee of the world bank.

Members of the Joint Coordination Group have a role in planning for rapid response to a priority pathogen and they are from WHO, GAVI, EMA, FDA, MSF, UNICEF, IFRC, AVAREF, NIBSC, and Wellcome.https://cepi.net/about/whoweare/

CEPI has also received single-year investments from the governments of Belgium and the UK. The European Commission foresees substantial financial contributions to support relevant projects through its mechanisms.

GAVI

Global Alliance for vaccines and immunisations,

GAVI to which the UK Govt is one of the biggest donors, has on its governing board, many pharma industry representatives, this group sets the price for vaccines, stimulates needs and using public money and money from "donors" is highly involved in the vaccine process.

The pharma industry sell vaccines to other countries, which is paid for by GAVI. The pharma companies can then collect that money back from a special fund called the Advance Market Commitment. So they can set the price of vaccines involving the same companies that stand to profit, a clear example of conflicts of interest.

Global health organisations like this are complicit in ensuring corporate welfare at the expense of the public and the public's health!

The AMC is a special financing mechanism set up in 2007 by Gavi and six donors (Italy, the United Kingdom, Canada, the Russian Federation, Norway, and the Bill & Melinda Gates Foundation) to stimulate development of vaccines.

It is clear that vaccine manufacturers, govt agencies and financial institutions are embedded in a revolving door of a vast industry that is constantly pushing the 'pandemic' button in the hope of a world wide vaccine programme.

The Medicines and Healthcare products Regulatory Agency (MHRA) is an executive agency of the Department of Health and operates as a government trading fund. The Secretary of State for Health determines the policy and financial framework within which the Agency operates.

The corruption of this agency is well documented here: https://www.modernghana.com/news/858966/the-corrupt-unbalanced-british-healthcare-system.html

In the meantime, we have the The ID2020 Alliance.

Launched with an initial grant from the Rockefeller Foundation.

Bill Gates is a founding partner in another company, this one is called the ID2020 Alliance, and its goal is to give every human being on earth a digital ID. How do they plan on accomplishing this feat? By combining mandatory vaccinations with implantable microchips.

The ID2020 Alliance is a digital identity program that aims to "leverage immunisation" as a means of inserting tiny microchips into people's bodies. In collaboration with GAVI.

Curious emblem? Very similar to this?

Put into perspective, Bill Gates is part owner of the coronavirus vaccine via Pibright Institute, he helped to create a pandemic exercise with the Chinese CDC just a few months before the reported 'outbreak' using the same virus.

He is involved with CEPI who are funding the vaccine manufacture, GAVI who sets the price for the vaccine and ID2020 who will use vaccines to microchip the public in line with the UN,s agenda 20/30. This is then passed onto the DNA vaccine company, Inovio who have links to other vaccines that were contaminated in the past, who claim to have a vaccine in a very short time, against all vaccine protocols.

This event is going to be used to forward the agenda that is Agenda 20/30 and they lost no time in creating this with the first case being reported on the 31st December 2019.

The 'mock up' scenario which is also funded by Gates and other globalists, goes on to express how this event will create the very circumstances that are needed to implement the UN,s policy of complete control over future populations.

On 30th January 2019, the WHO declared the corona virus to be international public health emergency.

In 2009, Professor Chossudovsky, a former employee of WHO,exposed the corruption of the WHO during the H1N1 flu campaign, he disclosed that WHO is a political body and NOT a health organisation.
Countries that are members are obligated under treaty to instigate policy on a national level.
He revealed that the data to support the decision to to call for a pandemic was fabricated by WHO.
They also discouraged independent testing and exaggerated the occurrence and number of deaths.
Big Pharmaceutical corporations advise WHO, they are NOT to be trusted and neither is the media who will push this fear mongering to make people accept dangerous vaccines.
WHO officials have collaborated with drug firms to create a campaign of panic and this time is no different.

WHO has been extremely successful in raising funds and is now receiving more than half of its yearly budget from private sources .
Bill Gates has for example given more than one billion dollars to the WHO. Private funding of WHO has brought WHO much closer to the pharmaceutical industry.

The biggest enemy we have right now is our acceptance of paternalism: the idea that these organisations, and psychopathic "leaders" are benevolent overlords

The hospital built in China, Huoshenshan Hospital, which was modelled on a facility set up in China's capital, Beijing, in 2003 to help tackle an outbreak of SARS, or Severe Acute Respiratory Syndrome is a prison!

When did you ever see a hospital with locks on the outside and bars on the windows?

Update 6/02/20

Pirbright Institute has a patent for corona which has links to Gates and was also an animal research facility and has ties to Dr Adrian Hill of the Jenner Institute.

This is the man who was involved in Ebola vaccine studies!Innovate UK who are the agency who are pushing the smart/5G agenda are also linked to Pirbright and fund trials.

Dramatic increase in the UK vaccine capability

In 2018, a new vaccine centre was set up called Vaccines Manufacturing Innovation Centre with Hill registering the new organisation, this was a supposed not for profit company.

The centre will cost around £66m to build and is scheduled to be up and running by the spring of 2022.https://www.vmicuk.com/

This organisation has members who are involved in the Pirbright Institute that is responsible for creating the Corona virus.

Here is Adrian Hill discussing his links to Pirbright!

In this interview he discusses how Ebola vaccines failed because they came after the 'event'!

In this interview Hill mentions the partnership between Jenner and Pirbright at 40 mins in.

https://www.abc.net.au/radionational/programs/bigideas/vaccines-for-ebola:-tackling-a-market-failure/7285468

A WEEK BEFORE the first reports of the Corona virus outbreak on 31st December 2019, this organisation created a new company called VMIC UK services Ltd.

An organisation, govt affiliated, that is supposedly' not for profit' for two years suddenly creates a private company ?

One of the directors is Prof Robin Shattock is linked to Horizon 2020 who are the biggest EU funding body pushing the smart agenda.

The CEO of this new company is named Dr Matthew Duchars who is also the CEO of the UK's Vaccines Manufacturing Innovation Centre (VMIC) not due to open until 2022.

So if its not due to be opened till 2022, why did they create a private company a week before Corona virus was mentioned?

Astonishingly, ebola vaccines have now been given to 'reported' corona victims!https://www.nytimes.com/reuters/2020/02/01/business/31reuters-health-china-gilead-sciences.html?fbclid=IwAR2cuDm4sBkjyMcU0gkKPZkyoeGQ4ndF1Hax2bvcewDScL4yaqOTghSHMR4

It is no wonder they have called this virus 'corona' because this imagery has been showcased in every Olympic games ceremony for decades.Here are such images that have been shown during Olympic Games ceremonies.

Complete with cut out faces of all the people in the world!

A Corona

A Corona virus image

How many people are aware that the epicentre of the reported 'Corona' virus, in Wuhan, held an Olympic type games ceremony just months before the reported outbreak? Yes, exactly, probably none! All kept very much quiet despite the extensive and grandiose games.

This was the 7th Military World Games held in Wuhan, the first time they had come out of the barracks and in the public domain!
With attendance by 103 countries and an opening ceremony that not only competed with every Olympic games ceremony but was a clear depiction of a military world under the UN, yet no main stream media even touched upon it!

This attunes to all my research showing the mass media events such as opening and closing ceremonies of other sporting events being used to showcase their intentions and Wuhan military games is NO exception. The pictures speak for them selves, here is a link to the opening ceremony.
https://www.youtube.com/watch?v=cKIfgkxaJSE

The 7th Military World Games was the first international military multi-sport event to be held in China and also it was the largest military sports event ever to be held in China, with nearly 10,000 athletes from over 100 countries competed in 27 sports.

Countries participating in the military games

5G also used at the event!

https://www.shine.cn/news/nation/1910184043/

Gilead have began testing unapproved Ebola vaccines in Wuhan even though it has never been passed for any safety requirements. https://www.zerohedge.com/markets/wuhan-begins-human-trials-new-gilead-coronavirus-vaccine

And the UK Government have given police in the UK, unprecedented powers to arrest people anywhere they choose if they "suspect" any person or group of people have the virus.

https://www.legislation.gov.uk/uksi/2020/129/introduction/made?fbclid=IwAR1AIbUXGzGk3nk9sKWOy_xCe2CcboFaI1DTTuQ0w8Uo40HLAO3_hScDWmc

As far as I am concerned this whole thing is a hoax, another fake pandemic on the way. The usual players are involved, they claim to have a vaccine in 2 hours, there is a mock up of the very same thing just a couple of months before involving the US CDC and the Chinese CDC as well as representatives from all the usual agencies and companies such as the Gates foundation, it gives 5G the opportunity to be showcased and seen as a great asset, it also gets a lockdown at a time when the public in that area were protesting against the incinerators that were causing respiratory problems, what better way to make use of the situation than to use it against the people.I also think that the pulsed waves of 5G have the same actions as that of the electroporation method perfected by Dr Weiner, the same man who has been given the contract to create the vaccine so it would appear that 5G pulsed waves would enable any pollutants to penetrate the body more easily and give the appearance of a viral infection.

Dr. Stefan Lanka, virologist and molecular biologist, is internationally mostly known as an "AIDS dissident" (and maybe "gentechnology dissident") who has been questioning the very existence of "HIV" since 1994. In the past years, however, he stumbled over a breathtaking fact: Not even ONE of the (medically relevant) viruses has ever been isolated; there is no proof of their existence. http://neue-medizin.com/lanka2.htm

NEW BOOK RELEASE – ARE WIRELESS DEVICES REALLY SAFE?

LEARN MORE HERE: Are Wireless Devices Really Safe?

http://radiationdangers.com/5g/is-the-coronavirus-actually-microwave-illness/

Is The "Coronavirus" Actually Radiation Sickness?

January 31, 2020 admin 145 Comments

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Note – this article is a work-in-progress. As new information comes to my attention, I will add it to the article if appropriate.

To learn more about the effects of 5G and other forms of non-ionizing radiation including 3G and 4G frequencies, please see my book, *The Dark Side of Prenatal Ultrasound and the Dangers of Non-Ionizing Radiation.*

Please also register in the sidebar to the right for updates about my books, "*Are Wireless Devices Really Safe*" and *"The Ultrasound-Autism Connection".*

* * * * * *

Source

Let me get right to the point. Anyone that is still denying the link between this allegedly deadly "coronavirus" and the symptoms associated with radiation sickness should not be trusted.

The evidence is POURING in that people are, indeed, getting sick from wireless radiation.

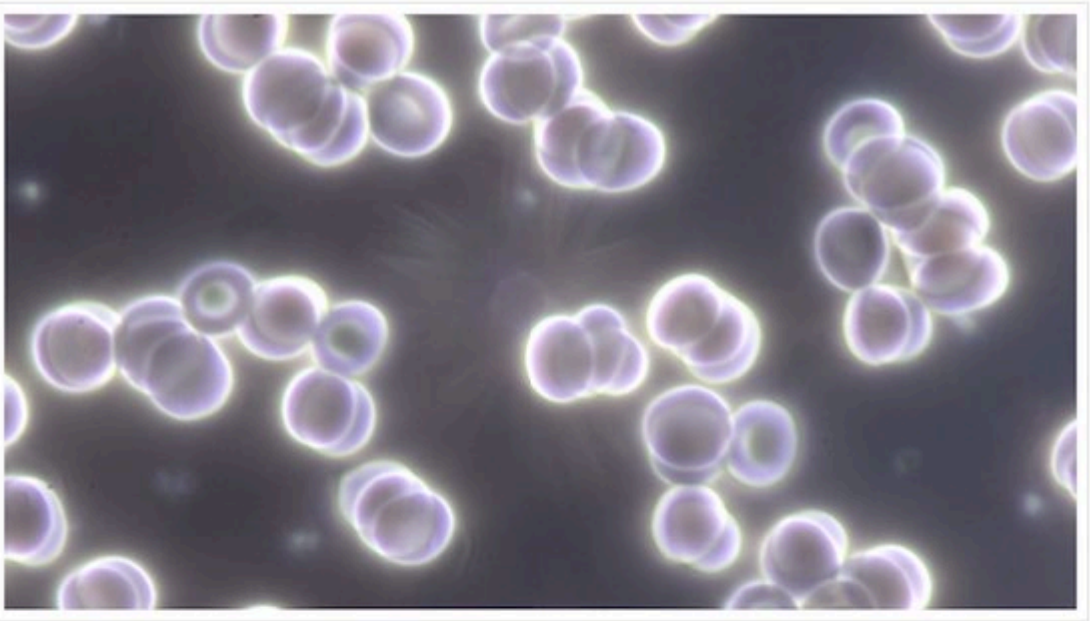
THE PROBLEM IS NOT JUST 5G.

ALL TYPES OF MANMADE RADIATION ARE HARMFUL including ultrasonic radiation, radiowaves, microwaves, and millimeter waves – and that includes 2G, 3G, 4G, and 5G.

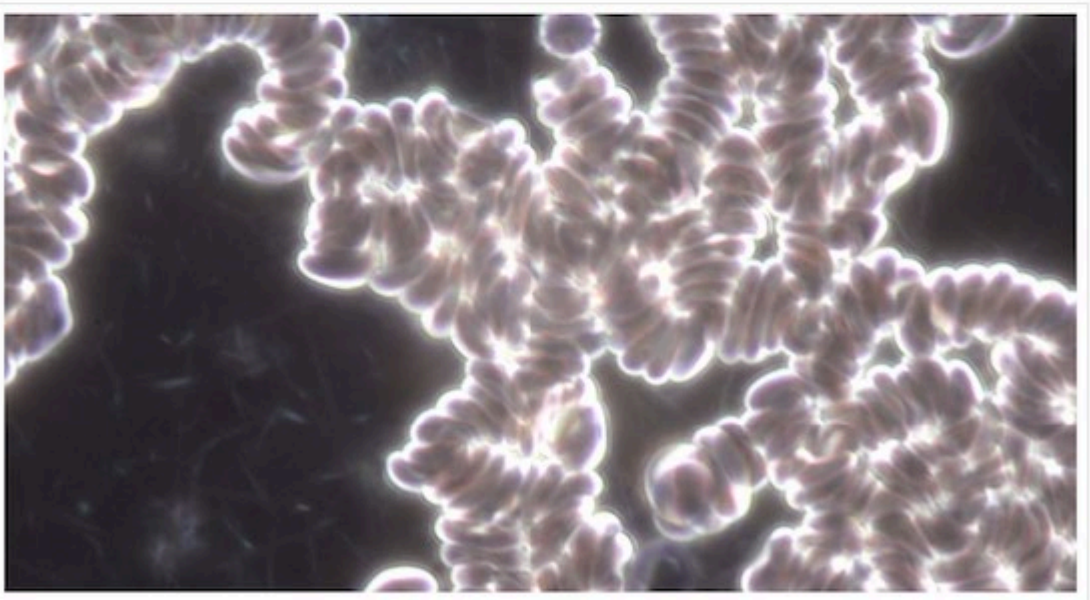
There are tens of thousands of studies documenting this (see also here and here). But we have been lied to incessantly about this fact and the time is now to set the record straight.

The symptoms people are experiencing that are being attributed to a "virus" are the exact same symptoms of radiation sickness. Just look at these symptoms!

- **loss of taste and smell**
- **stroke and seizures**
- **"fizzing" and an electrical feeling on the skin**
- **a burning feeling on the skin (which is EXACTLY what happens with 5G military weapons)**
- **neurological problems such as dizziness, headaches and impaired consciousness**
- **heart problems and heart attacks (which are CLEARLY a result of exposure to PULSED MICROWAVES that disrupt the electrical signaling of the human body – see also here)**
- **damage to men's testicles!!! (in case you did not know – exposure to any form of manmade radiation destroys male fertility)**
- **clotting of the blood that immediately makes me think of what happens to the blood when it is exposed to the 2.45 GHz frequency used for wifi, cell phones, baby monitors, etc.**



Normal Blood Cells



Same Patient – Rouleaux formation of red blood cells after 10 min exposure to 2.45 GHz

Dr. Magda Havas, PhD and Professor Emeritus at Trent University in Ontario,

Source

Respiratory problems are also being association with this virus, but in fact, are much more likely to be caused by exposure to 4G devices and also 5G (see below for a slew of information regarding the 60 GHz 5G frequency interfering with the body's ability to absorb oxygen).

Listen to the woman below describe her symptoms, all of which are clearly signs of RADIATION SICKNESS but that the medical establishment is claiming are the result of a virus. From a facebook post. Link not provided.

Back in March, right before everything shut down in my state, my husband went to lunch with a friend. A few days later, his friend started feeling very sick. A few days after that, my husband started feeling slightly sick for a day or two himself, and then I got brutally ill. His friend called later that week to tell us he tested positive for COVID. I spent weeks thinking I was actually going to die. I couldn't get tested anywhere no matter how sick I was, and when I could barely breathe my doctor told me "whatever you do, don't go to the hospital" . There were several nights where my husband packed my things for the hospital and watched me to see if I would get to a critical enough state that he needed to call 911. I was close so many times, but I'm here, and I'm suffering long term symptoms. I'm a "long hauler". One thing I noticed is that my fingers feel like they're getting chemical burns when I use my touch screen or phone for longer than a few minutes at a time. I would honestly believe my skin was actually starting to blister, and I would constantly check my hands to find out everything was in tact and unharmed. I work from my computer, and I noticed that at the end of the day I would start getting severe stroke-like symptoms. On the days I wasn't using my computer much, I would be mostly fine. My mom and aunt ordered those gun sensor thermometers, and I HATE THEM. I keep telling them to stop checking my temp with them because they feel like they're burrowing a hole into my brain. It sets me off. They think I'm insane. I had let them check my baby a couple times with it, but now I'm terrified of it. I don't want it anywhere near my baby's head. I notice when I'm able to take gentle walks with my baby, the closer I get to certain areas the more stroke-like symptoms I get. I was walking with my husband yesterday and I couldn't finish my conversation. I started having severe nerve pain, walking diagonally, dim vision, severe headache, slurred speech. We went to the shore and the only time I seem to feel well is in the morning on the beach, so sometimes I just go to the beach with my phone in airplane mode and sit in the sand for a while not touching any electronics. ***My brain and whole body feels like it's buzzing all the time. I do genuinely believe I've suffered severe nerve and vascular damage from this, and now I'm painfully sensitive to electronics****. I can feel when electronics turn on in my house. My husband loves the air fryer, and I have to make sure I'm a safe distance away from it or I get awful headaches. I mean, I have way more going on than just this, but I notice my stroke-like symptoms only seem to happen or become more severe around electronics or EMFs. It's a nightmare… honestly. I don't know what I'm looking for here, but I just needed to vent.*

And note that children, too, are becoming ill with symptoms of radiation sickness that the lying medical establishment is calling a "virus" or "Kawasaki disease."

Children are appearing with "multi-system inflammation with flu-like symptoms," and "with blood parameters consistent with severe COVID-19." The children may be agitated, confused, have severe difficulty breathing, have seizures, low blood pressure, inflammation of the heart, abdominal pain, skin rash and, especially in teenage boys, testicular pain. The disease is being called a variant of either toxic shock syndrome or Kawasaki disease. But the symptoms are all classic effects of radio wave sickness.
Arthur Firstenberg – Source

Friends, I believe there is a MASSIVE cover-up happening right now and if we do not expose it, then shame on us. Several studies have already demonstrated a connection between the 5G rollout and the prevalence of "COVID 19" (see here, here, and here).

Frankly, I DON'T THINK THERE IS ANY DEADLY VIRUS AND THE VIRUS STORY IS NOT ONLY A COMPLETE FABRICATION, BUT A REVERSAL OF TRUTH. The facts are below. Please share widely.

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Note: This information was originally published on Jan 31, 2020 and has been repeatedly updated.

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Dear friends – alot of information has been circulating around the internet regarding the alleged "coronavirus pandemic" that started in China.

Alarmist headlines began almost immediately, such as this one from Alex Jones' Infowars:

"Computer Models Show 183 Million Infected by Coronavirus February 29"

and this one from Mike Adams of Natural News:

"Over the Last 7 Days, Coronavirus Infections Have Increased 1000%"

Yet Alex Jones is now screaming that COVID-19 is a hoax – and this is ocurring just a few months after he instigated so much fear concerning this non-existent virus. I received this headline in my email today (6/11/20).

The World Health Organization declared a "Global Coronavirus Pandemic" at a time when there were allegedly 4,250 deaths WORLDWIDE from the virus. The United States declared the coronavirus to be a "*public health emergency*" in January of 2020 when there was not a single death registered from this fake virus in America. In fact, as of March 2020, only 110 people in the U.S. were alleged to have died from the virus.

The speed with which the emergency declarations were made, combined with the fact that there was no emergency, clearly indicate that this "viral pandemic" is completely fictitious and something else is going on.

Of course, the dark ones are gearing up to introduce yet another allegedly "life-saving" vaccine, and they are rubbing their hands together with glee, imagining that this latest "viral pandemic" will be the one that will finally enable them to mandate vaccines around the globe.

The CDC produced test kits that were contaminated with a lab-created coronavirus. UK tests were also contaminated. Canada also was caught with contaminated test kits. And if that were not enough, the tests are completely bogus anyway and do not really detect any virus.

Z Save Xing Bing Xue Za Zhi. 2020 Mar 5;41(4):485-488. doi: 10.3760/cma.j.cn112338-20200221-00144. [Epub ahead of print]

[Potential false-positive rate among the 'asymptomatic infected individuals' in close contacts of COVID-19 patients].

[Article in Chinese; Abstract available in Chinese from the publisher]

Zhuang GH[1], Shen MW, Zeng LX, Mi BB, Chen FY, Liu WJ, Pei LL, Qi X, Li C.

Author information

Abstract in English, Chinese

Objective: As the prevention and control of COVID-19continues to advance, the active nucleic acid test screening in the close contacts of the patients has been carrying out in many parts of China. However, the false-positive rate of positive results in the screening has not been reported up to now. But to clearify the false-positive rate during screening is important in COVID-19 control and prevention. **Methods:** Point values and reasonable ranges of the indicators which impact the false-positive rate of positive results were estimated based on the information available to us at present. The false-positive rate of positive results in the active screening was deduced, and univariate and multivariate-probabilistic sensitivity analyses were performed to understand the robustness of the findings. **Results:** When the infection rate of the close contacts and the sensitivity and specificity of reported results were taken as the point estimates, the positive predictive value of the active screening was only 19.67%, in contrast, the false-positive rate of positive results was 80.33%. The multivariate-probabilistic sensitivity analysis results supported the base-case findings, with a 75% probability for the false-positive rate of positive results over 47%. **Conclusions:** In the close contacts of COVID-19 patients, nearly half or even more of the 'asymptomatic infected individuals' reported in the active nucleic acid test screening might be false positives.

KEYWORDS: COVID-19; Close contacts; False-positive; Nucleic acid test; Screening

PMID: 32133832 DOI: 10.3760/cma.j.cn112338-20200221-00144

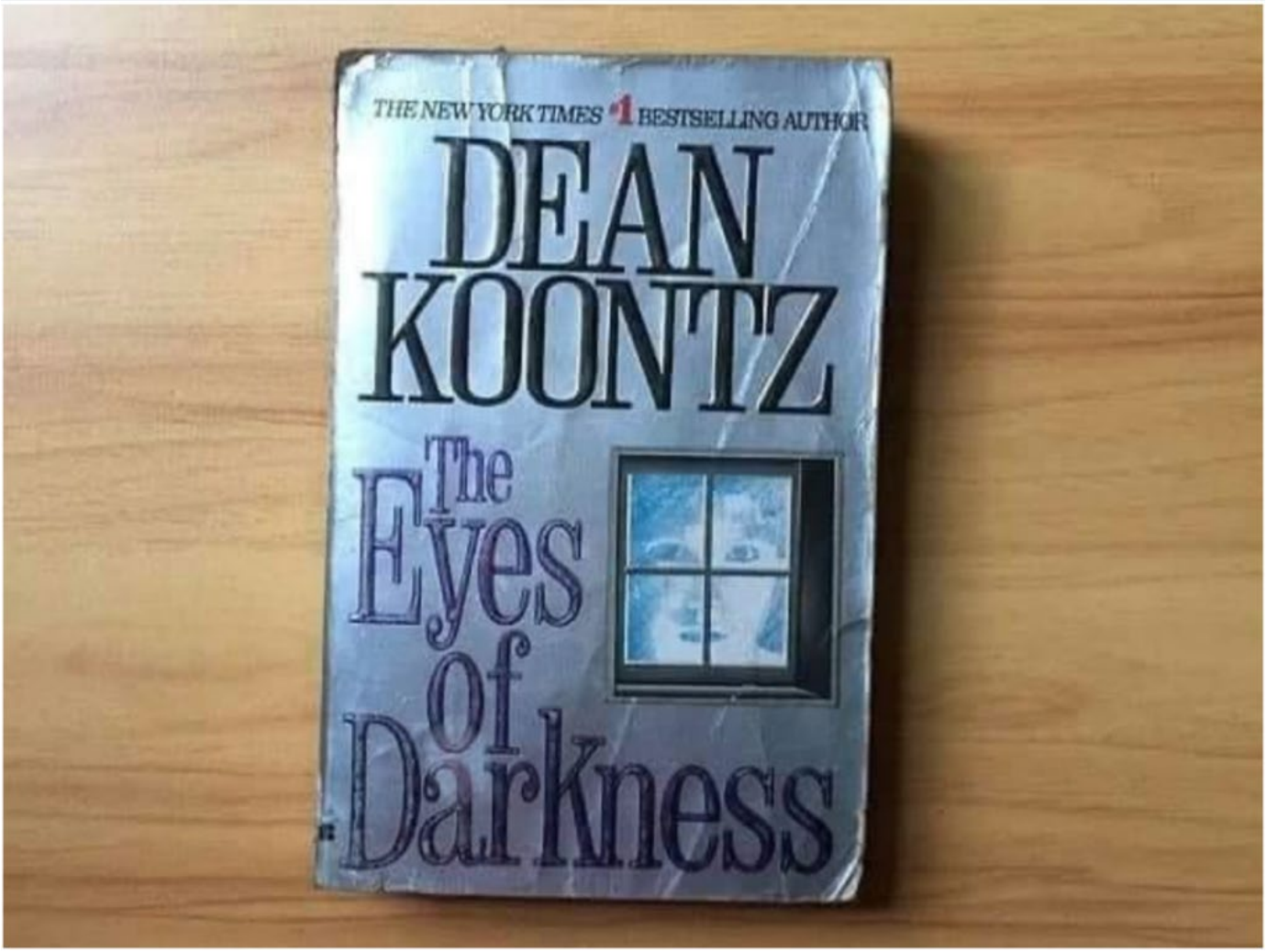
Source

What *is* happening is that people are developing various symptoms of radiation sickness and governments worldwide are blaming it on a fictitious virus.

Notice how all of these people have their faces in their phones. They people believe that wearing masks will protect them from a non-existent viral threat. Yet, in Truth, their radiation-emitting devices will weaken their immune systems and make them *more vulnerable* to becoming deathly ill.

It is important to note that the dark ones have been planning to unleash this so-called "viral" threat for decades. The images you are about to see are what is called "*revelation of the method*" — the process by which the psychopathic "elite" tell us ahead of time what they plan to do. They make these announcements ahead of time because, in their warped and twisted minds, they believe if they tell us what they are going to do and we do not object, then they have our tacit or implied consent and therefore, cannot be held spiritually accountable or liable for the harm they cause since we were all OK with it.

Behold the insanity of those who deviously plan over decades and centuries about the ways they intend to harm us and/or gain control over us. This book was published in 1981.


THE NEW YORK TIMES #1 BESTSELLING AUTHOR
DEAN KOONTZ
The Eyes of Darkness

"I'm not interested in the philosophy or morality of biological warfare," Tina said. "Right now I just want to know how the hell Danny wound up in this place."

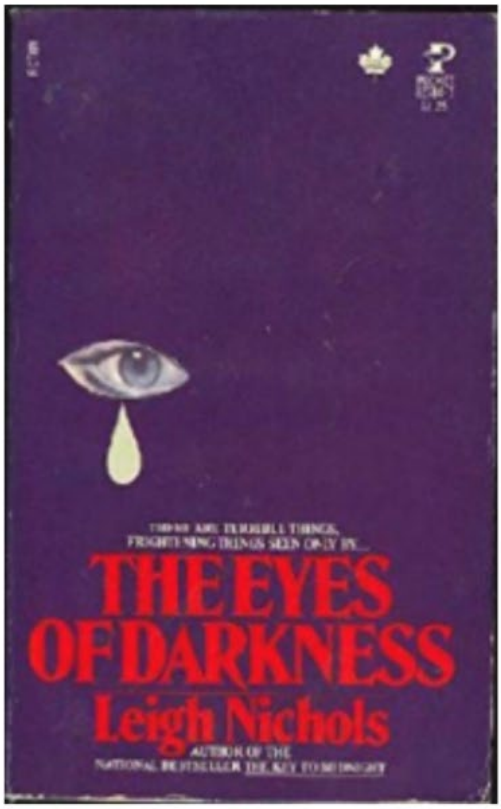
"To understand that," Dombey said, "you have to go back twenty months. It was around then that a Chinese scientist named Li Chen defected to the United States, carrying a diskette record of China's most important and dangerous new biological weapon in a decade. They call the stuff 'Wuhan-400' because it was developed at their RDNA labs outside of the city of Wuhan, and it was the four-hundredth viable strain of man-made microorganisms created at that research center.

"Wuhan-400 is a perfect weapon. It afflicts only human beings. No other living creature can carry it. And like syphilis, Wuhan-400 can't survive outside a living human body for longer than a minute, which means it can't permanently contaminate objects or entire places the way anthrax and other virulent microorganisms can. And when the host expires, the Wuhan-400 within him perishes a short while later, as soon as the temperature of the corpse drops below eighty-six degrees Fahrenheit. Do you see the advantage of all this?"

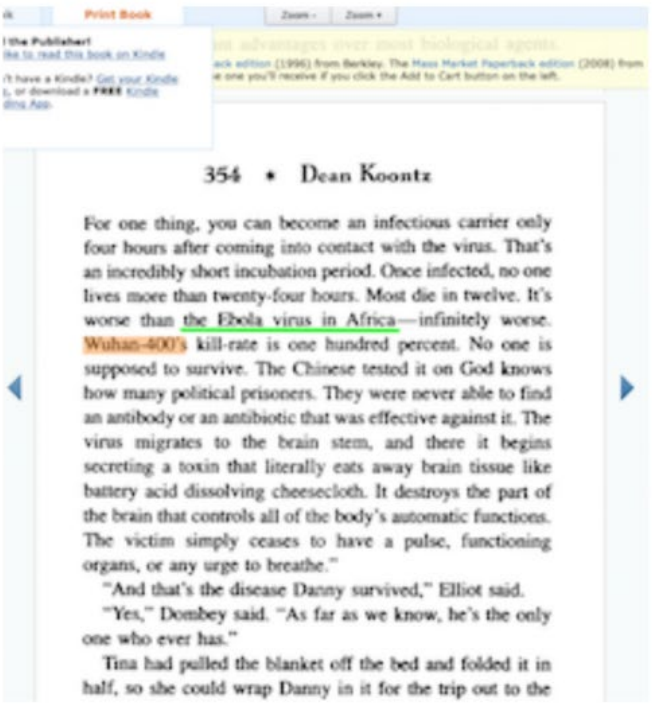
Tina was too busy with Danny to think about what Carl Dombey had said, but Elliot knew what the scientist meant. "If I understand you, the Chinese could use Wuhan-400 to wipe out a city or a country, and then there wouldn't be any need for them to conduct a tricky and expensive decontamination before they moved in and took over the conquered territory."

Dombey said, "And Wuhan-400 has other, ... over most biological agents.

"Koontz" has apparently written many books under various pseudonyms. And so it was the case with *The Eyes of Darkness*, which was originally released in 1981 under the fake name of Leigh Nichols. Not only does this book mention a "bioweapon" from Wuhan, China, but on the very next page, also mentions the "ebola virus" from Africa.



Original title and pseudonym published in 1981



354 • Dean Koontz

For one thing, you can become an infectious carrier only four hours after coming into contact with the virus. That's an incredibly short incubation period. Once infected, no one lives more than twenty-four hours. Most die in twelve. It's worse than the Ebola virus in Africa—infinitely worse. Wuhan-400's kill-rate is one hundred percent. No one is supposed to survive. The Chinese tested it on God knows how many political prisoners. They were never able to find an antibody or an antibiotic that was effective against it. The virus migrates to the brain stem, and there it begins secreting a toxin that literally eats away brain tissue like battery acid dissolving cheesecloth. It destroys the part of the brain that controls all of the body's automatic functions. The victim simply ceases to have a pulse, functioning organs, or any urge to breathe."

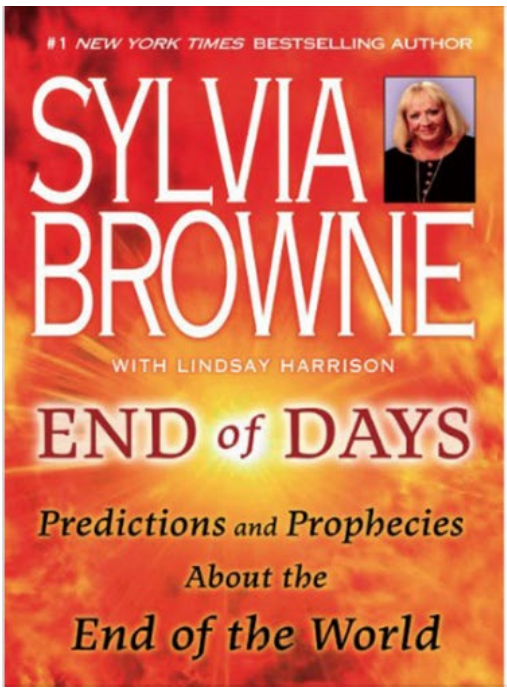
"And that's the disease Danny survived," Elliot said.

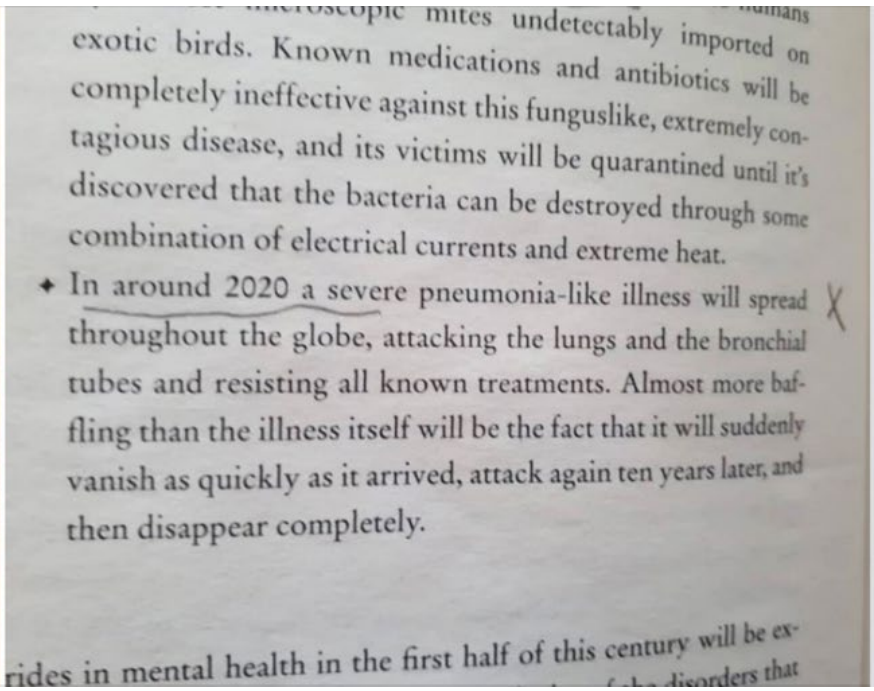
"Yes," Dombey said. "As far as we know, he's the only one who ever has."

Tina had pulled the blanket off the bed and folded it in half, so she could wrap Danny in it for the trip out to the

The Eyes of Darkness p. 354
Click image to enlarge

Even more interesting is the fact Dean Koontz is not the only author to 'predict' this nasty "virus." According to [The Sun Daily](), author Sylvia Browne published a book in 2008 called *End of Days: Predictions and Prophecies About the End of the World.* Check out her "prediction"!!!!





microscopic mites undetectably imported on exotic birds. Known medications and antibiotics will be completely ineffective against this funguslike, extremely contagious disease, and its victims will be quarantined until it's discovered that the bacteria can be destroyed through some combination of electrical currents and extreme heat.

• In around 2020 a severe pneumonia-like illness will spread throughout the globe, attacking the lungs and the bronchial tubes and resisting all known treatments. Almost more baffling than the illness itself will be the fact that it will suddenly vanish as quickly as it arrived, attack again ten years later, and then disappear completely.

rides in mental health in the first half of this century will be ex-

Source: [The Sun Daily]()

On top of all of this, the psycopaths actually staged a pandemic "exercise" (otherwise called a drill) called Event 201 in New York in October of 2019.

Event 201 was a 3.5-hour pandemic tabletop exercise that simulated a series of dramatic, scenario-based facilitated discussions, confronting difficult, true-to-life dilemmas associated with response to a hypothetical, but scientifically plausible, pandemic. 15 global business, government, and public health leaders were players in the simulation exercise that highlighted unresolved real-world policy and economic issues that could be solved with sufficient political will, financial investment, and attention now and in the future.

The exercise consisted of pre-recorded news broadcasts, live "staff" briefings, and moderated discussions on specific topics. These issues were carefully designed in a compelling narrative that educated the participants and the audience.
Source

And… 10,000 military personnel from 110 nations gathered in Wuhan, China on the exact same day for the "*2019 Military World Games*"!

One aspect which is very interesting and has been covered extensively here, is Event 201. The pandemic exercise simulating a global Coronavirus pandemic which took place on October 18th 2019 only 6 weeks before the first case of the virus was reported in Wuhan China. What not many people are talking about, is that on this exact same day, October 18th, the 2019 Military World Games held its opening ceremony followed by a U.S. mens soccer match in Wuhan China, ground zero of the outbreak!
Source

You cannot make this stuff up folks! They have been planning this hollywood-style plannedemic for a long time. And now it is clear, they are planning to air another round in the fall of 2020.

Expect coronavirus to return in the fall, says Fauci
https://youtu.be/IM3sIf7aMfU

What these psychopaths are actually doing is literally causing illness with their microwave and millimeter weapons, while simultaneously hiding the real cause of the illnesses people are suffering by claiming they are due to a "virus."

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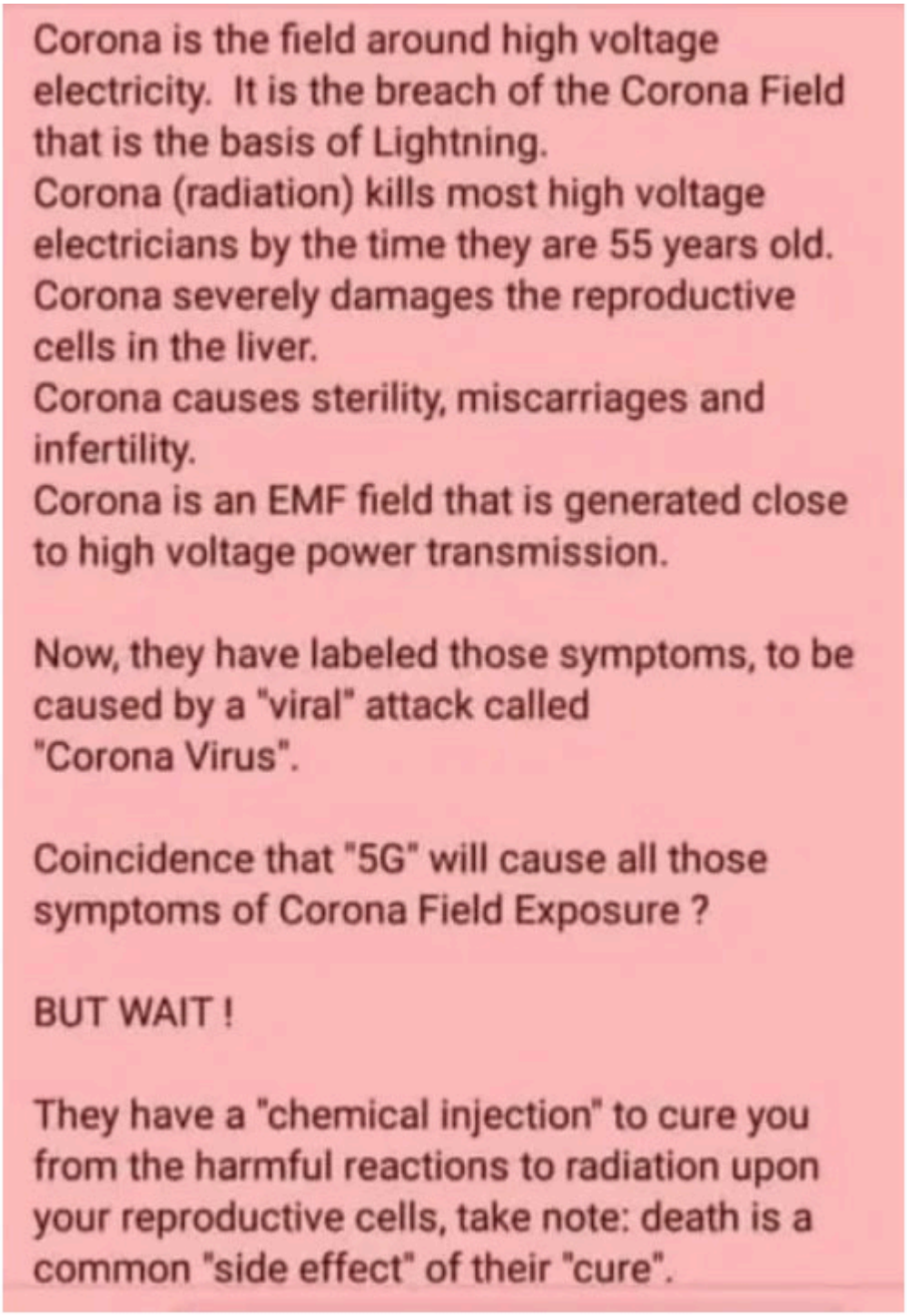
So let's take a moment to decode the word "coronavirus", and notice first that the word "virus" means "poison"and the word "corona" is used to describe the RADIATION FIELD that is sometimes emitted by high voltage devices! (See here, here and here for more info).

Thus the word CORONAVIRUS literally means RADIATION POISONING!

A corona discharge is an electrical discharge brought on by the ionization of a fluid such as air surrounding a conductor that is electrically charged. Spontaneous corona discharges occur naturally in high-voltage systems unless care is taken to limit the electric field strength… In many high voltage applications, corona is an unwanted side effect. Corona discharge from high voltage electric power transmission lines constitutes an economically significant waste of energy for utilities. In high voltage equipment like Cathode Ray Tube televisions, radio

transmitters, X-ray machines, and particle accelerators the current leakage caused by coronas can constitute an unwanted load on the circuit. In the air, coronas generate gases such as ozone (O3) and nitric oxide (NO), and in turn, nitrogen dioxide (NO2), and thus nitric acid (HNO3) if water vapor is present. These gases are corrosive and can degrade and embrittle nearby materials, and are also toxic to humans and the environment.
Source



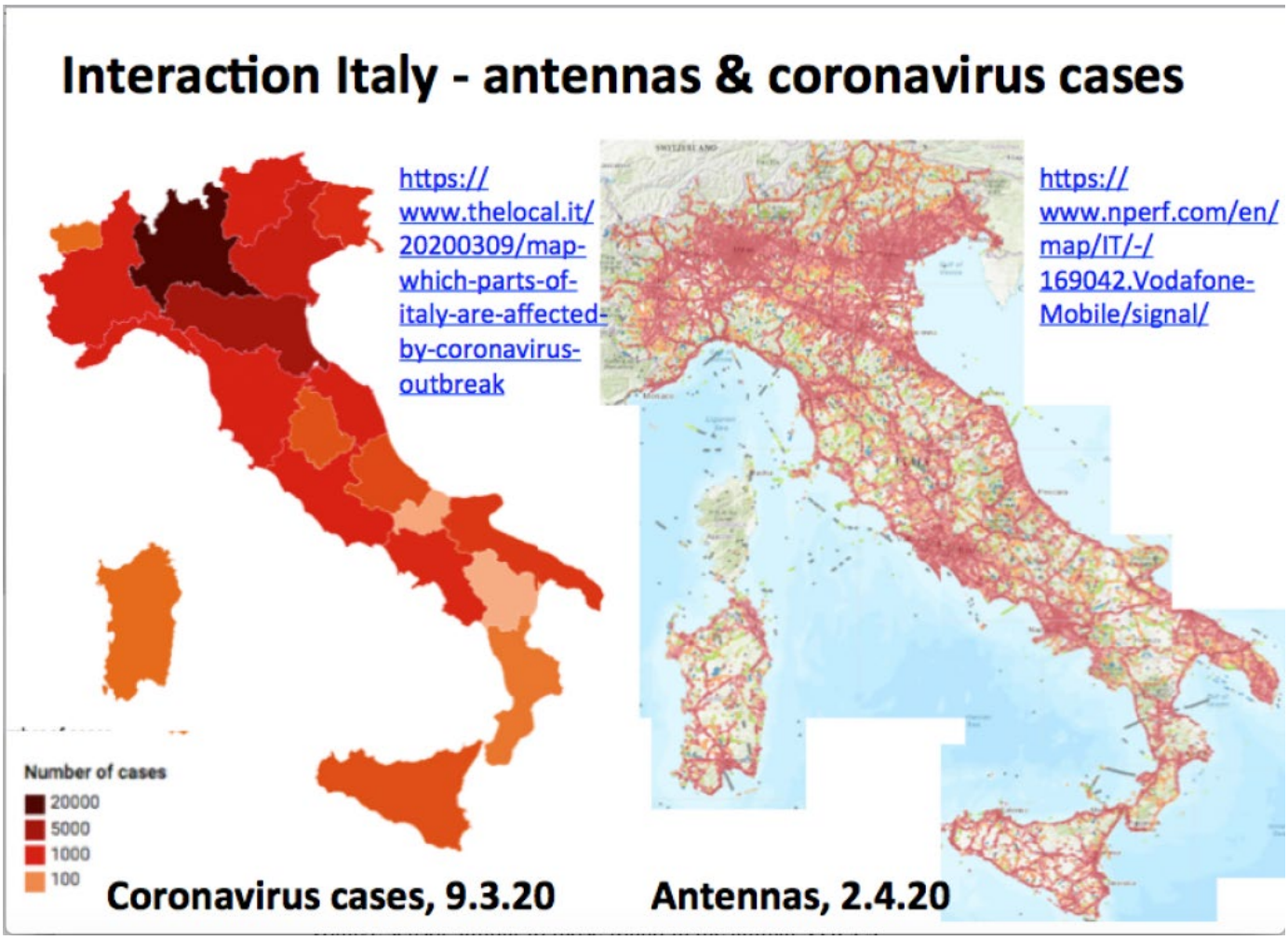
Source

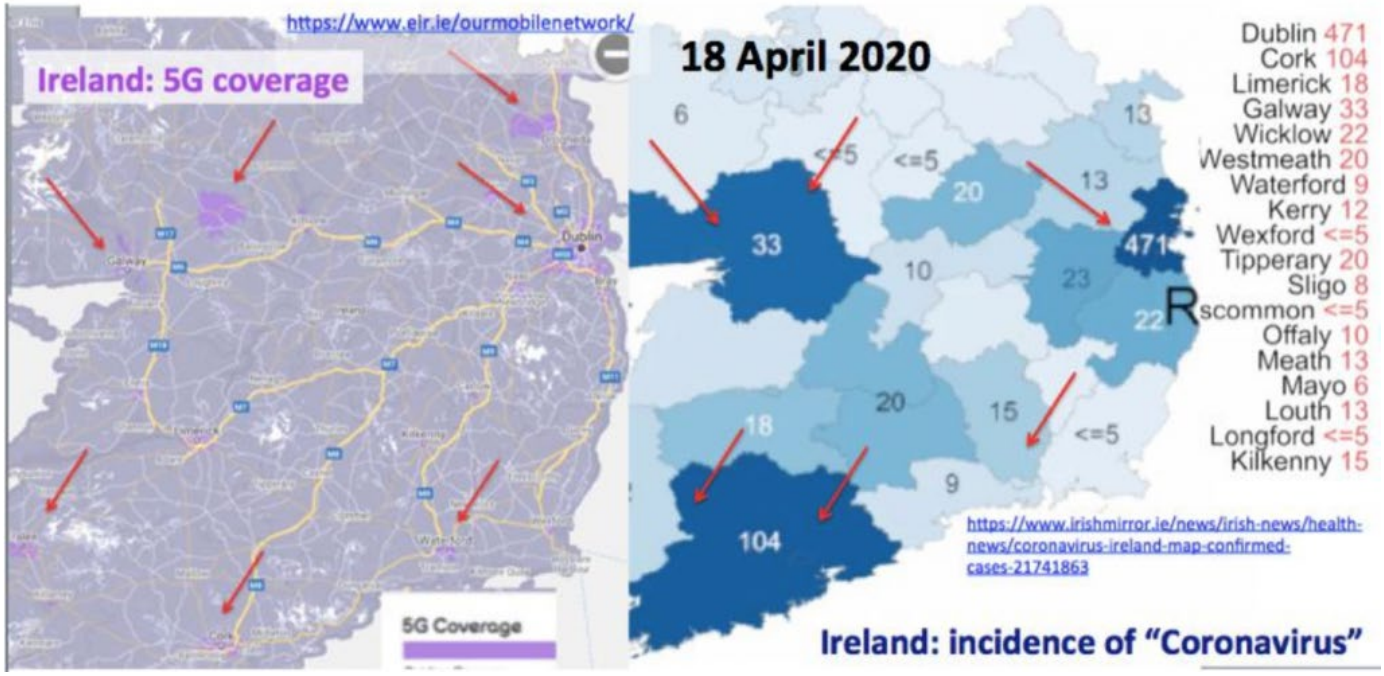
Is it just a coincidence then that the symptoms of this “virus” match precisely the symptoms of radiation sickness which symptoms are no doubt being brought on by increased cell tower density and the 5G rollout which has happened in Wuhan (see here and here) and other parts of China. See also here for a plethora of information about the radiation situation in China.

Look at this picture analysis of what is happening with the 5G roll-out in America and the places where people have gotten sick with this "virus."

Then read this article that documents how "coronavirus" outbreaks happen in the same locations where 5G has been rolled out.

Claire Edwards has documented this brilliantly in the following images.





The mainstream media and the powers-that-shouldn't-be will never tell us the Truth about this. Instead, they will babble on about an allegedly dangerous virus, while simultaneously presenting us with bogus ideas about so-called "climate change" so that nobody will ever suspect that any warming of our planet is likely due to radiation heat from increased cell tower density along with billions of wireless microwave devices (microwaves do COOK things), or that any

epidemics we experience over the next 5-15 years are going to be related to radiation poisoning from exposure to increasing densities of noxious, non-ionizing radiation.

So let's begin at the beginning. But first, here's a comment I recently made on a youtube video that is being censored…

Since 5G frequencies are known to negatively effect the absorption of oxygen in the cells and the body (see here and here);

And since all of the symptoms they are reporting are also listed as the very same symptoms associated with "microwave sickness" (i.e., radiation illness which can be induced from exposure to all wireless devices, including 4G devices — see here http://wa.grdn.net/microwave-sickness/);

And since "the flu" and microwave illness share many of the same symptoms (see here: http://wa.grdn.net/microwave-sickness/the-flu-and-microwave-sickness-share-many-of-the-same-symptoms/);

And since "the flu" has been shown to NOT be the result of a "virus" but rather an electrically-induced illness (see Arthur Firstenberg's book, "The Invisible Rainbow");

It is a fair estimation to assume that wherever 5G is being rolled out, people are going to rapidly become deathly ill. Wake up people. The entire wireless grid is designed to destroy us. They will blame these radiation-induced illnesses on a variety of things, but one thing they will not do is tell you that your devices and your entire wireless society are the problem. You have to figure this out on your own.

Please see my book for much more information about this: https://www.birthofanewearth.com/1/paperback-release-the-dark-side-of-prenatal-ultrasound/

People wearing masks is obviously not going to protect them from radiation-induced illnesses. Avoidance of radiation and/or radiation-shielded clothing are the only things that work.

Source

1. 5G IS ACTIVELY BEING DEPLOYED IN WUHAN.

"WUHAN — Central China's Hubei province has built more than 300 5G base stations and achieved full 5G signal coverage in its prefecture-level cities, local telecom sources said.

The China Mobile's Hubei branch said more than 300 5G base stations have been built since February 2018, and a dozen 5G experience centers have been completed in cities including Xiaogan, Yichang and Jingmen."
Source

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"So far, China Mobile has installed 100 5G base stations in Wuhan, the capital of Hubei, and is launching large-scale tests, according to Fan Bingheng, general manager of the company's Hubei branch."
Source

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China, in its rush to take the lead in the 5G race, had by the end of 2019… installed 130,000 5G antennas throughout the country,[19] **with 10,000 antennas installed in Wuhan alone**.[20]…

China already has a total of more than 80,000 **5G macro base stations**, typically cellular towers with antennas and other hardware that beam wireless signals over wide areas, government officials said. They said China will end the year with about 130,000, while Bernstein Research estimates South Korea will be in second place with 75,000…

This basically means that China had suddenly turned on the 5G switch, just less than two months before the COVID-19 outbreak, suddenly blanketing many cities with this 5G wireless radiation. And as of this writing, South Korea's numbers of COVID-19 cases are also starting to skyrocket. As we can see from the above article, **South Korea** has the s**econd highest number of 5G antennas with 75,000**. That is a lot for a country its size. Is there a connection? I think there is."

Source

2. 5G FREQUENCIES ARE KNOWN TO CAUSE SEVERE DISRUPTIONS IN THE BODY'S ABILITY TO ABSORB AND UTILIZE OXYGEN.

"The FCC has opened up the millimeter wave band and they're going to be broadcasting at 60 GHz… for the new 5G and the new Wifi. It's called wi-gig… This stuff is wicked. 60GHz is the oxygen molecule absorption spectrum… This is the frequency that the oxygen molecules start reacting to… They're gonna be using 5G to mess with oxygen… When you hit oxygen molecules with 60GHz millimeter emissions, it effects the orbital properties of the electrons… [This will affect] how oxygen is absorbed into your body… When you start effecting the oxygen molecules' ability to bind with the hemoglobin in the blood, you can't transport the oxygen into your tissues… It also effects your ability to produce Vitamin D. There are two locations in the United States where this was rolled out in schools. It produced paralysis, arrhythmia, neurological problems, problems with tingling in the extremities, people passing out, people having fatigue, malaise, all these bizarre ailments. These people have managed to get you to kill yourselves, and enjoy it, and kill your children, and pay for it."
Source

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"60 GHz… gets stuck in air. It doesn't travel well at all. So it's a bit bizarre that Ofcom [Office of Communications in the UK] are going to give [that part of the spectrum] away… If I was to blast enough 60 GHz amplitude into an oxygen molecule, I might break it. And that oxygen atom will attach with other oxygen molecules and create 03. 03 kills. At 50ppm, it will kill all biological life. So it's a bit bizarre that Ofcom would even want anyone to use this part of the spectrum—nevermind giving it away."
Source

"We are just beginning to recognize that Covid pneumonia initially causes a form of oxygen deprivation we call "silent hypoxia" — "silent" because of its insidious, hard-to-detect nature…

Pneumonia is an infection of the lungs in which the air sacs fill with fluid or pus. Normally, patients develop chest discomfort, pain with breathing and other breathing problems. But when Covid pneumonia first strikes, patients don't feel short of breath, even as their oxygen levels fall. And by the time they do, they have alarmingly low oxygen levels and moderate-to-severe pneumonia (as seen on chest X-rays). Normal oxygen saturation for most persons at sea level is 94 percent to 100 percent; Covid pneumonia patients I saw had oxygen saturations as low as 50 percent."
Source

Please watch this short video of a New York City ICU doctor explaining what he is seeing with respect to his "coronavirus" patients.

"It is as if tens of thousands of my fellow New Yorkers are on a plane at 30,000 feet and the cabin pressure is slowly being let out. Patients are slowly being starved of oxygen."

https://www.bitchute.com/video/i1lCAUEcMtlg/

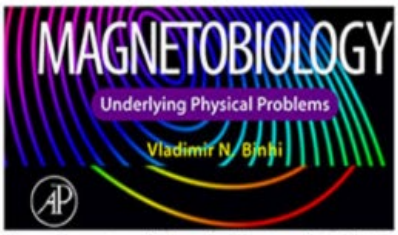
This is NOT typical pneumonia symptoms! In fact, this is exactly what can and will happen when people are exposed to the 60GHz 5G frequency. Keep in mind that 5G has been unleashed in NYC (see here and here). And also in Italy. Please see this link for details about the 5G rollout in Italy.

The past 48 hours or so have seen a huge revelation: COVID-19 causes prolonged and progressive hypoxia (starving your body of oxygen) by binding to the heme groups in hemoglobin in your red blood cells. People are simply desaturating (losing o2 in their blood), and that's what eventually leads to organ failures that kill them… Patients returning for re-hospitalization days or weeks after recovery suffering from apparent delayed post-hypoxic leukoencephalopathy strengthen the notion COVID-19 patients are suffering from hypoxia despite no signs of respiratory 'tire out' or fatigue.
Source

The POINT we would like to emphasize here- where the Dr notes in the hospital -Kirkland,WA where the death rate went to about 60% – not only was the area leading 5G rollout – also the level of wifi electrosmog measured there was highest they had ever measured. It has also been suggested not only was Wuhan leading 5G rollout- but also that Princess cruise ship- was rolling out 5G. (major cities leading the rollout -lead the deaths??) – We are finally getting a bit of biophysics depth here on how the hi ghz in the 5G causes oxygen loss in the blood / viral susceptibility – intro: https://www.youtube.com/watch?v=CtfqUtW_8AA… I suggest when we calculate the biophysics of the electron spin rates at the oxygen bond sites on the hemoglobin- we will find why when the critical ghz in 5G electrosmog densities go over a certain threshold the electron spin excitation necessary to phase lock the oxygen bond is inhibited. Harald says that happened near Berlin when they launched the extra microsatelites to boost the 5G saturation.
Source

Research on microwave radiation at lo power levels - 42 ghz in this case
5G tech is likely on this order- showing reduced oxygen solubility
in water- EVEN AT LO POWER LEVELS OF ELECTRO POLLUTION

exerpt from



Water and water systems have been traditional objects of study in many fields of science. Eisenberg and Kauzmann (1969), Franks (1982), and Antonchenko *et al.* (1991) considered physical and chemical properties of water, and presented a history of pertinent research. Privalov (1968), Watterson (1988), and Aksenov (1990) discussed the role of water in biological systems and processes. We confine our attention to papers devoted to water memory or metastability in connection with electromagnetic exposure. Below we give a few recent publications on the subject. A review of engineering applications of magnetically conditioned water, researched in the 1960s and 1970s, may be found in a book of Klassen (1973).

- Berezhinsky *et al.* (1993) demonstrated that conditioning a liquid water by a few mW/cm^2 of microwave radiation at 51.5 GHz for 5 min changed its refractive index by $\triangle n = 2.5 \cdot 10^{-4}$. This variation is 10 times the change in the sample index achieved with an equivalent thermal power. The effect had a frequency selectivity. It was measured with a He–Ne laser interferometer. Evidently, structural changes in water revealed by the polarizability of electrons have a relaxation time of at least 5 minutes.

- Singh *et al.* (1994) reported that water conditioned by microwave radiation influences the production of blue-green algae (cyanobacteria).

- Fesenko *et al.* (1995) demonstrated that a water solution used in measurements of the activity of calcium-dependent potassium channels memorizes exposure to microwave radiation. The activity of channels were measured by the "patch-clamp" method where a microscopic area of a membrane with channels covers the tip of a mini-pipette submerged in a solution and forms a part of an electric circuit.

Changes in channel activity changed current in the circuit. Since there were only few channels on the test area and each of them can be in an open or closed stat the current changed discretely. Data processing yielded the probability of a chann to be in an open state. In these experiments, either the solution–membrane–pipett system (Geletyuk *et al.*, 1995) or the solution alone were exposed to 0.1–2 mW of CW 42.25-GHz microwave radiation for 20–30 minutes. In the last case, th conditioned solution was moved to replace an identical unconditioned solution i the system to observe how channel activities changed within a few minutes. Change were the same as in the case of direct system exposure.[32] The changed state of th solution persisted for as long as 20 min. The effect of microwaves on the state ion channels was attributed, at least partially, to changed properties of solution It was speculated that these changes might be due to gas transfer at the surfac of solutions, specifically to a change in dissolved oxygen induced by microwav irradiation.

Indeed, Kazachenko *et al.* (1999) found that microwave radiation at this fr quency, power density around 5 mW/cm^2, and the above time of exposure reduce the concentration of oxygen dissolved in water and weak brines approximately by 1 3 %. The conditioned water acquired a new physicochemical state stable to mechan ical agitation and thermal convection. The new state persisted for over 4 h. Aera tion of the water by bubbling changed the concentration of molecular hydrogen, bu this change decayed within 10–20 min. A frequency dependence of this phenomeno was noted along with the fact that this dependence exists only in the presence impurities (ions). The authors concluded that microwave radiation can affect th macrostructure of water set by impurities.

Fesenko and Gluvstein (1995) used a different physical method to study change in water caused by microwave radiation. They measured how voltage oscillation across a capacitor filled with water decayed after a pulse excitation of the circuit. computer analysis of low-frequency oscillations revealed two pronounced peaks nea 5 and 47 Hz. Exposure of the cell to a 36-GHz field for several minutes suppressed th 47-Hz peak. This state of water persisted for several minutes or hours (dependin on the strength of the exposure field) after the microwave field was shut down. It remarkable that exposure to a 50-μW/cm^2 field had a far more pronounced effec on the system than a hundred times stronger field. The authors discussed stabl water-molecular associates that have a memory of electromagnetic conditioning.

Source

3. THE "CORONAVIRUS" IS CLAIMED TO PRODUCE "ATYPICAL PNEUMONIA" AND SEVERE RESPIRATORY DISTRESS THAT HAS LED TO DEATH.

"It started with a light cough. He burped constantly, and complained of shortness of breath… The doctor said he seemed to have heart problems and suggested him to stay in the hospital. He appeared healthy except for a minor infection in one lung area. Two weeks later, he was dead, with both lungs infected and organ failure. His doctors at the Wuhan Jinyintan Hospital determined the cause of death as "unknown pneumonia." It was days before Chinese health authorities identified the cause of the new viral pneumonia as 2019-nCoV, a coronavirus that first emerged in December in the commercial city of Wuhan, his home city."
Source

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"Coronaviruses are types of viruses that typically affect the respiratory tract of mammals, including humans. They are associated with the common cold, pneumonia, and severe acute respiratory syndrome (SARS) and can also affect the gut."
Source

==========

"The symptoms of corona virus initially mimic the flu—fever, headache, cough, fatigue and muscle aches. The 41 patients admitted to the hospital all developed pneumonia."
Source

==========

4. ALL RADIATION-EMITTING FREQUENCIES — INCLUDING THOSE IN THE RADIO, MICROWAVE AND MILLIMETER RANGE (3G, 4G, and 5G) — CAN CAUSE SEVERE RESPIRATORY DISTRESS.

"In the first study of its kind, scientists strapped magnetic field monitors on pregnant women to determine their level of exposure, and studied whether it was associated with the risk of asthma in their children. They found that children born to women with the highest levels of exposure to electromagnetic fields (EMF) — including from microwaves, hair dryers and power lines — had a more than three-fold higher rate of asthma compared to those whose moms had the lowest exposure."
Source

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"The irradiation inhibited the oxygen consumption rate by the mitochondria… and slowed down the rate of respiration upon exhaustion of the ATP."
Source: *N.P. Zalyubovskaya, Biological Effect of Millimeter Radiowaves, Kiev, Vrachebnoye Delo, in Russian, 1977, No. 3: 116-199.*

5. THE MEDICAL ESTABLISHMENT HAS KNOWN FOR DECADES THAT EXPOSURE TO THEIR SO-CALLED "RADIATION TREATMENTS" CAN LEAD TO PNEUMONIA.

"Radiation pneumonitis is the acute manifestation of ***radiation-induced lung*** **disease**… Symptoms typically include:

- cough
- dyspnea (exertional or at rest)
- low-grade fever
- chest discomfort
- pleuritic pain"

Source

6. EXPOSURE TO MICROWAVES CAN ALSO LEAD TO VARIOUS FORMS OF LUNG DISEASE AND PNEUMONIA. SYMPTOMS OF "*MICROWAVE ILLNESS*" – A CONDITION FIRST DESCRIBED BY THE RUSSIANS IN THE 1970's – INCLUDE ASTHMA, BRONCHITIS, PNEUMONIA, INFLAMED SINUSES, ETC. SEE HERE FOR MORE INFO.

NOTE THE SYMPTOMS PEOPLE ARE EXPERIENCING IN CHINA AND COMPARE THESE WITH THE SYMPTOMS LISTED FOR MICROWAVE ILLNESS BELOW.

Symptoms of the coronavirus include a fever, cough, shortness of breath, and breathing difficulties. However, according to Chinese state media, some are not experiencing any of these symptoms and are instead **experiencing**

nausea, diarrhea, tiredness, bad concentration, headache, irregular heartbeat, chest pain, cornea inflammation, and muscular pains in the limbs, back, and waist.
Source

As the NY Post reported in this April 10th story, nearly half of severe covid-19 cases have also shown neurological symptoms including dizziness, headaches and impaired consciousness. And with the Daily Mail reporting in this April 11th story that another very strange symptom people are reporting has been a sort of *'**fizzing**'* or *'**buzzing**'* or *'**electrical feeling**'* upon or underneath their skin, we couldn't help but noticing that all of those *'symptoms'* are also symptoms of microwave illnesses…
Source

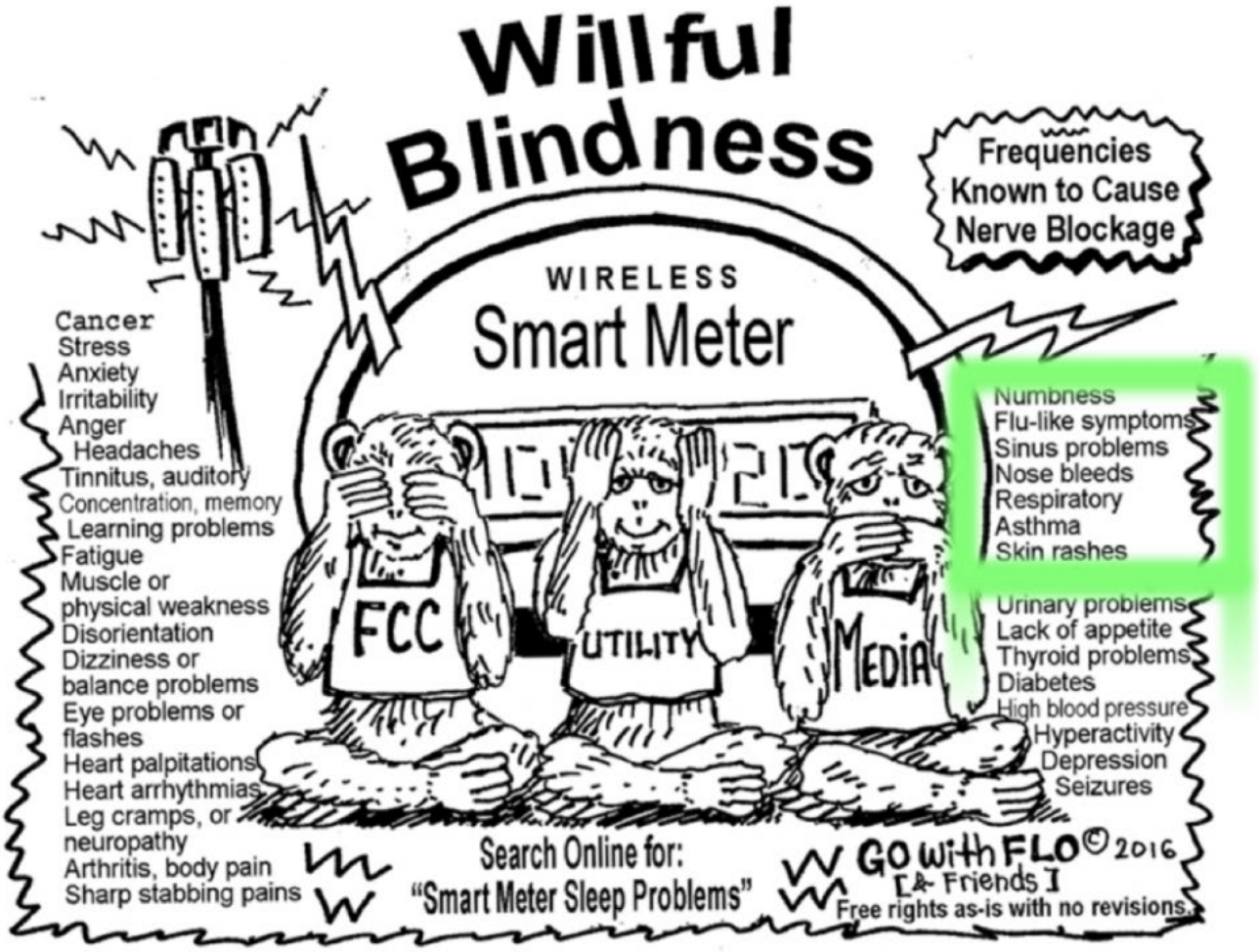
"Fizzing, electric sensations, heart attacks, and a drowning sensation are only a few of the extremely unorthodox manifestations of COVID-19. So much so that it presents less like a virus and more like radiation poisoning…"
Source

Many [doctors] are also reporting bizarre, unsettling cases that don't seem to follow the textbooks they've trained on. They describe patients with startlingly low oxygen – so low that they would normally be unconscious or near death – talking and swiping on their phones. **Asymptomatic pregnant women suddenly in cardiac arrest. Patients who by all conventional measures seem to have mild disease deteriorating within minutes and dying in their homes.**
Source

Symptoms of Microwave Illness

https://www.microwavedvets.com

Headaches	Difficulty Concentrating	Tinnitus
Dizziness	Memory Loss	Hearing Loss
Nausea	Brain Damage	Irregular Sleep Pattern
Skin Rash	Mood Disorder	Insomnia
Itchy Skin	Personality Disorder	Chronic Fatigue
Burning Skin Sensation	Increased Irritability	Deteriorating Vision
Tingling Sensation	Decreasing Trust in People	Pressure in/behind eyes
Tremors	Depression	Eye Damage
Muscle Spasms	Anxiety	Cataracts
Muscle and Joint Pain	ADHD/ADD	Immune Abnormalities
Restless Leg Syndrome	Digestive Issues	Altered Sugar Metabolism
Foot Issues	Abdominal Pain	Asthma Attacks
Low/High Pressure	Enlarged Thyroid	Bronchitis
Facial Flushing	Hair Loss	Pneumonia
Dehydration	Testicular/Ovarian Pain Low	Inflamed Sinuses
Body Metals Redistribution	Sperm Motility	Chest Pain/Pressure
Leukemia	Miscarriage	Heart Arrhythmia
Lymphoma	Electromagnetic Sensitivity	Heart Palpitations



Art Courtesy of Floris Freshman

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7. THE SO-CALLED "FLU" AND MICROWAVE ILLNESS SHARE MANY OF THE SAME SYMPTOMS

"As someone who has experienced symptoms of microwave illness first hand (thanks to the installation of a wireless solar system on my home and the simultaneous placement of an "opt-out" digital smart meter which has since been removed), I can confirm that the above-mentioned symptoms can come on fast and furious and bring a person close to death before a person even realizes what has hit him or her. Within a year of having the solar wifi module and digital "opt-out" smart meter put on our house, one family member developed severe skin rashes, hair loss, chronic mouth ulcers, and twice went into respiratory failure. Another family member suffered from rapid onset memory loss, balance problems, chronic leg and muscle cramps, olfactory changes including loss of taste and smell, and thyroid cancer. I, myself, suffered from "tinnitus," insomnia, abnormal heart function, chronic dizziness and nausea, vision problems, hearing problems, temporary loss of smell and taste, intense headaches, sharp pains and pressure in my head, joint and muscle pain, muscle spasms, feelings of extreme weakness and fatigue that made me feel like I was close to death, and repeated, severe bouts with "the flu."
Source

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In my series on the China epidemic (archive here), I've pointed out that pneumonia—the key indicator of the "coronavirus"—can be caused by many other factors… And Chinese authorities no longer require direct testing for the coronavirus. Instead, CT scans of the chest are employed. If these scans show signs of pneumonia, the "coronavirus epidemic" label is absurdly applied to the patient.

I've also pointed out that, historically, pneumonia has been a major disease in China. Long before "the emergence of the new human coronavirus," people in China have been dying of pneumonia at the rate of about 300,000 a year. Now those people, passing away from the disease in 2020, can be falsely called "deadly epidemic cases." How convenient.

Well, it turns out the US Centers for Disease Control (CDC) has been running its own pneumonia scam for a long time.

Some years ago, when I was writing about the flu, I received emails from Peter Doshi and Martin Maloney. They fed me data from the CDC's own charts detailing flu deaths in the US. And they pointed out the lies. Doshi went on to write an analysis for the journal BMJ Online (December 2005). Here is a key quote from his report:

"[According to CDC statistics], 'influenza and pneumonia' took 62,034 lives in 2001—61,777 of which were attributable to pneumonia and 257 to flu, and in only 18 cases was the flu virus positively identified."

You might want to chew on that sentence for a while.

You see, the CDC has created one overall category that combines both flu and pneumonia deaths. THEY CALL THIS CATEGORY "FLU." Why do they do this? Why do they deceptively assert the pneumonia deaths are complications stemming from the flu? Because they want to sell doctors and the public on the "dangers of the flu."
— Jon Rappoport
Source

8. IN HIS BOOK, "*THE INVISIBLE RAINBOW*", ARTHUR FIRSTENBERG ASSERTS THAT THE FLU IS NOT A VIRAL ILLNESS AT ALL, BUT RATHER AN ELECTRICALLY-INDUCED DISEASE!

The speed at which influenza travels, and its random and simultaneous pattern of spread, has perplexed scientists for centuries, and has been the most compelling reason for some to continue to suspect atmospheric electricity as the cause, despite the known presence of an extensively studied virus. Here is a sampling of opinion, old and modern:

Perhaps no disease has ever been observed to affect so many people in so short a time, as the Influenza, almost a whole city, town, or neighborhood becoming affected in a few days, indeed much sooner than could be supposed to spread from contagion.

Mercatus relates, that when it prevailed in Spain, in 1557, the greatest part of the people were seized in one day.

Dr. Glass says, when it was rife in Exeter, in 1729, two thousand were attacked in one night.
Shadrach Ricketson, M.D. (1808), A Brief History of the Influenza:

"The simple fact is to be recollected that this epidemic effects a whole region in the space of a week; nay, a whole continent as large as North America, together with all the West Indies, in the course of a few weeks, where the inhabitants over such vast extent of country, could not, within so short a lapse of a time, have had the least communication or intercourse whatever. This fact alone is sufficient to put all idea of its being propagated by contagion from one individual to another out of the question.
Alexander Jones, M.D. (1827), Philadelphia Journal of the Medical and Physical Sciences:

"Unlike cholera, it outstrips in its course the speed of human intercourse.
Theophilus Thompson, M.D. (1852), Annals of Influenza or Epidemic Catarrhal Fever in Great Britain from 1510 to 1837:

"Contagion alone is inadequate to explain the sudden outbreak of the disease in widely distant countries at the same time, and the curious way in which it has been known to attack the crews of ships at sea, where communication with infected places or persons was out of the question.
Sir Morrel Mackenzie, M.D. (1893), Fortnightly Review

"Usually influenza travels at the same speed as man but at times it apparently breaks out simultaneously in widely separated parts of the globe.
Jorgeen Birkeland (1949), Microbiology and Man'
Source

WHAT CAUSED THE 1918 "SPANISH INFLUENZA"?

This is not the first time a scare about a viral pandemic has swept the world. We have previously heard predictions — none of which came true — that swine flu, bird flu, SARS, MERS, West Nile virus, Zika virus and Ebola were going to kill millions of people. Notably, all of these scares have occurred after the Internet replaced human contact as the predominant means of communica-tion, and words and pictures on a screen replaced reality. Today, this has gone so far that people are finally willing to shut down the world rather than notice what is going on around them.I do not pretend that there is no basis at all for these predictions. Behind all the hysteria is a fear that the catastrophe that was the "Spanish Influenza" of 1918-1921 will repeat itself. The 1918 flu, after all, sickened one-third of the world's population and killed an estimated fifty million people.

But there are a number of important facts about the 1918 flu that are not widely known:

- The 1918 flu was not caused by a virus.
- The 1918 flu was not contagious and did not spread by direct human-to-human contact.
- The 1918 flu began on U.S. military bases where soldiers were being trained in wireless telegraphy. It spread throughout the world on ten thousand U.S. Navy ships equipped with state-of-the-art wireless stations. It became much more deadly in September 1918 when the first round-the-clock voice radio station powerful enough to be received in most parts of the world went on the air in New Brunswick, New Jersey in service of the U.S. war effort, thereby launching the modern era of radio communication.

Efforts by doctors working for the U.S. Public Health Service to prove the contagious nature of the 1918 flu were heroic and resulted in resounding and repeated failure. In November and December 1918 and in February and March 1919, they attempted to infect one hundred healthy volunteers with influenza in the following ways:

- They put secretions from the mouth, nose, throat and bronchi from hospitalized influenza patients into the nose, throat and eyes of volunteers;
- They injected blood from sick patients into volunteers;
- They filtered mucous material from sick ptients and injected it under the skin of volunteers;
- They had volunteers shake hands with sick patients, talk to them, faces close together, for five minutes, then had the patient breathe out as hard as he could while the volunteer, two inches away, was breathing in, then had the patient cough directly into the face of the volunteer, five times.

None of the volunteers in any of these experiments got sick in any way.Similar attempts to infect healthy horses with secretions from horses sick with influenza resulted in the same resounding failure.

These experiments, and other facts about the 1918 flu, as well as about influenza in general, are thoroughly discussed and documented in chapters 7, 8 and 9 of my book, *The Invisible Rainbow: A History of Electricity and Life* (AGB Press 2017, Chelsea Green 2020).

Historically, influenza was an unpredictable disease that struck without warning and without a schedule and disappeared as suddenly and mysteriously as it had arrived, not to be seen again for years or decades. It did not exist on this earth as an annual disease prior to the worldwide deployment of AC electricity for lights and power

that occurred in 1889. Many of the doctors who were flooded with influenza in 1889 had never seen a case before. But influenza has not been absent anywhere on earth since.

What is most difficult for people to let go of is the notion, so deeply engrained in our society, that a disease is the same as a bacteria or a virus. This way of looking at the world, as a battlefied instead of a community, is wrong. Yes, there is a respiratory virus associated with influenza. No, the virus does not cause the disease. Influenza is a neurological disease that can affect almost every organ, with or without respiratory symptoms. It is caused by electricity.
— Arthur Firstenberg

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9. ALL OF MY RESEARCH ON THE TOPIC OF VIRUSES INDICATES THAT THEY ARE A NATURAL PART OF THE IMMUNE SYSTEM AND ARE NOT HARMFUL! THEY EMIT SOME TYPE OF CHEMICAL OR SOLVENT THAT HELPS TO BREAK DOWN TOXINS, MAKING THE TOXINS EASIER FOR THE BODY TO RELEASE.

Viruses are pieces of DNA or RNA, with a few other proteins…They happen when the cell is poisoned. **They are not the cause of anything**… When your cells get poisoned. They try to purify themselves by excreting debris, which we call viruses…

So, what happened 1918? There was a huge pandemic – and every pandemic in the last 150 years, there was an a quantum leap in the electrification of the Earth, in 1918, late, late fall of 1917, there was the introduction of radio waves around the world.

Whenever you expose any biological system to a new electromagnetic field, you poison it, you kill some and the rest go into a kind of suspended animation, so that interestingly, they live a little bit longer – and sicker.

And then starts in World War Two, with the next pandemic.

With the introduction of radar equipment all over the Earth, blanketing the entire Earth in radar fields, was the first time humans have ever been close to that.

In 1968, there was the Hong Kong Flu and it was the first time the Earth has a protective layer in the Van Allen Belt, which essentially integrates the cosmic fields from the Sun and the Earth from the Moon and Jupiter, etc., integrates that and essentially distributes that to the living beings of the Earth.

And we put satellites emitting radioactive frequencies in the Van Allen Belt. Within six months, we had a viral pandemic. Why viral? Because the people are poisoned. They excrete toxins. They look like viruses. People think it's a flu epidemic…

And I will only finish by pointing out that there has been a dramatic and quantum leap in the last six months with the electrification of the Earth. And I'm sure a lot of you know what that is, it's called: 5G, where there now have 20,000 radiation-emitting satellites, just like the radiation-emitting thing in your pocket and on your wrist and that you use all the time.

That is not compatible with health.

— Thomas Cowan, MD
Source

Source

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“There is highly convincing evidence that your body actually creates these particles [i.e, viruses] as part of a self-cleaning process. So it’s not a virus that attacks you from outside [and then] robs the DNA from your cell and destroys the cell. No. Your body creates these particles…in order to break up damaged cells before they can make the cells next to them ill… So, that which we’ve been told are viruses that make you ill are actually particles which your body creates in order to make you well.”
Source

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“There are very serious questions about whether a variety of viruses have ever been isolated, proven to exist, and proven to be causing disease. An OPEN, lengthy, ongoing, published debate needs to be undertaken among researchers—including independent researchers.”
Source

“There is more to discuss along this line… It involves asking the questions, “How do researchers actually isolate a new virus and identify it?” and, “What are the correct standards for proving a particular germ causes a particular disease?” When you ask those questions and pursue the answers, you find yourself wading hip-deep in a swamp. The garbage floating around you is formidable.” Source
— Jon Rappaport

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Viruses are basically bits of genetic information/material that I think it is fair to say is ALWAYS produced INSIDE our own bodies. They are deployed for all kinds of reasons, genetic information transfer between cells, etc

- Janine Roberts book “Fear of the Invisible”
- very often they are produced in response to stress and micro-waves, chemicals, etc.
- a virus is about a BILLIONTH the size of a normal cell in the body, AND it is not ‘alive’ it has no metabolism of its own to reproduce or do anything.
- this idea of a virus ‘mutating’ is not accurate. They are constantly different because they are being produced by us in response to different challenges and situations.
  — Patrick G.

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Joe Imbriano’s idea that the virus is the clean-up crew of the body. He says blaming the virus is like blaming the rescue crew at a car accident just because they are always to be found there.

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“The Germans were getting ready to announce—and they were on the verge of proving—that viruses have been misdescribed and they are actually electromagnetic in nature… A virus may be better described as an electromagnetic vampire…” Source
— James Lee

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From 1933 to the present day, virologists have been unable to present any experimental study proving that influenza spreads through normal contact between people. All attempts to do so have met with failure.
— Arthur Firstenberg

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Yes, as shocking as it sounds, even the so called AIDS virus is also a big hoax. AIDS is real of course, but it’s not caused by any particular virus. Instead, AIDS is caused by an extremely weakened immune system from

recreational drugs to enhance deviant sex, too many antibiotics and other legal drugs, venereal diseases especially from sodomite/deviant sex with many partners over time, and a poor diet in general. And the drugs to treat people who supposedly are infected with the AIDS virus are also quite deadly, especially chemo drugs like the AZT that they used to use many years ago to treat AIDS.
— JSchmitt

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[There are] thousands of cases of AIDS without HIV in the United States alone. Peter Duesberg found 4,621 cases recorded in the literature, 1,691 of them in this country.
— Scientists Charles Thomas, Karen Mullis, and Phillip Johnson

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There is no virological, nor epidemiological, evidence to back up the HIV/AIDS hypothesis… The virus is biochemically inactive and harmless. [There real causes of AIDS include] AZT, chemotherapy, radiation and radiation treatment, street drugs like popper and MDMA etc., along with antibiotics which break down the immune system and malnutrition and starvation as seen in Africa. 'These are the causes of AIDS and AIDS is not sexually transmitted and HIV doesn't exist.'"
– Dr. Peter Deusberg

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However, for those who have reached the unfortunate yet inevitable conclusion that global crimes and conspiracies not only exist but are in fact one of the major driving factors shaping history, it is dreadfully non-shocking to consider the possibility that there is no HIV or AIDS, and the entire fraud is in reality a global ploy to sell fraudulent drugs, and to hide the true cause of millions of deaths. Source
— Louis James

And here's an astute observation by Jim Stone:

My original assessment right in the beginning was that the Coronavirus was a basically harmless virus that gave people the sniffles. Now that the cruise ship has played out to more than 550 infected with zero deaths it does not seem plausible that any of it was real… Tomorrow, Japan is letting everyone on the cruise ship go. Not a single person died or even got seriously sick. There's a hoax somewhere, a hoax with a motive. Source
— Jim Stone

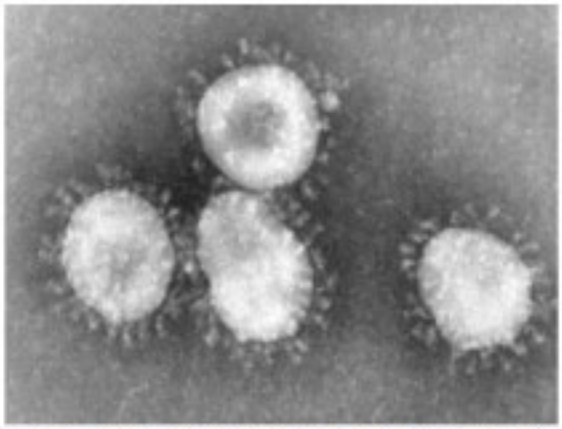
Here's a short video that explains what viruses are and why you cannot catch or spread a virus.

https://www.brighteon.com/7134f098-46f8-4dd2-bf5a-653b251046f1

11. IMAGES OF THIS ALLEGED CORONAVIRUS ARE THE EXACT SAME IMAGES THAT WERE USED TO ILLUSTRATE SARS, MERS AND OTHER ALLEGED "COV" VIRUSES. SO IT APPEARS THERE IS NOTHING NEW HERE AT ALL.

I found the corona virus images claimed to be from electron microscopes and they are identical, actually the same exact images used for the Sars and Mers virus scams of the past. They are the same exact images!!!!!!!!!!!!!!!!
Robert Arnett Otey

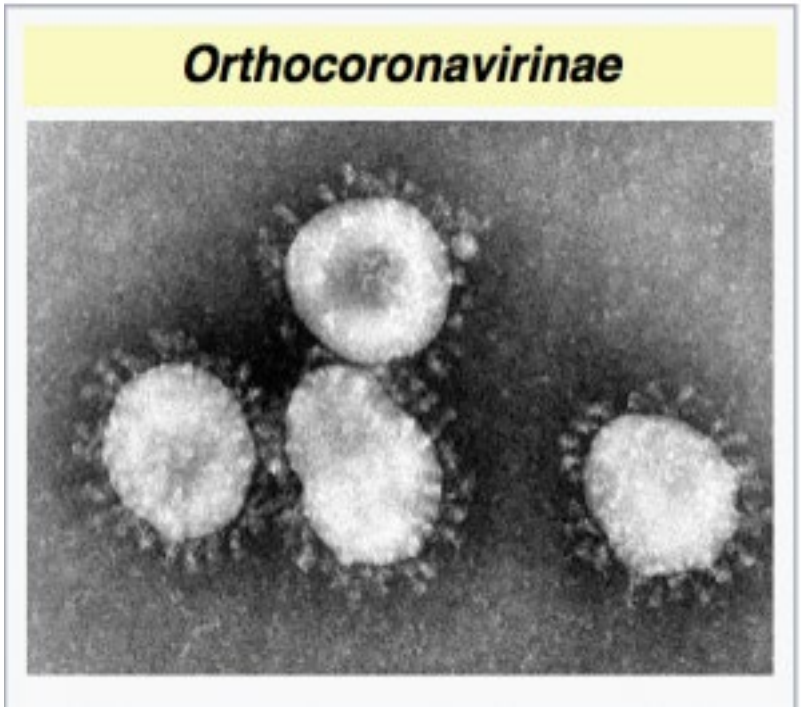
SARS CoV



Coronavirus Electron Micrograph - Image Source: CDC/Dr. Fred Murphy

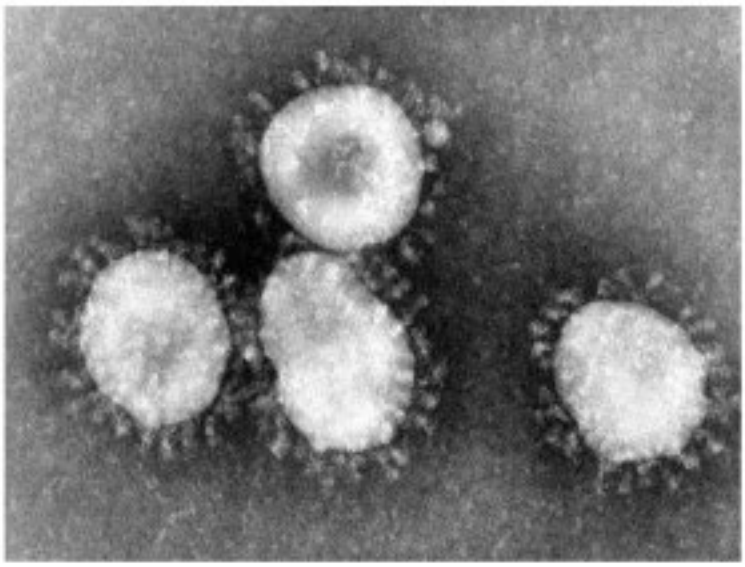
Source: https://www.ncbi.nlm.nih.gov/genomes/SARS/SARS.html

Source: https://newyork.cbslocal.com/2014/05/19/experts-mers-virus-still-poses-low-risk-to-general-public/



Source: https://en.wikipedia.org/wiki/Coronavirus

(Wuhan Virus was Dropped)



Source: https://ufospotlight.wordpress.com/2020/02/13/chinese-intelligence-officer-reveals-true-magnitude-of-chinas-coronavirus-crisis/

https://www.youtube.com/watch?v=S-CkBVqFjh0&feature=youtu.be

11. THIS ENTIRE CORONAVIRUS SCARE IS A SCAM AND THE WIRELESS GRID NOW SURROUNDING US IS PART OF A WELL-DESIGNED WEAPONS SYSTEM WHOSE TRUE PURPOSE IS TO DESTROY US!

"Microwave weapons, by stimulating the peripheral nervous system, can heat up the body, induce epileptic-like seizures, or cause cardiac arrest. Low-frequency radiation affects the electrical activity of the brain and can cause flu-like symptoms and nausea."
Source

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"They're going to kill people…by giving them flu-like symptoms [that will] cause fluid in their lungs and pneumonia… Then it's going to cause the body to begin going into convulsions and then heart palpitations. And then the heart is just going to give out."
Source

13. NOTICE THE SIX-POINTED STAR AT THE CENTER OF THIS WICKED WEAPONRY AND KNOW THAT THIS IS NOT A COINCIDENCE. ISRAEL IS, INDEED, AT THE CENTER OF THE CREATION OF THESE LETHAL TECHNOLOGIES.


Source

13. THIS VIDEO SHOWS US THE SOLUTION. NOTE THAT WHEN THE CELL PHONE CONNECTION IS FINALLY GONE, THE THE PEOPLE FINALLY EXPERIENCE PEACE. NOTE ALSO THE CRUISE SHIP FLOATING ALONG THE SEA (YOU CAN'T MAKE THIS UP!), AND THE FACT THAT THIS COUPLE DOES NOT RETURN TO THE WIRELESS WORLD!

https://www.youtube.com/watch?v=XToHkp3mVZ8&feature=youtu.be&t=109

CONCLUSION

WHAT IS HAPPENING IN WUHAN IS VERY LIKELY A RESPONSE TO RADIATION EXPOSURE. HOWEVER, THE MEDIA AND MEDICAL ESTABLISHMENT WILL LIE ABOUT THIS, CLAIMING THAT THE ILLNESSES ARE DUE TO A VIRUS AND THAT THIS VIRUS CAN BE PREVENTED WITH ONE OF THEIR NEUROTOXIC VACCINES.

DO NOT GET ANY VACCINES!

INSTEAD, GET RID OF ALL WIRELESS DEVICES AND REPLACE THEM WITH WIRED DEVICES, GET RADIATION SHIELDING FOR YOUR HOME, PURCHASE RADIATION SHIELDED CLOTHING, AND DO EVERYTHING YOU CAN TO PROTECT YOURSELF AND YOUR FAMILY FROM EXPOSURE TO WIRELESS AND ULTRASONIC IRRADIATION.

THE MORE PEOPLE THAT BECOME AWARE OF THIS, THE QUICKER WE CAN EXPOSE MEDIA AND MEDICAL ESTABLISHMENT LIES.

The medical establishment continues its ruse, promoting its highly toxic,[i] [ii] extremely dangerous,[iii] [iv] and completely useless,[v] [vi] flu vaccines, yet somehow neglects to mention that the illnesses most people are suffering from have nothing to do with influenza at all, but rather are symptoms of microwave radiation poisoning.[vii]
Source

[i] Gary Null PhD and Richard Gale, **The Toxic Science of Flu Vaccines**, GreenMedInfo.com, Nov 2, 2016. **http://www.greenmedinfo.com/blog/toxic-science-flu-vaccines**

[ii] W. Myers, **Flu Vaccines are Toxic**, MyersDetox.com, **https://myersdetox.com/flu-vaccines-are-toxic/**

[iii] Brian Shilhavy, **Get Your Flu Shot? DOJ Report From Vaccine Court Reveals Flu Shot is Most Dangerous Vaccine in U.S.**, HealthImpactNews.com, Sep 7, 2018. **http://healthimpactnews.com/2018/get-your-flu-shot-doj-report-from-vaccine-court-reveals-flu-shot-is-most-dangerous-vaccine-in-u-s/**

[iv] Paul Fassa, **If You Know Anyone Considering a Flu Shot This Year, Show Them This**, RealFarmacy.com. **https://realfarmacy.com/ditch-flu-shot-instead/**

[v] C. Del Mar and P. Collingnon, **The Flu Vaccine Is Up To 99 Per Cent Ineffective**, LifeHacker.com, Jun 8. 2018. **https://www.lifehacker.com.au/2018/06/the-flu-vaccine-is-99-per-cent-ineffective/**

[vi] Mike Stobbe, **Flu vaccine ineffective for people 65 and older last winter**, DenverPost.com, Jun 21, 2017 **https://www.denverpost.com/2017/06/21/flu-vaccine-elderly-ineffective/**

[vii] Arthur Firstenberg, **Transcript ~ The Hidden Dangers Of Wireless & CellPhone Radiation ~ Audio Interview ~ Part 2**, **https://multerland.files.wordpress.com/2019/01/2-the-hidden-dangers-of-wireless-and-cell-phone-radiation.pdf**. Video: **2/4 ~ The Hidden Dangers of Wireless & Cell Phone Radiation ~ Arthur Firstenberg ~ English subtitles,** Multerland Youtube channel, Feb 3, 2019, **https://youtu.be/yqxQZZM1K7I**

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Update 3/12/20

The people in Wuhan are openly stating this virus is FAKE.

https://youtu.be/Ytr16VQwrhY

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This video reveals how FAKE the numbers are!

https://www.bitchute.com/video/8wxxHr378n2S/

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MUST WATCH VIDEO

https://www.youtube.com/watch?v=zFN5LUaqxOA&feature=emb_title

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Update – 2/3/20

The video below should put the kabash on any talk about this allegedly deadly coronavirus being something new — something that threatens the entire world. An entire charade is now being played out in an attempt for the dark ones to further their satanic control system, including keeping people on lockdown and mandating deadly vaccines. We cannot let them get away with any of it. The time is now to say NO MORE!

"Today, America would be outraged if U.N. troops entered Los Angeles to restore order. Tomorrow they will be grateful! This is especially true if they were told that there were an outside threat from beyond, whether real or promulgated, that threatened our very existence. It is then that all peoples of the world will plead to deliver them from this evil. The one thing every man fears is the unknown. When presented with this scenario, individual rights will be willingly relinquished for the guarantee of their well-being granted to them by the World Government." *— Dr. Henry Kissinger, Evians, France, 1991*

Post Views: 165,466
Posted in: 5G, China, Coronavirus, Microwave Sickness, Radiation Sickness Filed under: 5G, China, Coronavirus, Microwave Illness, Radiation Sickness

Post navigation

← Radiation in Cars: A Public Health Threat
Is Your Smart Phone Stealing Your Memory? →

145 thoughts on "Is The "Coronavirus" Actually Radiation Sickness?"

1.  **elandra meredith** says:

   January 31, 2020 at 6:00 am

   brilliant, OMG, thank you! sharing asap!!!

   Reply

   1.  **Davide** says:

      April 2, 2020 at 9:49 am

      No its not
      Shut the fuck up and respect hygiene rules or all lf our parents and grands will fucking die.

      Reply

      1.  **admin** says:

         April 2, 2020 at 6:21 pm

Davide – either you choose to speak respectively to the people commenting here or I will block you. Your parents and grands are going to die from RADIATION SICKNESS. Masks and gloves are not going to help you, but go ahead and wear them. Tell your parents and grandparents to do the same. But if they have iphones, wifi, bluetooth devices, smart meters, etc., the masks and gloves are not going to help.

Reply

1. **Patrick Rohrbach** says:

   October 29, 2020 at 4:20 am

   Well said

   Reply

2. **melcee** says:

   April 7, 2020 at 8:16 am

   Agreed, Davide.

   Reply

3. **Ted** says:

   June 16, 2020 at 12:33 pm

   YOU poor misguided individual.

   Reply

4. **Ted** says:

   June 16, 2020 at 12:42 pm

   Check out this
   http://stateofthenation.co/?p=12846

   Plus the all the additional EMFs being used points to humanity being microwaved to death.

   Reply

5. **truthwise** says:

   July 24, 2020 at 4:31 am

   Bah Bah little lost lamb now back you go in line with the rest of the sheep led to slaughter.

   Reply

2.  **Elite destroyer** says:

   June 9, 2020 at 2:00 pm

   I find only this article that done some research in a profound manner.
   But I only want you to take a factor in consideration that
   "it's never one disease and one cause"(by Jon rappoport sir)

   To say that 5g is causing all the things, than I might take a step back.
   But I think that 5g play a very prominent role in what is going on.
   Like in New York doctors say that they are seeing things that they never seen before, (patients lungs are fine, but they are deprived of oxygen. They got protocols to treat it like ARDS but it's not like ARDS)

   AND here in my country (India)
   Doctors are saying that it's like a normal flu. Some are also saying that you can treat yourself by staying at home. Patients who recover also say not to fear, it's like a normal flu.

   Why there is difference between this county? Is the virus is county biased?

   And then I got a clue that it might be 5g what is causing this. Then I start my research over this topic. I find this article

   http://www.holistiq.com/covid-19-hypoxia/
   (which was removed where it was originally published)

   That article also say what those doctors are saying in New York. But in that article it says that a VIRUS is causing all the stuff
   (toxicity by hemoglobin) but I don't believe that viruses exists as the way doctors say, they infect play a supportive role in our body.
   And in my mind another clu popup. That 60 GHz can split the property of oxygen molecules. But I haven't find any relation between 60 ghz, oxygen and hemoglobin.

   And also the fact that 60ghz is not used in 5g towers which are in New York (and here my research got a major stone)

   But I will continue to look on this topic. You are doing good work.

   Than you.

   Reply

   1.  **admin** says:

      June 9, 2020 at 2:36 pm

      Elite Destroyer – I do not believe there is any deadly virus either. I do not believe viruses cause disease. This is a medical lie that has been perpetuated for about 100 years and needs to be exposed.

      I also do not think 5G is causing any virus, but rather is causing symptoms of radiation sickness. 3G, 4G, and 5G — all G's — cause symptoms of radiation sickness. Chronic exposure to any "G" will lead to sickness and ultimately death.

So 5G is not THE problem. It is a MAJOR problem. But it is not the only problem. All of this radiation is the problem.

Reply

1.  **Elite destroyer** says:

   June 9, 2020 at 4:09 pm

   Yes I agree with your view on viruses. But my main question is why there is a difference between covid patients in places like New York or Italy and in India. Why virus act differently on different countries.

   There's something suspicious about this. What make this difference?

   Reply

   1.  **admin** says:

      June 11, 2020 at 8:33 pm

      There is no deadly virus and I am not at all sure why you think something that does not exist can act differently in different places. People are sick from radiation exposure. Radiation affects people differently so there are a variety of symptoms that are being expressed. And the denser the radiation exposure, obviously the more sickness we are going to see.

   2.  **Colette** says:

      August 25, 2020 at 3:57 pm

      It depends on the lifestyles of the populace. Those being foods, pollutions in their country, and level of health and wellness. China a heavily industrial country, lots of pollution, has lots of toxic waste already in their bodies. Italy lots of older populace, having usual aging problems. So you can see where this would change from country to country.

   3.  **admin** says:

      August 26, 2020 at 9:18 pm

      Both places – China and Italy – were heavily saturated with 5G at the time of the "outbreak." See the posts on this website regarding studies done on this issue.

2.  **Dennis** says:

   October 12, 2020 at 3:41 am

Virus “theory” has never been proven to cause anyone to have ever gotten sick from exposure. It is not a “germ” by definition, but has been portrayed as such by the medical establishment led pharma-based smearings.

Virus’s are lumped into the germ camp along with mold, fungus, bacteria, and “germs” but while you can “kill” mold, fungus, bacteria, and “germs” it is in fact impossible to kill something which is not alive in the first place!

A virus is comprised of small amounts of either DNA, or RNA wrapped with one or more proteins. It has no way to to exhibit any form of life with only those components, nor can it “live” on hard surfaces longer than it can on soft surfaces as the Covid virus has been bandied about by the powers that be.

I believe through my research that what is called a virus which are expelled by cells when they are toxic and in need of cleansing, are shed out of the body removing toxins and potentially damaged RNA/DNA which happens when the body is toxic and run down. We don’t “catch” a virus, we shed them. If you were to have ingested a virus that was shed from somebody else it would get expelled through normal channels without harm to you. However if it were introduced into the body through a show like a “flu” shot than you are starting to play Russian Roulette!

Now as far as wireless signals go it is a known fact through live blood microscopy that the red blood cells will start clumping up and start stacking (rouleau effect) when they are exposed to radio waves like cell phone usage. Red blood cells are responsible for the delivery of oxygen throughout the body, and when hit with frequencies that cause them to stack up on each other there is little room to carry oxygen so blood oxygen levels will drop no matter how much you are pumping into the lungs.

There are pictures of this effect of cell phone usage on the blood on the internet. 5G will effect the blood more efficiently than what we are used to with the 3G and 4G. If you think back to where the Covid outbreaks were the most prolific starting at the beginning of 2020 it hit 3 places the hardest . . . Wuhan, Italy, the cruise ship and than New York. All had 5G and people that were the oldest and had the most issues did the worst especially when being forced onto ventilators. However did anyone notice that none of the people on the cruise ship died?

Interestingly enough, in seeing some video clips of people falling over from lack of oxygen in China and hearing what the doctors were saying about how it appeared that their patients were showing symptoms of high altitude sickness, and then people actually doing worse when forcing oxygen into their lungs makes perfect sense that their blood was not capable of transferring CO2 to oxygen from the lungs with the red blood cells all clumped up.

Now the good news! You can help un-clump your blood cells by grounding . . . walking barefoot on grass, or oceanside, or lakeside, or the best is to do PEMF which can in fact re-energize your cells which are ultimately little batteries.

Reply

1.  **admin** says:

   October 13, 2020 at 1:00 am

Excellent commentary! Thank you very much.

2. **zdb** says:

   November 14, 2020 at 10:14 pm

   like button

2. **Scott** says:

   July 4, 2020 at 5:24 pm

   I very much believe that 5g is a major part, if not all of the problem. The question I have, that has been with me all night since reading this is: why are more Doctors and Nurses not getting sick? I have heard that the hospitals have 5g, and yet you would think it would be a major place where people are getting sick.

   Reply

   1. **admin** says:

      July 5, 2020 at 5:37 pm

      Hi Scott – I'm not sure hospitals have 5G. But it is no matter. Doctors and nurses probably have various symptoms of radiation sickness (such as headaches, insomnia, tinnitus, heart palpitations, etc.), but have not yet made the connection between their symptoms and the radiation they are being exposed to. I've no doubt that within the next five years, many, many people are going to become ill. Some will realize what is causing their illness. Some will not. But for sure, it is the radiation that is going to take people (along with their children and their pets) down. I have no seen one single butterfly this entire season. Precious few bees. Plants are not doing that well either. The radiation is destined to hurt many living things. 5G is not required for this destruction. What we are currently being exposed to is more than enough to destroy many lives. It already has.

      Reply

      1. **ROGER REINER** says:

         September 7, 2020 at 9:48 pm

         Let's also not forget nature's part in all this. I read that the Sun's 11 year cycle peaked in late 2019 and that natural EMF is then combined with the toxic electro-smog that we are creating. This natural EMF then begins to dissipate but that can either happen quickly or over several years before it starts to again build up for it's next cycle. If the combination of all this is then exposed to various people then those people are more likely to develop the symptoms that can eventually make them sick or even die from over-exposure. At the same time there are indications that tens of thousands of more satellites have been approved and will be launched in the not-to-distant

future, thus creating additional “straws to break the camel’s backs”, with more outbreaks, more sicknesses, more deaths, etc.

The vaccine hoax will then follow for several reasons, including the fact that it is going to be a real money-maker for those who manufacture, promote, produce, and administer it, but there are scary possibilities that go along with it. For one, the advance notice to people that it will alter their DNA and/or RNA and that side-effects may include death, and also that technology now exists to include nanobots or microscopic computers within the injection which can then allow global snooping of every individual as well as possible mind-control, etc. We live in a brave new world so just like in past times when everyone said “buyer beware”, now it has to be something like “user-beware” and that includes devices as well as things we put or allow to be put into our bodies.

With the present technological revolution that develops solutions daily for problems of all kinds, it is not unthinkable that we could also develop much safer means of things like 5G, but until the masses demand such, this will simply go forward. Whether or not the resulting damage to life is intentional or not, it remains that it will begin to sterilize the planet in short order. Insects good and bad are nearly gone already. We were prompted to plant gardens this year but basically to no avail as they did not do well. Weather patterns have changed as well where nearly every time it rained all summer long, it included hail and high winds.

They speak of global warming but fail to speak of contributing factors other than greenhouse gases. Carbon dioxide is essential for plant growth but they are trying to eliminate it. Volcanoes produce more CO2 in a few hours than people do in a year, yet the eventual result is lush and green ground better than all the fertilizers people have ever produced. It is interesting that super-hurricanes have hit the Philippine Islands several times in the past few years, but there are never any correlations made as to attempts to control weather. Conspiracy theories are only theories as long as the truth is unknown. After we finally learn the truth, we then must act accordingly if possible, if not for ourselves, then for future generations. If not now, then when? If not us, then who? Far too many people are sheeple, and afraid to speak out about things, or are so addicted to their tiny machines that they cannot remove the hoodwinks from their lives.

2.  **admin** says:

   September 11, 2020 at 1:13 am

   Spot-on Roger, and extremely well said Thank you for sharing.

3.  **zdb** says:

   November 14, 2020 at 10:13 pm

   This site is not available
   http://www.holistiq.com/covid-19-hypoxia/

   Reply

3. **Stacy Stark** says:

   August 7, 2020 at 3:09 pm

   Conspiracy Theories are dangerous for many reasons.
   Amoung other things, they provide a way to reduce mental distress by changing our perception on a problem without actually doing anything to solve the problem.
   They are the mental equivalent of a pacifier.

   Reply

   1.  **admin** says:

      August 10, 2020 at 1:15 am

      Stacy – your refusal to look at all the facts and evidence presented in this article, combined with your obvious cognitive dissonance, also act as a pacifier. You can remain in denial until the end of your life if you like, but if you believe the obvious lies of the lamestream media about a non-existent virus, and you pretend that the radiation all around us is not a threat, then it is likely you will not live long. Please wake up.

      Reply

   2. **zac** says:

      August 22, 2020 at 7:27 pm

      One who ignores the facts about a conspiracy is known as a Conspiracy Ignore-ramus

      Reply

2. Pingback: Aktuelle patriotische Umschau – Januar 2020 – Deutsches Herz
3.  **Jean Hudon** says:

   February 1, 2020 at 2:57 am

   Thanks for your effort and time with compiling all this material. However, you have neglected to verify a key aspect that is central to our main concerns about 5G. The question you and everyone should ask before contriving all kinds of theories is : Which part of the radiowave spectrum is China's 5G operating on? If they can make it work properly*, the real 5G based on millimeter waves, the really dangerous one, is expected to have major detrimental effects on the skin and eyes and much much more, according to various experts as you can read at https://mdsafetech.org/5g-telecommunications-science/ – if you want to have a thorough understanding of the multiple health impacts millimeter waves can have. Here is a telling excerpt:

   "An older Russian paper, "Biological Effects of Millimeter Wavelengths" by Zalyubovskaya (1977) was declassified by the CIA in 2012. This paper disturbingly describes the research on both humans and animals showing a myriad of adverse effects of millimeter wavelengths. The author notes that millimeter wave technology had been used for years without any studies on biological effects. The researchers found that "millimeter waves caused changes in the body manifested in structural alterations in the skin and internal organs, qualitative and quantitative changes in the blood and bone marrow composition, and changes in the conditioned reflex activity, tissue respiration…and nuclear metabolism. The degree of

unfavorable effect of millimeter waves depended the duration of radiation and individual characteristics of the organism." The author confirmed that millimeter waves do not penetrate skin but act on nerve receptors in the skin to cause such diverse biological and metabolic effects as a reduction in hemoglobin and erythrocytes, higher blood cortisol levels, adrenal stimulation, mitochondrial dysfunction, and suppression of the central nervous system with notable changes in liver, kidneys, heart and brain. The declassified paper is Biological Effects of Millimeter Wavelengths. Zalyubovskaya-Declassified by CIA -1977."

You should know that the real 5G millimeter waves start at 24 gigahertz – 24 billions of hertz. So as you can verify at https://www.rcrwireless.com/20190603/5g/5g-spectrum-allocations-china, China is only using now the mid-band frequencies for their current false 5G system. These frequencies are all in the same range of existing WiFi routers — emitting either on 2400 megahertz (MHz – millions of hertz) or on 5000 MHz.

Nearly the entire Earth's population has already been exposed to these frequencies at close range for the past 10 years in their houses, schools, work places, hospitals, restaurants, etc. and no such virus has emerged. You can check at https://bit.ly/2UgffbO the VERY high level of pervasive WiFi radiation people are exposed to in the US. Check at https://bit.ly/37OpckC for the WiFi exposure in Europe. The false 5G exposure of people in China is therefore nothing new and it could mean that your theory is bogus. Yet what is new with the 5G networks is the high proximity of antennas relative to where people live. As in North Korea (see below) to try to provide higher download speed, the number of antennas necessary for the new false 5G networks to work means that in the end there will be on average 30 times more antennas, located at very close range from people, than with all the 4G and 3G antennas combined.

According to the following article "South Korean minister dismisses 5G health and environmental concerns" at https://bit.ly/2S6otVv (which is full of lies!), it is mentioned (and this looks plausible to me) : "In China, for example, 5G base stations have a radiation standard of fewer than 40 microwatts (μW) per square centimetre." (end of quote). Since no one understands what "40 microwatts (μW) per square centimetre" means in term of exposure level, you have to convert this in term of microwatts per square METER which is what we are using as a reference in North America. Using the conversion table at http://cqlpe.ca/pdf/ConversionTable.pdf, we see that it means people (at what distance from the antennas ? … we don't know…) can be exposed to 400,000 microwatts/m2 of radiation. This is outrageously high and dangerous!

According the Resolution 1815 adopted by the EU Parliamentary Assembly in 2011 (see at https://bit.ly/2RMjxGk), people, in indoor settings, should not be exposed to a level higher than 0.6 volts per metre and, ideally, to no more than 0.2 volts per metre. Once converted (using the calculator at https://www.powerwatch.org.uk/science/unitconversion.asp), this means no one should be exposed to more than 1000 microwatts/m2 (rounding 954 to 1000) and, ideally, to 100 microwatts/m2 (rounding 106 to 100). This determination was based on the best independent scientific studies in 2011, not on industry-commissioned bogus studies. Dig this! People should – ideally – not be chronically exposed to levels of EMF radiation beyond 100 microwatts/m2… In China, the WiFi-like frequencies of their false 5G is exposing a significant portion of the population to what allegedly is 400,000 microwatts/m2 of radiation… And this extreme level of exposure comes on top of the very high exposure levels from all existing 3G and 4G antennas. Such a toxic electrosmog, which is only increasing everywhere around the world, is the real genotoxic, neurotoxic and carcinogenic trigger and catalyzer for all kinds of physical and mental ailments, severely impacting billions of people right now. Could it be involved in opening the pandora box of a new plague? Perhaps. But one thing sure, it does not help anyone. And it is high time everyone starts focussing on this actual threat rather than concocting all kinds of speculative theories.

* So far in South Korea where they have a limited offering of real 5G — using the 28 GHz spectrum – see https://bit.ly/2OjdS8F — it has a dismal record in terms of stability and reliability as one can read in "South Koreans complain at poor quality of 5G network" at https://www.ft.com/content/1ff639a4-a85a-11e9-984c-fac8325aaa04

Excerpt: The world's first and largest 5G mobile network has come under fire from customers for poor quality, slow connections and lack of applications that use the new standard. (…) There are 14 times as

many South Koreans using 5G as there are Americans, because of aggressive marketing by telecoms operators and generous subsidies. But consumers are now complaining that the promise of internet speeds up to 100 times faster than 4G has so far not been met. Users said they often have weak signal and poor connections instead. (…) Analysts explained that so far there are not enough base stations for nationwide coverage. (…) Telecom operators are scurrying to improve service quality, by building more base stations and developing new content. They have built about 63,000 5G base stations across the country, which is only 7 per cent of the number of 4G stations, according to government data.

Reply

1.  **admin** says:

   February 2, 2020 at 12:37 am

   In response to your questions/comments, it appears that China is using frequencies between 24.25 – 27.5 GHz and 37 – 43.5 GHz (see here: https://www.rfwireless-world.com/Tutorials/5G-frequency-bands.html). In order to make 5G work, they also have to use "midband" frequencies and it appears that China is using 3300-4990 MHz. So 5G involves using multiple frequency ranges that are pulsed and modulated, creating a massive biological assault against all living things.

   And no doubt the 5G system is completely inefficient in terms of as a communications system. That's because it is designed to be a weapons system, and in terms of its ability to inflict lethal damage on all living things, it is quite effective.

   Humanity and all life forms are currently being exposed primarily to the 2.4GHz frequency, which is also pulsed (through cell phones, cordless phones, baby monitors, smart meters, smart TVs, etc), and incredibly biologically damaging. Still, this is far less damaging than being surrounded by 5G technology, which will expose us to SEVERAL DIFFERENT FREQUENCY RANGES ALL AT THE SAME TIME.

   Are you aware that each 5G small cell contains **1024 antennas** (according to Brendan Carr at the FCC), and that these antennas operate in "phased arrays" — each directing laser-like energy into people's homes and at their devices. Imagine having one of these noxious small cells outside your bedroom window, blasting multiple pulsed, microwave frequencies directly at you and your family 24/7. That is what is happening to people in China (and also part of the US), and there is no way people are going to walk away from this unscathed.

   Reply

   1.  **Jean Hudon** says:

      February 3, 2020 at 11:29 pm

      Thanks for your comment. I'm perfectly aware of how the 5G small "death boxes" are designed: 512 emitting antennas and 512 receiving antennas. Their MIMO phased arrays are also directed from multiple sources (multiple antennas) towards a single 5G device to try to provide a stable signal. The total effect can be lethal. But I've not seen any scientific indication that such high levels of exposure can cause the emergence of new viruses. It is true that most people with severe reactions (and sometimes a deadly pneumonia) to this new virus are older people with a compromised health – which can be aggravated by EMF exposure. But surmising that 5G is causing this plague is pure speculation. In fact theories like yours are a distraction from the real threats and damaging effects of ever growing EMF exposure. That the message I'm trying to convey. To get solid references, check what I've

been chronicling for years at http://www.cqlpe.ca/Developpements2019.htm – http://www.cqlpe.ca/Developpements2018.htm – http://www.cqlpe.ca/Developpements2017.htm etc.

Reply

1.  **admin** says:

   February 4, 2020 at 12:00 am

   Just to be clear – I did not say 5G is causing any plague or virus. Viruses, as far as I know, may not even exist in the way we have been told and may, in fact, be a normal part of human biology and not harmful at all. 5G, on the other hand, is extremely harmful and potentially deadly. And one of the many effects of this radiation and these frequencies involves severe respiratory distress, which can effect people of all ages, including small children who have asthma.

   So that is the point of my article. We need to be much more concerned about 5G (and 3G and 4G and all forms of noxious, non-ionizing radiation) than any so-called "virus."

   Reply

   1.  **Jean HudoN** says:

      February 13, 2020 at 10:05 am

      "We need to be much more concerned about 5G (and 3G and 4G and all forms of noxious, non-ionizing radiation) than any so-called "virus."

      I completely agree with you in this! BTW Switzerland is leading the way,,,

      Switzerland halts rollout of 5G over health concerns (Feb 12, 2020) https://www.ft.com/content/848c5b44-4d7a-11ea-95a0-43d18ec715f5

   2.  **admin** says:

      February 13, 2020 at 5:41 pm

      It looks like the info about Switzerland halting 5G was fake news. See here: https://www.takebackyourpower.net/switzerland-environmental-agency-restricts-5g-calls-for-studies/

2.  **Liz** says:

   February 16, 2020 at 2:07 pm

   Thanks for the information. So do you think this new thing is a combination of 5G plus a virus or bioweapon release?

   Reply

1.  **admin** says:

   February 17, 2020 at 5:25 pm

   Liz – I don't think there's any "virus." I think people are experiencing symptoms of radiation poisoning and it is "spreading" – not because of contagion but because of the radiation density that now plagues parts of China. This video speaks volumes about this:
   https://www.youtube.com/watch?v=eja3g2wpbV0

2.  **John Ferreira** says:

   March 16, 2020 at 1:28 pm

   I don't necessarily agree that this virus is not causing people problems. The virus is either a red herring or it is only now a danger, likely triggered by the sudden saturation of small cells in close proximity to people. However, the writing has been on the wall since the introduction of wireless devices in everyone's home, workplace, school, restaurant/cafe, store, and pocket/bra, long before 5G. In my opinion, if the virus is a problem, it would likely not be a threat to most if people's immune systems had not been compromised over the last 10-20 years by radiation-emitting devices. As per Olle Johansson's 2008 publication called "Disturbance of the immune system by electromagnetic fields" (https://iddd.de/umtsno/odpsejm/artJohanssonaEN.pdf):

   "Is biology compatible with the ever-increasing levels of electromagnetic fields (EMFs)? Or, to put it in more layman's terms: Can we, as human beings, survive all the radiation? Are we built for a 24-h, whole-body irradiation life? Are we immune to these signals, or are we actually playing with our planet's future, putting life at stake? The answers appear to be: No, we are not designed for such EMF exposure loads. We are not immune. We are gambling with our future."

   There are plenty of independent scientific publications concluding that there are adverse effects to the immune system. Most of us are likely walking around with weakened immune systems and all it takes is a trigger to take us down.

   But there are scientific publications that also discuss microbe activation from EMF radiation. Here are examples:

   https://www.nature.com/articles/s41598-019-51046-7
   https://www.ncbi.nlm.nih.gov/pubmed/28956351

   However, and interestingly, shielding from EMF radiation can improve autoimmune disease. Does shielding somehow let the immune system clean up or is there another pathway?

   https://www.shieldyourbody.com/2018/04/emf-autoimmune-disease/

   This is just a small sample of publications. But corrupt, greedy, and ignorant telecom, politicians, bureaucrats, health-professionals, and the media

continue to pipe their horns that this is all fake news and they know what they're doing and what's best for us. Meanwhile, we're all being locked up because of their mistakes. Remember that these "experts" were also the clowns who approved Thalidomide, tobacco, DDT, asbestos, etc. Remember all the doctors who appeared in ads promoting how great cigarettes were decades ago? Ya, they know what they're doing.

3.  **admin** says:

   March 16, 2020 at 4:05 pm

   John – that was a brilliant comment. Thank you for all the information. You have clearly understood the nature of the EMF problem, and 5G is NOT the only issue. What we are currently surrounded by is extremely dangerous and you are right. We are gambling with our future — our very survival. Thanks for the links too. I will be checking them out.

   BTW – I don't think there is any "virus" causing illnesses. This situation has taken me deep into the literature about viruses and they are not something that makes people sick. They are like the clean-up crew when the cells become poisoned. The body then creates viruses to help detox the cells. We cannot "catch" or "spread" viruses. This is complete and utter bullshit. Alien viruses can only enter our bodies through injection. Do not get any vaccines.

4.  **Corey** says:

   April 8, 2020 at 2:22 am

   Hello Admin,

   I believe in these facts or otherwise I would just be on 99.9 % of other cover up/sheep websites. So thank you for all you do and this website. One thing I am still not sure why 14 people who all work together just tested positive simultaneously at a Psychiatric . They have wifi which I know is not good either and they have had it for a while. No 5G towers in my state yet. I realize this is not contagious, so I am wondering about these tests, why would 14 people all at the same time test positive? What are COVID-19 looking for in their tests to determine this. Strange that 14 of them would test positive all at the same time if not contagious. Thank you.

5.  **admin** says:

   April 8, 2020 at 2:42 am

   Corey – our bodies create viruses when our cells become toxic. The viruses are designed to help the body detox and heal. They are a natural part of our immune system. Since most of us are exposed to technologically produced radiation, most of us are likely to have cells that are being poisoned from the radiation. Therefore, our bodies will have viruses in order to help us heal. Additionally, the test for the alleged COVID 19 virus does exist. The test they are using does not actually test for the virus! Check out Jon Rappoport's work (his site is NoMoreFakeNews.com) for more about this. Also watch this

great video. It explains everything: https://www.brighteon.com/1bbbce8e-acbf-4358-a9ce-397ceaf9ba42. I hope this helps.

3. **sim8t3** says:

   June 22, 2020 at 9:54 am

   I feel I need to interject here and inject this piece of vital information that will explain why every leap in technology as also been accompanied by viral "pandemics" or is this case "plandemics" I can't find the site I read it, this comes closest https://www.reddit.com/r/Jesuitworldorder/comments/fpgl2z/coronavirus_spanish_flu_influenza_marconi_tesla

   Reply

2. **Violet** says:

   February 6, 2020 at 6:02 pm

   3300 – 4990 MHz is actually known as sub GHz, and it is urban radar.

   They are rolling out a weapons system on top of us it is bloody terrifying. It is the same technology that cooked your eyes like eggs in world war 2!!!

   Reply

   1.  **admin** says:

      February 6, 2020 at 6:25 pm

      Violet – do you have a link for that info? I'd love to add it to my book. Tx.

      Reply

      1. **Violet** says:

         February 6, 2020 at 7:00 pm

         Admin, I heard about this info on a video called 5G apocalypse the extinction event, it was from a scientist from Gateshead in the UK called Mark Steele, if you haven't seen it yet I would highly recommend it.

      2.  **admin** says:

         February 6, 2020 at 7:09 pm

         OK. Tx Violet. I have seen it. I will have to look at it again.

3. **Violet** says:

   February 6, 2020 at 7:17 pm

   https://youtu.be/d7z8yGGKhU4

   Hope this helps.

4. **zdb** says:

   November 13, 2020 at 11:40 pm

   Violet or anyone. Any information on Mark Steele's background? The little I can find about him indicates him as an English bouncer (doorman) who had a weapons incident years ago at a bar. Beyond that I found nothing of any kind that indicates a CV or resume of any kind. All I have ever heard him state is that he has a weapons background and lots of knowledge. Is he some kind of limited hangout or counter intelligence smoke screen? Thank you

5.  **admin** says:

   November 14, 2020 at 2:30 am

   I don't know about Mark's background either. Annie Logical had written some not good things about him but it looks like her site was taken offline.

6. **zdb** says:

   November 13, 2020 at 11:42 pm

   btw, that is not to say that Steele's statements have not been accurate. He reminds me of Robert David Steele who also has many surprising and accurate statements and then runs down many wild pointless rabbit holes to blackwash most of the truths he highlights.

7. **zdb** says:

   November 14, 2020 at 10:25 pm

   Admin, that makes me more suspicious. How is it that Mark is so much less censored considering the hard sell he is making against 5G while so many others with less to say get censored so much harder. I wonder about Deborah Taveres that way too. Considering the speed and efficiency of what gets censored today, it's stranger and stranger what does not get censored.

8.  **admin** says:

   November 14, 2020 at 10:49 pm

I have similar suspicions about these people.

3. **Carolyn** says:

   April 16, 2020 at 7:48 pm

   Not to mention it is being transmitted via satellite. Both the Us Navy and the Princess cruise lines are vessels receiving these satellite transmissions. I think everybody by now has heard of the “corona outbreak” on these ships.

   Reply

   1.  **admin** says:

      April 16, 2020 at 7:50 pm

      Indeed. Thank you for bringing up this most important point!

      Reply

   2. **zdb** says:

      November 13, 2020 at 11:43 pm

      Also there have been many suspicious accidents in the last few years where entire ships crews seem to have gone to sleep while the ships went on autopilot into ridiculously stupid and dangerous paths.

      Reply

2. **Thea** says:

   February 7, 2020 at 7:53 pm

   im sorry but they use low bands (already pathogenics , “emitting either on 2400 megahertz (MHz – millions of hertz) or on 5000 MHz. ” that already dreadful to living organisms

   Millimeter waves : quote :”You should know that the real 5G millimeter waves start at 24 gigahertz – 24 billions of hertz. So as you can verify at https://www.rcrwireless.com/20190603/5g/5g-spectrum-allocations-china, China is only using now the mid-band frequencies for their current FALSE 5G system.

   That was in 2018 and were Trials

   then we find that now it different bands , were added to the ‘low’ bands that you say are ‘ not dangerous’ for years, but its because u know nothing about radiation poisoning from 2, 4 GHz wifi that is everywhere.

   now: CHINA ;https://www.rfwireless-world.com/Tutorials/5G-frequency-bands.html?fbclid=IwAR1q2Ni_zhU8gDWyX_CfpCix5yHCbeNXGn6uN5SAyaT7OSfdpm3ggdz61IA

Higher 5G Frequency Bands in mmwave

The table-2 below lists countrywise 5G frequency band allocations across the world. These are higher 5G millimeter wave bands used above 6 GHz.

Country 5G Frequency Bands
USA 27.5 – 28.35 GHz , 37 – 40 GHz
Korea 26.5 – 29.5 GHz
Japan 27.5 – 28.28 GHz
China 24.25 – 27.5 GHz, 37 – 43.5 GHz
Sweden 26.5 – 27.5 GHz
EU 24.25 – 27.5 GHz

Reply

1.  **admin** says:

   February 7, 2020 at 10:26 pm

   Thanks for this intelligent and informative reply Thea. It is clear that Jean Hudon was just being a bit pissy about all of this. But you are absolutely right. The 2.4 GHz frequency now being used in most of our wireless devices is the very same frequency used in microwave ovens to cook things. This is because it MAXIMIZES THE ABSORPTION OF RADIATION IN MAMMALIAN TISSUE. So we and our children are literally being cooked by this radiation and, in fact, this has been the plan all along. The 2.4 GHz frequency is well-known to be one of the most destructive frequencies in the entire spectrum. Yet the FCC has seen fit to allow this particular frequency to be used freely and without licensing, ensuring that our entire society will be SATURATED with this particular frequency.

   The agenda behind all of this is 100% evil and people are seriously in denial of what is happening. It is probably too late for most bloodlines. The children will not be able to reproduce, and if they can, there is a very high likelihood that THEIR children will be genetically defective.

   What we are currently being exposed to has already done serious and irreversible damage. This is a great, short video explaining some of the harm: https://www.youtube.com/watch?v=ojZIYfb72ME&feature=emb_title. 5G will simply speed up the amount of time it takes for people to become seriously ill and die. Of course, they are now trying to distract everyone from the real issue by getting them all to focus on this “virus.” This is how they play the game — a game that definitely needs to end this year with the complete removal of these entities from our reality. Time to vaporize them and beam them off the Earth permanently. We cannot co-exist with this creatures. They will never cease trying to destroy us and the Earth.

   Reply

   1.  **Joe Shmuk** says:

      March 13, 2020 at 8:23 pm

      My first time on your site. All very interesting, as if I didn’t already have enough on my mind. But who precisely are ‘“they?”

Reply

1.  **admin** says:

   March 13, 2020 at 8:27 pm

   That, my friend, is something you will need to discover through your own research. However, it should be becoming more and more obvious to those with eyes to see.

2.  **Chorney Toni** says:

   October 30, 2020 at 5:07 pm

   The New World order.
   Mortal enemy of humanity Bill Gates George Soros Rothschilds Rockefeller's The UN Agenda 2021 2030 we are currently in project lockstep. Look up these things on a non google search engine.

2.  **sim8t3** says:

   June 22, 2020 at 9:57 am

   You are so right, let us visualize their departure this year and let the planet ascend to higher vibration, love and light.

   Reply

2.  **Elite destroyer** says:

   June 6, 2020 at 6:56 am

   Why there is so much fuss about 60 GHz when they are not using it. I know that 60 ghz is unlisenced frequency, but people are saying countinusly that 60ghz is harmful.

   Reply

1.  **admin** says:

   June 7, 2020 at 3:52 pm

   All GHz are harmful. 60 GHz was brought up now because people are experiencing breathing problems and 60 GHz messes with the oxygen molecules.

   Reply

3.  **Liz** says:

   February 16, 2020 at 2:17 pm

Hi thanks for the info. To me I think that there are also viruses in addition to the electricity and radiation factor. Viruses can be seen under microscope. And the flu slows down in summer thisnis a fact and shouldn't happen if it's only from electricity and radiation. So I think it's possible that the radiation weakens us as you say, and then throw a new virus bioengineered and this can devastate us faster as in Wuhan. I will work on lowering my radiation exposure for sure but I still think we may see the virus spread – I guess to places with more radiation at a faster rate. Also the footage in Wuhan is real unlike sandy hook or other fake events- maybe you abbey seen enough footage to see how real it is.

Reply

1.  **admin** says:

   February 16, 2020 at 5:30 pm

   Liz – there are some who say that viruses don't exist. Others claim they are a natural part of the body's immune system and not harmful. I can share some interesting quotes with you to get you thinking about these alleged "viral" scares. Here they are and they definitely provide food for thought. Jon Rappaport has done some good work exposing these virus lies.

   Viruses are bits of electric material generated to amplify internal healing by the body itself

   Jenny Lake's research led her to the theory that West Nile fever showed up where the LTE 3G networks were first being tested. However, there is no VIRUS that causes West Nile. Concluding that the body makes viruses to deal with EMF is not supported in any literature…

   Patrick
   Viruses are basically bits of genetic information/material that I think it is fair to say is ALWAYS produced INSIDE our own bodies. They are deployed for all kinds of reasons, genetic information transfer between cells, etc
   ν Janine Roberts book "Fear of the Invisible"
   ν very often they are produced in response to stress and micro-waves, chemicals, etc.
   ν a virus is about a BILLIONTH the size of a normal cell in the body, AND it is not 'alive' it has no metabolism of its own to reproduce or do anything.
   ν this idea of a virus 'mutating' is not accurate. They are constantly different because they are being produced by us in response to different challenges and situations.

   Joe Imbriano's idea that the virus is the clean-up crew of the body. He says blaming the virus is like blaming the rescue crew at a car accident just because they are always to be found there.

   Jim O'Kelly
   Are you worried about the CORONIAVIRUS? You needn't be. They just made it up. It is fake news. How do I know? Because I discovered a long time ago that viruses do not exist. Free your mind of the virus crap they injected into it in order to inject their vaccines into your body. I have put a book together that will relieve your mind of this medical/ pharma fraud. I call it The Virus That Never Was.

   Jon Rappaport
   There are very serious questions about whether a variety of viruses have ever been isolated, proven to exist, and proven to be causing disease. An OPEN, lengthy, ongoing, published debate needs to be undertaken among researchers—including independent researchers.

https://blog.nomorefakenews.com/2020/02/04/the-chinese-virus-hiv-and-a-stranger-on-a-train/

JSchmitt
Yes, as shocking as it sounds, even the so called AIDS virus is also a big hoax. AIDS is real of course, but it's not caused by any particular virus. Instead, AIDS is caused by an extremely weakened immune system from recreational drugs to enhance deviant sex, too many antibiotics and other legal drugs, venereal diseases especially from sodomite/deviant sex with many partners over time, and a poor diet in general. And the drugs to treat people who supposedly are infected with the AIDS virus are also quite deadly, especially chemo drugs like the AZT that they used to use many years ago to treat AIDS.

thousands of cases of AIDS without HIV in the United States alone. Peter Duesberg found 4,621 cases recorded in the literature, 1,691 of them in this country.

[T[here is no virological, nor epidemiological, evidence to back up the HIV/AIDS hypothesis… The virus is biochemically inactive and harmless. [There real causes of AIDS include] AZT, chemotherapy, radiation and radiation treatment, street drugs like popper and MDMA etc., along with antibiotics which break down the immune system and malnutrition and starvation as seen in Africa. 'These are the causes of AIDS and AIDS is not sexually transmitted and HIV doesn't exist.'"
– Dr. Peter Deusberg

However, for those who have reached the unfortunate yet inevitable conclusion that global crimes and conspiracies not only exist but are in fact one of the major driving factors shaping history, it is dreadfully non-shocking to consider the possibility that there is no HIV or AIDS, and the entire fraud is in reality a global ploy to sell fraudulent drugs, and to hide the true cause of millions of deaths. — http://www.examiner.com/article/hiv-aids-the-biggest-lie-the-cdc-ever-told – Louis James

A new virus story always sounds good. It will have legs. People will want to know about it. Some reporters—blithely accepting the existence and dire impact of a virus—will take that ball and run with it into new territory: "the virus was created in a lab." They don't stop and consider the possibility (confirmed by history) that the hoax goes all the way to the bottom—no virus was actually discovered, or if it was, there is a zero proof that it's harmful. They miss that vital step.

There is more to discuss along this line—and I have, in print. It involves asking the questions, "How do researchers actually isolate a new virus and identify it?" and, "What are the correct standards for proving a particular germ causes a particular disease?" When you ask those questions and pursue the answers, you find yourself wading hip-deep in a swamp. The garbage floating around you is formidable.

Reply

1. **Alina** says:

   March 15, 2020 at 6:37 am

   Hello,
   Where do I get the book the Virus that never was? Thank you

   Reply

1.  **admin** says:

   March 15, 2020 at 4:56 pm

   You will need to send an email to jimokelly@yahoo.com to request the book directly from the author.

4.  **Manu Costa** says:

   April 9, 2020 at 5:28 pm

   Some search results I found for key-words “virus microwave radio frequency activate”:

   Diplomats’ mystery illness linked to radiofrequency/microwave radiation, researcher says
   https://www.sciencedaily.com/releases/2018/08/180829115456.htm

   Resonant Dipolar Coupling of Microwaves with Confined Acoustic Vibrations in a Rod-shaped Virus
   https://www.nature.com/articles/s41598-017-04089-7

   Effects of microwave exposure on the hamster immune system. II. Peritoneal macrophage function
   https://onlinelibrary.wiley.com/doi/abs/10.1002/bem.2250040205

   Epstein Barr Virus can be reactivated by Electromagnetic Field
   https://kasiakines.com/epstein-barr-virus-ebv-emf-exposure/

   Reply

   1.  **admin** says:

      April 9, 2020 at 7:57 pm

      Great research! Thanks!

      Reply

4.  **Toxi Com** says:

   February 1, 2020 at 4:23 am

   Epigenetics — the influence if not outright control of environment upon genetics. Not just a debilitating ‘slow cooking’ as 4G and predecessors, is 5G assembling, creating, powering diseases such as 2019-nCoV / Coronavirus ?

   Reply

5.  **Ingri Cassel** says:

   February 1, 2020 at 7:35 am

Thank you, Jeanice, for your astute comments. I found this article early on as I was also researching this topic – http://www.xinhuanet.com/english/2019-05/27/c_138094302.htm
It would be good to investigate further the comparisons between the USA and China regarding exposure levels of radiation. For instance, microwave ovens that were approved in the USA do not meet safety standards in other countries — that information is from memory from 20+ years ago… I do agree with Jeanice that wearing medical masks will not impact the spread of this illness.

Reply

6. **stop5g.cz** says:

February 1, 2020 at 9:41 am

#Stop5g – 5G and Coronavirus – https://stop5g.cz/us/nanotechnology-coronavirus-bioweapon-activation-by-5g-physical-genocide-misused-a-i/

Nano-particles can be activated by 5G microwaves in the human body, so someone can influence them, control them, change our information field, quantum field or our DNA This is so call "Neural Mesh" or NanoCore network. All data are collected and algorithms are used on them – abused A.I.. Activation of nano-particles can be done via 5G ground stations or via satellites.
WUHAN – China – 5G – Coronavirus

WUHAN, Feb. 13 2019 (Xinhua) — China's telecommunication and expressway operators have agreed to launch the country's first 5G-based smart highway project in central Hebei Province. China Mobile's Hubei branch is planning locations for 5G base stations across the highway sections in the province to run tests on smart toll stations, according to the operator. The 5G-based smart expressway would make it possible to gather real-time traffic information and make predictions based on the big data, according to the network operator. Thirty-one 5G base stations have been built in Wuhan, capital of Hubei, by the end of 2018. China Mobile plans to spend one billion yuan (147 million U.S. dollars) this year to build another 2,000 stations in the province.
Coronavirus – Patent – U.S. Pat. No. 10,130,701. (Nov. 20, 2018)

CORONAVIRUS was funded and patented by Wellcome Trust (UK, fake sold to GlaxoSmithKline), Bill & Melinda Gates Foundation, DARPA, DEFRA (UK), World Health Organization, European Commission (EU) via THE PINBRIGHT INSTUTUTE (UK)

CORONAVIRUS. Assignee: THE PIRBRIGHT INSTITUTE (Woking, Pirbright, Great Britain), funded by Wellcome Trust, DARPA, Bill & Melinda Gates Foundation, EU. U.S. Patent Office.

Coronavirus et al Patent Assignee for Pat. Nos. 10,507,237; 10,294,277; 10,202,578; 10,130,701; 9,969,777; 9,457,075; 9,243,230; 9,145,548; 8,828,407; 8,501,466; 8,455,201. U.S. Patent Office.
Google, Facebook, Neuralink Sued for Weaponized AI Tech Transfer, Complicity to Genocide in China and Endangering Humanity with Misuse of AI

Endangering Humanity with the misuse of Artificial Intelligence, Complicity and Aiding in Physical Genocide inside of China by transferring AI Technology, Engaging in Cultural Genocide of Humanity, & Controlling and programming the Human Race by Social Engineering via AI coding and AI algorithmic biometric manipulation

The Wuhan coronavirus has killed 81 people and infected more than 2,800. Here's everything we know about the outbreak.
The Belt and Road Initiative

The Belt and Road Initiative (BRI, or B&R[1]) is a global development strategy adopted by the Chinese government in 2013 involving infrastructure development and investments in 152 countries and international organizations in Asia, Europe, Africa, the Middle East, and the Americas.[2][3]
5G and NanoCore Network

In fifth generation WWWW (World Wide Wireless Web, Dynamic Ad-hoc Wireless Network (DAWN) are developing. Fifth generation network technology is depend on nanotechnology and all IP network. 5G networks make use of this flat IP concept to make it easier for different RAN to upgrade in to a single NanoCore network. The 5the Generation networks have an approach to use Nanotechnology also as defensive tool for security concern that arises due to IP Address. Certainly Flat IP network is the key concept to make 5G acceptable for all kind of technologies.
With the shift to flat IP architectures mobile operators can:

i)Mitigate the network elements in low cost and expenditure.
ii)As per emerging applications delivering service should be partially decouple.
iii)Minimize system latency and enable applications with a lower tolerance for delay;
iv)Should be greater flexibility in network planning and deployment.
v)Develop a flexible core network that can serve as the basis for service innovation across both mobile and generic IP access networks
vi)Create a platform that will enable mobile broadband operators to be competitive, from a price /performance perspective, with wired networks.

5G include latest technologies such as SDR, cognitive radio, cloud computing, nanotechnology based on All IP Platforms with high data rate. By using nanotechnology, mobile phones should act as intelligent sensors which have various applications in many industries or in military.
Nano Dots

Nano dots have the number of discrete balls which are made of hundred nickel atoms. It allows holding a single bit of data 1 or 0. Nanodot is implemented on both Nano Equipment as well as Nano Core.

Reply

7. **Liz A.** says:

February 1, 2020 at 10:43 pm

I theorize that the people in china were given the “vaccine” for this, as Guinea pigs, with or without their knowledge… also, with the current adjuvants in the vaccines today, wouldn’t it be logical to think these metals as reacting to the radioactive wavelengths?? They say, never put aluminum foil in a microwave… maybe this is happening on a molecular level?? Hence the deaths only in China, where 3G,4G, 4G+,&5G are all over. …. just my 2 cents.

Reply

1. **admin** says:

February 2, 2020 at 12:10 am

Yes Liz, the metals make us more conductive to the frequencies. That is why they have sprayed our atmosphere with all these metals — so that we (and all living things) will be full of these metals and thereby become strong “attracters” of the frequencies.

Reply

8.  **Neil** says:

   February 6, 2020 at 1:55 pm

   So how do they manage to get so far with this “genocidal procedure” if you know about it surely people building and testing these things must have noticed thesevside effects…do they not have children or are they not concerned about their own health ? How did they manage to get so far with it.. All these government agencies that sold out.. Are they all gonna move underground.. Or have they got a special device that they wear making them impervious to It’s effects ?

   Reply

   1.  **admin** says:

      February 6, 2020 at 5:52 pm

      Great questions Neil, and I’m not sure I know the answers. I have NO IDEA how they think they will be exempt from the effects, except to say that people like Trump have made sure that the areas where he is will not have 5G. So the entire 1 mile radius (if I remember correctly) will not have 5G, and neither will Palm Beach, FL where he has a home. Here’s links so you can read about this: https://www.kirsten6b.org/wp-content/uploads/2018/08/FINAL-DRAFT-SMALL-CELL-DESIGN-GUIDELINES-08232018.pdf and https://www.palmbeachdailynews.com/news/20170503/official-palm-beach-exempt-from-5g-wireless-law. People building these things do, indeed, feel the effects and some have had to stop work, of course, for their own survival. I have lots of information in my book about this. I recommend you read it. https://www.birthofanewearth.com/1/paperback-release-the-dark-side-of-prenatal-ultrasound/ As for their children, we have to remember that luciferian’s are willing to sadistically torture and even murder their own children. Some of them are so insane, they actually engage in rituals where they eat the body parts and drink the blood of their dead or dying children. I am not making this up. They do not have the capacity to love. I do not even know if they are human. I actually think many are not. They take great delight in turning children into psychopaths, and with these frequencies and radiation, they can turn the children into altered humans who have no capacity for love. And these children are groomed to serve the dark side while they are alive. Many do not live very long — some are lucky to make it to 30. All of this info is in my book. Please consider reading it so you can get a more grounded sense of the mentality of these monsters. Hope this helps.

      Reply

      1.  **Troy** says:

         February 16, 2020 at 2:31 am

         Please look up “Nano Domestic Quell”
         That is the real “virus”

         Reply

      2.  **ROGER REINER** says:

         September 7, 2020 at 11:21 pm

I have talked to several and most do not have a clue as to the side-effects of what they are doing. Most only work on one small part of the whole, and get paid handsomely, I might add. One gal moved from CA to practically nowhere, WY in the middle of a windmill farm, and was getting paid around $4,000 per week. She was not going to give that up for anything and wanted not to hear about anything contrary. Another guy was working in MN and then transferred to AZ, and the same results, but he was only working on tiny electrical connectors and things. Obviously the work settings have yet to experience any serious detrimental effects, perhaps by design. They can always wipe them out later on when they are no longer needed, or send them elsewhere if they want to re-use them. When you think of the haves and have-nots and what people will do who have never had a true opportunity to earn a decent living, people in general will sell their souls to get ahead, and for the most part one cannot blame them. It is the designers and decision-makers, the leaders who turn a blind eye, that are mostly at fault.

Reply

9. **Violet** says:

   February 6, 2020 at 6:15 pm

   The war against 5G heats up.

   http://stateofthenation.co/?p=6517

   Reply

10. **Frank Oliveira** says:

    February 7, 2020 at 3:59 pm

    It’s definitely here on Maui. Wake up Kanaks! For everybody else bottom line :Consider yourself expendable Imua!!! Deliver Us From Evil □☒□□□

    Reply

    1.  **admin** says:

       February 7, 2020 at 5:53 pm

       Frank – are the kanaka maoli awake to this issue?

       Reply

11. **Frank Oliveira** says:

    February 7, 2020 at 4:03 pm

    REALLY WHEN

    Reply

12. **Troy** says:

    February 16, 2020 at 2:37 am

    https://youtu.be/UJbB6naiwuQ

    Nano Domestic Quell is what is happening in China

    Reply

    1.  **admin** says:

       February 16, 2020 at 2:47 am

       Absolutely makes sense to me.

       Reply

13. **Mr.J** says:

    February 17, 2020 at 4:32 pm

    Normal Cell = Innocent Life,entity,People
    Mercenary Cell= We!
    (Elite) Virus Cell=Shaping the System With their Perspective only.
    Minerals,Vitamins,
    Chemical,Metals,5gKillerWaves(Vaccine) =
    Recources

    Reply

14.  **Virginia** says:

    February 19, 2020 at 2:30 am

    I cannot thank jeanice enough for her fight against evil by the sharing of truth and facts! I think the world of this very special lady with a beautiful soul for all of mankind. At first I was fearful, not so much for myself, but my family. Then Jeanice's email came and I realized that much to my dismay, I fell into the "fear" that is quickly enclosing many today. I watched Joe Imbriano's youtube videos as well and it had never dawned on me that it appeared that most police and military officers, were all immune to this virus! I mean you would think that they would be completely suited up as those of the CDC suit up, yet they were not!

    Wondering how long they could possibly continue this charade without eventually running out of people to replace all the hundreds of officers that are exposed removing and taking people. God forbid any children are harmed through this….but it is odd that we have not heard of any……..GOOD! There is definitely MUCH more to what is really going on and Jeanice is awesome pointing out all the dangers of what 5G and any other energized weaponry can do to the body, etc..

    Thank you Jeanice once again! Much love, abundance and health!

Reply

15. **Jasper** says:

    February 21, 2020 at 8:09 am

    Can anyone explain why there are no children (15 & under) in wuhan suffering from the ‘virus’ ? Or have I got this wrong.

    Reply

    1.  **admin** says:

        February 21, 2020 at 4:31 pm

        Good question!

        Reply

    2. **Julie Grover** says:

        April 5, 2020 at 10:40 pm

        Children’s bodies are able to repair cellular/dna damage very rapidly. So their bodies are repairing the damage from wireless almost as fast as it occurs. That ability decreases with age. Thus, lending even more credence to the theories propounded here.

        Reply

        1.  **admin** says:

            April 5, 2020 at 10:49 pm

            Children’s bodies, like the bodies of adults, can only repair radiation damage if they are able to sleep in a non-irradiated environment. For most children, this is not possible, since their parents have filled the house with wireless devices that are never turned off. Moreover, many homes now have smart meters which pump pulsed microwaves into the house 24/7.

            It is not wise to imagine that the children are not being strongly affected and strongly damaged by this radiation exposure. Take a look around. Look at how many autistic children there are. How many with ADHD and asthma. How many with childhood cancers like leukemia?

            Our children are NOT safe in this environment. We have to take action now to protect them. Please see here and here for more information about the danger to the children. Please also see my book, *The Dark Side of Prenatal Ultrasound and the Dangers of Non-Ionizing Radiation*, for detailed information about this.

            Reply

16. **Billy Smart** says:

February 21, 2020 at 6:24 pm

I'm sure that 5G and all of our excessive electromagnetic devices are causing great harm, but if the 'dark ones' are intent on constructing a global network to kill everybody, or at least many millions, then won't they themselves be killed?

It may well be that the 5G radiation is allowing the coronavirus to become more deadly due to weakened immune systems and nervous systems, but can we say that it's a deliberate agenda, or is it more likely that it's just a consequence of humanity's ignorance and the genies which have been let out of the bottle.

Reply

1.  **admin** says:

   February 21, 2020 at 6:45 pm

   There's definitely an agenda Billy, and it's been explained in some detail in my book. It's been ongoing for several decades — centuries even — as these creatures plot and scheme and devise ways to take over the Earth (or what's left of it when they get through with it). As I mentioned in my book (and also in one of the comments here) — they have devised ways to create pockets of protection for themselves. So, for example, Trump has seen to it that the one mile radius around the White House will be exempt from 5G. Palm Beach, Florida, where he has a home, will also be exempt.

   Go figure.

   Please read: https://www.birthofanewearth.com/1/paperback-release-the-dark-side-of-prenatal-ultrasound/

   Reply

2.  **admin** says:

   February 21, 2020 at 6:53 pm

   I'm going to post an excerpt from Appendix A of my book. Please contemplate the information I am about to share…

   ———

   As the graph below shows, by the year 2025, the U.S. population is expected to drop from 327 million people to 100 million. In the U.K., the predicted reduction is from 66 million people down to 15 million. In Germany, the population is planned to be reduced from 81 million people to 28 million by the year 2025.
   See the graph here: http://www.deagel.com/country/United-States-of-America_c0001.aspx

   Dr. Rima Laibow has spoken about this genocidal agenda:

   "[Years ago], we had a head of state who was our patient… So, one day this very pleasant, chatty lady said 'you know, it's almost time for the great culling to begin…' I said 'What? What are you

talking about?' She said, 'You know, the culling of the useless eaters.' I said, 'Who are the useless eaters? She said, 'You know, everyone who is consuming our non-renewable natural resources… We are the neo-aristocrats. We are the people at the top of the pyramid. Around us will be our servants and around them will be our technicians. And we only need 10% of the population.'"

According to Dr. Laibow, this woman, who was a head of state, was "truly bonkers" and a "nutjob." But as can be clearly seen, she was nevertheless privy to an agenda that most people are completely unaware of. Remarkably, she felt perfectly comfortable discussing this agenda with Dr. Laibow.

Dr. Laibow goes on to state that:

"The World Health Organization, the United Nations, the United States Government, the Club of Rome, the Illuminati, the Council on Foreign Relations, have all said 'We have too many people in the world. In order to create a sustainable planet… we have to eliminate 90% of the population…' Since 1974, the World Health Organization has had a commission to develop and deploy vaccinations to permanently end the fertility of the women who receive the vaccines"

After seeing many children die from vaccination in Australia, Dr. Archie Kalokerinos, M.D. concluded that:

"My final conclusion after forty years or more in this business is that the unofficial policy of the World Health Organisation and the unofficial policy of 'Save the Children Fund' and almost all those organisations is one of murder and genocide. They want to make it appear as if they are saving these kids, but in actual fact they don't. I am talking of those at the very top. Beneath that level is another level of doctors and health workers, like myself, who don't really understand what they are doing. But I cannot see any other possible explanation: It is murder and it is genocide. And I tell you what: when the black races really wake up to what we have done to them they are not going to thank us very much. "

A recent Bloomberg article entitled "*Earth Needs Fewer People to Beat the Climate Crisis, Scientists Say*," lends support to the idea that there is a real need for people to either die or stop reproducing. To bolster this notion, 11,000 scientists signed an "emergency declaration" warning that reproduction must change immediately. The article babbles on about the severity of today's "climate crisis" due to alleged carbon emissions, and naturally blames the "useless eaters" for causing this problem. Not surprisingly, no mention is made of the global geoengineering programs that are intentionally causing massive weather changes in our world, nor is there any talk of radiation heat or the alien frequencies that now permeate our air space and are contributing to the climate issues we are facing. Both the mainstream media and the scientific community are being used to distract people from the facts while simultaneously trying to convince everyone that it is a good thing if the human population dies out.

Below are comments made by well-known "elite" people who speak of the need to depopulate the Earth.

David Rockefeller: "The negative impact of population growth on all of our planetary ecosystems is becoming appallingly evident."

HBO personality Bill Maher: "I'm pro-choice, I'm for assisted suicide, I'm for regular suicide, I'm for whatever gets the freeway moving – that's what I'm for. It's too crowded, the planet is too crowded and we need to promote death."

Planned Parenthood Founder Margaret Sanger: "All of our problems are the result of overbreeding among the working class." "The most merciful thing that the large family does to one of its infant members is to kill it."

Paul Ehrlich, former science adviser to president George W. Bush and author of "The Population Bomb": "Basically, then, there are only two kinds of solutions to the population problem. One is a 'birth rate solution,' in which we find ways to lower the birth rate. The other is a 'death rate solution,' in which ways to raise the death rate — war, famine, pestilence — find us."

CNN Founder Ted Turner: "A total population of 250-300 million people, a 95% decline from present levels, would be ideal."

David Brower, the first Executive Director of the Sierra Club: "Childbearing [should be] a punishable crime against society, unless the parents hold a government license … All potential parents [should be] required to use contraceptive chemicals, the government issuing antidotes to citizens chosen for childbearing."

Source of these quotes can be found here: https://www.activistpost.com/2019/11/45-population-control-quotes-that-show-the-elite-are-quite-eager-to-reduce-the-number-of-people-on-the-planet.html

Reply

1. **McGinty** says:

   April 5, 2020 at 9:55 am

   There is indeed a problem with over population. Humans are making themselves a viral scourge on this planet. If there are aliens they have probably placed a cordon around Earth to prevent us infecting the galaxy until we can learn to control our birth rate and therefore responsibly utilise resources instead of exhausting them which always leads to war.

   However… These cosmic 'watchers', that exist in my argument for arguments sake, will not be impressed by brutal, in humane means of achieving 'birth control/population control'. If our species can destroy its own so readily how would they treat other other worldly species?

   Depopulation and responsible living (which includes responsible breeding), must be learnt and achieved by all in the most humane way possible. In my humble opinion this means restricting children per family (though of course NOT retrospectively). This must be equal across the classes and continents. It must not be negotiable via money, status and influence. It must take place in a world in which gender isn't favoured (to prevent the apparent horrid murders of baby girls when these controls were applied in China).

   This is not an evil aim. This is not about police states and pyramidal power structures. Some would try to make it about these things from either side of the fray. It's about being a responsible species. It's about the human race growing up.

   Reply

   1.  **admin** says:

      April 5, 2020 at 3:44 pm

      McGinty – I disagree that there is a population problem but agree 100% that Mankind needs to get serious about conscious procreation. So many children are suffering from not being wanted. Millions are murdered every year in the womb. Even animals merge their bodies for the purpose of procreation only — and yet we

ourselves have been conditioned to fuck just about anything that moves, pretty much anywhere and at anytime. The grotesque elite go so far as to fuck animals — that is how sick they are! In any event, it is our conditioning that makes us have sex the way we do, which of course, results in misery for the unwanted children and those who are murdered. The misery also extends to those who are engaging in haphazard sex since they never seem to be able to manifest authentic and enduring human love.

I have given a talk about this sexual conditioning on my other website here: https://www.birthofanewearth.com/1/pornography-and-the-attack-on-human-love/. On that site, you will also find lots of information about the importance of conscious procreation and the path to achieving healthy families.

As for limiting the size of families, I disagree with you as I know that the white race, in particular, is right now being targeted for extinction. We need to have bigger families, but we need to do it CONSCIOUSLY. The key to a happy life is learning the keys to the preservation of love in families. Strong families are also the key to a strong state.

Reply

3.  **admin** says:

   February 22, 2020 at 1:14 am

   Here's an article that is very well done that addresses this issue. Please read:

   STAGED CORONAVIRUS PANDEMIC: An International Criminal Conspiracy of Epic Proportions
   http://stateofthenation.co/?p=6898

   Reply

17.  **Kelley Eidem** says:

    February 22, 2020 at 7:33 pm

    May it be suggested that viruses are real, and that they can also be beneficial to our health? Viruses are comprised of nucleic acid combined with a protein which can be seen dead via electron microscopes and alive with an Ergonom 500 microscope.

    Their beneficial task is to eat unhealthy and dead cells. As long as those types of compromised cells are few in number there is no problem.

    Viruses can't enter any cells that have the proper Membrane Potential. The MP inside the cells are negatively charged which make them perfect for repelling viruses which are also negatively charged. All viruses have the same negative charge, as do bacteria, even gram positive bacteria.

    This electrical defense is actually our primary immune defense, far outstripping the protection provided by immune cells. Immune cells are more like the police who show up after the microbial crime has been committed, so to speak. They do a good job so long as there aren't too many messes to clean up.

5G, 4G, Wifi, etc all lower our Membrane Potential. All those electrical insults can be relentless as they are operational 24 hours a day, many times a second. This invites the viruses (and bacteria) in to feast., turning a minor cold virus like the coronavirus into a potentially deadly event.

5G can and has taken many Wuhan residents out without a prior infection by short circuiting the neural cells of the heart. 4G qnsd the rest has done the same only in a somewhat slower and less recognizable fashion. In the last four years, for example, average lifespans in the US have declined. The biggest jump has been in those who are frequently the population that are the heaviest users of cell phones and WiFi. Their deaths are blamed on suicide and drug overdoses, but shouldn't we ask what drives a person to doing those sorts of things more than a short circuited brain would?

Because I am able to keep my Membrane Potential strong, I'm able to hug people who have the flu, yet never get it myself.

Reply

1. **JACINTA MOORE** says:

   February 26, 2020 at 2:44 pm

   I would be interested in how you do this as I would suspect others would.

   Reply

   1.  **admin** says:

      February 26, 2020 at 6:38 pm

      Interested in how we do what? I don't understand your question. Could you clarify?

      Reply

2. **JACINTA MOORE** says:

   February 26, 2020 at 3:07 pm

   Do lipid types such as Omega 3 6 and 9 and minerals such as potassium and phosphorus have some impact? Also proteins from seeds and nuts rather than legumes promote cell membrane integrity?

   Reply

   1.  **admin** says:

      February 26, 2020 at 6:38 pm

      I don't know Jacinta and I'm not sure how these questions fit in to what has been shared here. Do these things have an impact on what? Protecting you from radiation? I don't think so.

      Reply

18.  **Kelley Eidem** says:

    February 22, 2020 at 8:01 pm

    As totally and completely wrong headed the proponents of the 5G's are, i don't believe they are attempting to kill us intentionally. Oh yes, they do ignore every bit of contrary information in the process, there is no doubt.

    They so strongly want to believe that what they are doing is safe that they latch onto any misinformation they can to support their stance, such as relying on engineering hypotheses and approved guidelines. They must be good because they are "approved," right?

    They are in love with the 'nifty' possibilities and with the money aspect of course. Pots of gold that gleam so bright they blind one's eyes.

    The nature of 5G is such that no one's biology is immune to its ionic effects or to its repetitive pulses that act like a stuck alarm clock. Then there is the societal collapse as we are witnessing already in Wuhan and elsewhere. The shortage of goods is about to bitch slap everyone very soon. Not only will goods be in short supply, but so will incomes as jobs, commissions and profits are affected. China is already in the deep throes of these realities.

    The advocates of 5G will suffer from both. Their health and their livelihoods are are both barreling down the same road.

    We might think of them as enemies, when they are also fellow victims. Tower climbers have already died and suffered health effects including headaches and ear ringing. Some fall perhaps after becoming disoriented. It might be the most dangerous job in the US.

    A good approach might be to counter their arguments by calling out their reliance on engineering hypotheses and guidelines by letting them know their hypothesis and guidelines do not amount to a hill of beans when biological studies overwhelmingly reveal that the opposite is true.

    Tests on mannequins are worth less than zero, for instance.

    Reply

19.  **Kelley Eidem** says:

    February 22, 2020 at 8:11 pm

    What would happen to a group of people if they were living in a metal container with lots of Wifi pinging back and forth inside the container?

    I dunno – let's ask the passengers of the Diamond Princess for their input.

    BTW, if the floor space of the Diamond Princess were 20 acres, the death rate on the ship attributed to the coronavirus is 50 million times higher than anywhere outside of China. In the US for example 2,000 to 6,000 people died from the flu. Zero of them died from the corona virus.

    Reply

20.  **MorningStar** says:

February 28, 2020 at 1:45 am

18 February 2020
By Brandi Vincent
“Project Convergence”: Veteran Administration Reveals Industry Partners For First 5G-Enabled Hospital:
https://www.nextgov.com/emerging-tech/2020/02/va-reveals-industry-partners-first-5g-enabled-hospital/163172/

25 September 2019
By Brandi Vincent
Critical Update: The Hidden Threats Of 5G:
{4G connects everyone, 5G connects everything}
https://www.nextgov.com/podcasts/2019/09/critical-update-hidden-threats-5g/160124/

Geiger Counter World Map:
https://www.gmcmap.com

Reply

1.  **admin** says:

   February 28, 2020 at 1:53 am

   Thank you!

   Reply

21.  **Justin Klingensmith** says:

    March 5, 2020 at 7:55 am

    Idiots. Radiation-based depopulation methods were ruled out as not viable in the 70s. My city has installed a ton of new “5G” cells (which look exactly the same as “4G” cells, which is why I wonder if “5G” is even real at all. My phone is not getting faster) not far from my house and I feel fine. Heck, my arthritis has actually gone down a bit since last year. Stop wasting your time chasing what they want you to waste your time on. Doesn’t this seem all a little “too easy” to figure out? Agenda 21 is based on a real depopulation method, chemtrails.

    Reply

    1.  **admin** says:

       March 5, 2020 at 5:34 pm

       I hope you decide sometime soon to do some research Justin. You are in deep denial of the severity of the problem and it could cost you your life.

       Reply

       1.  **Justin Klingensmith** says:

March 6, 2020 at 4:52 am

Oh I know how severe the problem is. I see the clues are everywhere. There are so many of them, almost too many. Those YouTube videos above, they're not censored. We all know Google is evil's IT department, and YouTube is owned by Google. Why would Google let those videos stay up? Those videos blow the lid off of the 5G agenda, wouldn't you think they'd take them down? It's not like they came out yesterday, one of those vids is from 2018. Surely they know about it, and all it would take to remove it is a press of a button. So why don't they? I'm not saying you're wrong, just that this is fishy. They definitely plan on depopulating us somehow. It's just that slowly killing people with short range 5G antennas seems like an overtly complex and slow way to do it.

Reply

1.  **admin** says:

   March 6, 2020 at 3:32 pm

   Dear Justin – you will have to speak with the diabolically insane creatures who created 5G technology (and all wireless technology) in order to comprehend their logic. 5G will not be slow kill. Based on all my research, it will be one or two years before people stop dropping. With 4G, it is usually between 5-15 years of exposure, depending on the constitution of the person.

   In any event, the radiation danger is very real. It is extreme. And it is likely many are going to die over the next 20 years. Not just humans.

   Reply

   1.  **Justin Klingensmith** says:

      March 9, 2020 at 6:38 am

      One to two years is practically forever. People would realize what's up in a few months and storm the towers. No, chemtrail-based depopulation is much more likely. From what I've read people could start dropping in as little as five weeks. So much faster, easier, and also less costly than fancy microwave-based systems. From an engineering standpoint, it's a no-brainer. Chemical methods are "better" (to them, not us) in every way.

   2.  **admin** says:

      March 9, 2020 at 4:44 pm

      Justin – you seriously need to educate yourself. Otherwise, there is no point in having this conversation. You appear to have NO IDEA of how deadly microwave technologies are. This is not to imply that chemtrails are not a problem. They are. The metals that we are inhaling make us more conductive to the microwaves. We are sitting ducks at this point unless we become willing to shield our homes or relocate deep into the forest. Without a doubt, they intend to kill us. Please wake up.

22. **Rick** says:

    March 13, 2020 at 3:20 pm

    March 13, 2020
    From : Rick Potvin, anti-5g activist in Phoenix Az
    To: admin of this blog

    POINT OF ORDER: Your article above is the best concise statement of the problem I've seen so far. However, the image of the pregnant woman at the top makes it difficult to see the point of the article immediately. Can you consider reducing its size so the SUBJECT LINE of the article appears immediately upon entering the site? I note that you point out that you're continually updating this article… great! I'll be back in a few days.

    Reply

    1.  **admin** says:

       March 13, 2020 at 4:28 pm

       Sadly – I am unable to control the size of the image. It is very frustrating for me also. I need someone with more expertise than myself to figure out if there is a way. I have been unable to find the way myself. Thanks for the suggestion.

       Reply

23. **Neil** says:

    March 15, 2020 at 11:37 pm

    The deaths from 'coronavirus' are being attributed to cytokine storm syndrome. An immune system gone crazy.

    Reply

    1.  **admin** says:

       March 16, 2020 at 12:01 am

       Sounds suspiciously similar to what happens when people are exposed to radiation!

       Reply

24. **Patricia Brown** says:

    March 16, 2020 at 7:26 pm

    Totally disagree with this elaborate, yet very well put together, fictitious story. Call me uneducated and try to make me feel as if I'm not up on my information, I won't fall for that either. I think it is extremely wreckless and irresponsible to push this crap. ALL the conspirators, media, government, their families and

children, would be just as susceptible to these problems as the rest of the public, so why would they risk that? Do they go along with it because of coercion? No, it's AS ridiculous as chemtrails and all the other conspiracy theories out there!

Reply

1.  **admin** says:

   March 16, 2020 at 9:36 pm

   People go along with the lies, Patricia, because they are under a spell. It's called mind control, otherwise known as hypnosis. Clearly you are suffering from this very thing yourself since anyone that thinks chemtrails is "ridiculous" or a conspiracy theory is obviously not able to see what is right in front of their face. Perhaps you are under hypnosis as a result keeping your head in your cell phone? Or perhaps you watch alot of TV, and/or read the mainstream media newspapers, and/or have been well-"educated" by the twisted and perverse people in control of the education system. Congratulations! You have become a brainwashed biological robot. Perhaps you should consider a simple google search for the word "geoengineering" so you can learn the facts about the chemicals and heavy metals that are being sprayed in our skies — for decades now. These metals make us more conductive to the frequencies and radiation hence, more susceptible not only to illness but also mind control.

   If certain aspects of humanity refuse to snap out of the spell, there is no hope for their bloodlines. Perhaps this is as it should be. We can no longer tolerate an Earth that is filled with people in denial of the harm they are causing. It's either wake up or die Patricia. Which will you choose?

   Reply

25.  **Unknown** says:

   March 27, 2020 at 12:47 pm

   How does a microwave work?
   Using the same electromagnetic radiation as satellites (24/7 sending signals), routers, phones , base stations, etc., microwaves heat the food with the same signals. Food contains water. The particles of the water are: oxygen and hydrogen. One is positive and the other is negative (charge). The electromagnetic radiation is electricity divided (positive and negative separated). So positive attracts negative and negative attracts positive. That's how energy is produced and that is what makes the food hot.

   1/3 of the planet is water.
   More than 50% of human body is water.

   5G deployed this year thousands of satellites emitting electromagnetic radiation with the strength of the signal that passes even through walls (what about human bodies?)

   Just asking?
   Isn't electromagnetic radiation the cause of global warming? (the oceans are shaking more as the electromagnetic radiation when in contact with water, produces energy -> heat)

   Isn't electromagnetic radiation the cause of headaches? (the water inside us is moving constantly as the particles attract when in contact with electromagnetic radiation)

   Isn't electromagnetic radiation the cause of weak immune systems? (coronavirus effects)

Maybe the CEOs of big companies that rely on wireless technologies are smart, trying to take another path in life https://governmentslaves.news/2020/02/26/wtf-is-going-on-17-major-companies-had-their-ceo-step-down-in-the-last-30-days/

Reply

1.  **admin** says:

   March 27, 2020 at 4:57 pm

   You are spot-on in much of what you say. We are all living in a microwave oven right now. Microwave ovens use the 2.4 GHz frequency to cook things. This is the frequency that MAXIMIZES THE ABSORPTION OF RADIATION IN MAMMALIAN TISSUE so it is perfect for cooking. And guess what! They are using this very same frequency to power our cell phones, cordless phones, smart meters, baby monitors, smart TVs, etc. All the better to cook us along with the rest of creation.

   Headaches are caused by radiation-induced vasculopathy. When we are exposed to these alien frequencies and radiation, our blood vessels constrict due to the trauma of the frequency assault. The constriction cuts off blood and oxygen supply to the brain and causes headaches. It can also cause stroke, which is why so many young people today are experiencing strokes whereas this was hardly ever heard of before the introduction of wireless devices.

   Regarding global warming, here is an article I wrote pointing out that so-called "climate change" (otherwise called "global warming") is absolutely being caused by radiation heat: http://wa.grdn.net/babies-and-children/so-called-climate-change-is-caused-by-radiation-heat-not-carbon-dioxide-and-greenhouse-gases/ So you are spot-on about that too.

   Below is an excerpt from my book about how microwaves cook. Everyone needs to understand that what is happening to the food molecules is happening inside of our bodies as well.

   "Technically produced microwaves are based on the principle of alternating current. Atoms, molecules and cells hit by this hard electromagnetic radiation are forced to reverse polarity 1 to 100 billion times a second.' There are no atoms, molecules or cells of any organic system able to withstand such a violent, destructive power… This is how microwave cooking heat is generated – friction from this violence in water molecules. Structures of molecules are torn apart, molecules are forcefully deformed (called structural isomerism) and thus become impaired in quality… There is direct damage to cell walls and genes from microwaves… 'the cells are actually broken, thereby neutralizing the electrical potentials – the very life of the cells…'"
   Source

   Moreover,

   "Eating food processed from a microwave oven causes permanent brain damage by 'shorting out' electrical impulses in the brain.

   Eating microwaved food causes loss of memory, concentration, emotional instability, and a decrease of intelligence…
   Minerals, vitamins, and nutrients of all microwaved food is reduced or altered so that the human body gets little or no benefit. Regular consumption of microwaved food causes immune system deficiencies through lymph gland and serum alterations.

   The prolonged consumption of microwaved foods causes cancerous cells to increase in human blood. Moreover, these foods cause stomach and intestinal cancerous growths (tumors). This may

explain the rapidly increased rate of colon cancer in America."
Source

Reply

26. Pingback: 5G (An invisible Enemy) - ancientofdayshealth.com
27. **MyNameIsNobody** says:

    April 7, 2020 at 2:58 am

    Have you looked into the possibility that 60 ghz might also be causing ozone to form in the beam between the router and the person's device? The symptoms of the cornholio virus seem to be almost exactly the same as ozone poisoning. We know that oxygen absorbs the 60 ghz energy. Could it cause the O2 to split into O1 and recombine as O3? Could this be why people around the person start having trouble breathing too?
    Perhaps, do a duckduckgo search on: "corona ozone generators" or on "ozone poisoning".
    Hospitals, airplanes, airports, and winter city streets are a cool, dry environment, with low air flow so O3 takes longer to de-energize and revert back into 02.

    Reply

    1.  **admin** says:

       April 7, 2020 at 3:40 pm

       I think you are right about that. What you say makes sense. Mark Steele had commented about 60 GHz causing ozone. In this video (https://youtu.be/JQDViJDTCRE), he said: "If I was to blast enough 60 GHz amplitude into an oxygen molecule, I might break it. And that oxygen atom will attach with other oxygen molecules and create 03. 03 kills. At 50ppm, it will kill all biological life."

       I did not know that about hospitals, airplanes, etc. Thanks for the info!

       Reply

       1. **AndyJ** says:

          April 20, 2020 at 4:55 am

          Actually, Ozone (o3) and Peroxide (h2o2) are good for the body. Both are unstable in their molecular states, so when they come in contact with anaerobic (bad) bacteria, one Oxygen atom will leap off and oxidise (kill) that bacteria. You will be left with 02 (oxygen) or h2o (water). Both are good for oxygenating the body and helping aerobic (good) bacteria flourish.
          Note: Most good bacteria is aerobic and most bad bacteria is anaerobic, but not in every case. Still bacteria is not to be feared, your body lives happily with both, just keep the balance of good higher.

          Reply

          1.  **admin** says:

April 20, 2020 at 4:41 pm

Ozone can actually kill people and other things. It's very harmful to the lung. Here's a link: https://www.lung.org/clean-air/outdoors/what-makes-air-unhealthy/ozone. And yes, bacteria is beneficial.

Reply

2. **Stan** says:

September 27, 2020 at 12:46 pm

I believe this is it:
The absorption of (especially) 60 GHz radiation from 802.11ad/ay/5G machines in the atmosphere causes "photodissociation" of O_2 generating ozone:

$O_2 \rightarrow 2\ O$; $O_2+O \rightarrow O_3$
https://en.wikipedia.org/wiki/Photodissociation
https://scientists4wiredtech.com/wireless-at-60-ghz-has-unique-oxygen-absorption-properties/

Interesting reading:
What is ozone?, How long does ozone last?, Is ozone safe?:
https://purifyo3.com/what-is-ozone/
Basics about ozone, Ozone production, Safety information:
https://ozonesystemsolutions.de/wp-content/uploads/2019/10/OZON-PRODUCER-Handbuch-ENGLISCH.pdf

Reply

1. **admin** says:

September 27, 2020 at 9:43 pm

And ozone can kill people instantly. Thanks for this info.

Reply

28. Pingback: 5G Technology has to be stopped | Stan Rams
29. Pingback: Con las redes 5G.nos tratan como canarios enjaulados robando nuestro oxigeno en las minas de carbon – muelasgaitan
30. Pingback: Is Your Skin 'Fizzing'? Absolutely Bizarre Symptoms Of Covid-19 - The Daily Coin
31. **Nick** says:

June 1, 2020 at 7:36 pm

Great encompassing article. This site was offline a few days ago, did you know?
Anyway, you NEED to see this group and READ…

https://www.facebook.com/groups/supportgroupcovid19/

I have made a list of SOME of the symptoms being attributed to ‘covid19’ if anyone wants a shortcut. But tell me, what do you see?

I have noticed that some of this is being slowly slowly dripped out through the media. This gets it out there without anyone seeing a full list and thinking… ‘hang on….’

Reply

1.  **admin** says:

   June 1, 2020 at 8:19 pm

   Nick – where is your list? I would love to see it. I am not on facebook.

   Reply

   1.  **Nick** says:

      June 6, 2020 at 11:54 pm

      ‘Covid-19’ (not exhaustive)
      heavy feeling in chest /intense pressure on chest
      Slowed breathing/gasping for breath
      digestive issues (diarrhea)
      body aches all over
      fever, chills
      Constant dizziness for weeks or months
      Nausea
      bladder weakness
      shortness of breath
      extreme fatigue
      Brain fog/Confusion
      Sharp shooting pains in head and various
      Rash (various body parts)
      Blackouts
      Hair falling out
      Heart palpatations
      Loss of smell & Loss of taste
      Burming smell
      Facial drooping
      Swelling (various body parts)
      Aching eyes
      Burning eyes
      Intense pain (various body parts)
      Panic attacks
      Numbness (various body parts)
      Muscle spasms
      Tingling skin/electricity under skin
      Vertigo
      Blurred Vision
      Black tongue/swollen tongue/swollen gums/sores
      Very low blood oxygen levels <90
      Low blood pressure

Stroke/Seizures
Intense headaches
Ringing in ears/buzzing in ears
Very cold fingers/toes
Sunburnt feeling (various body parts)
Shaking limbs (electrical feeling)
Changes to menstrual cycle
Itching
Blood pressure spikes
'covid' toes
kawasaki disease
Source: https://www.facebook.com/groups/supportgroupcovid19/

Reply

1.  **admin** says:

   June 7, 2020 at 3:50 pm

   AMAZING! Almost of all of these are signs of radiation sickness. See my article for more info: http://radiationdangers.com/5g/is-the-coronavirus-actually-microwave-illness/

   Reply

   1.  **Nick** says:

      June 11, 2020 at 6:50 pm

      Yes, that is the article I'm reading.
      I'm afraid we have a serious problem. I was of the opinion that 'coronavirus' was just a cover for the 5g 'switch on'.
      Its not. It cant be. From examining recent events it is 100% clear that they were entirely orchestrated. The riots were MADE to happen, nothing was left to chance.
      It is difficult to comprehend the pure evil that is behind this. Google 'crowds chant I cant breathe' and click on news tab to see just how widespread that was. That is the predictive programming/symbology these sick fucks employ.

      They made it all happen so that there was reason for a 'second wave'.
      But you cannot create a 'second wave' from a single 'switch on'.
      Unless you surreptitiously have access and can pulse a more dangerous frequency, un-noticed, for a desired timeframe.

      They have the data now from the 'live exercise' and 'preparation drill'. These are quotes that were slipped by Trump and Cuomo. (I doubt they have a clue what is going on). Truthseekers have been hanging on to these because we are so used to everything being fake, this must be too. We have been played.

      I can see people online today saying 'this will be over soon'. Its barely started.

2.  **admin** says:

   June 11, 2020 at 8:31 pm

   Commie Cuomo and Trump know exactly what is going on. And this is an attempted Bolshevik/communist takeover not only of America, but the world. And the killing of George Floyd was just as fake as this non-existent deadly virus. It's all a great big Hollywood movie created by the very same tribal CULT that controls the media.

   It is definitely wakey wakey time for the American people.

32. **The Rebels** says:

    June 14, 2020 at 5:21 pm

    This is true, but its not just 5G, they've been using facilities like HAARP for years, and some people could feel it before, but since Corona its more the people realising this, sometimes erroneously thinking it's because of the virus, and that is because it's stronger now. Also, when its used for climate manipulation, the waves reflect back to earth. I tried to translate a post i wrote about this so you can read it if you like. You should also take a look to HAARP's patent and its effects on earth magnetic field, since they've been saying for years that there are holes in it.
    https://tapintotheunknown.wordpress.com/2020/05/15/unusual-symptoms-around-the-world/

    Reply

    1.  **admin** says:

       June 15, 2020 at 2:26 am

       Thanks. I will check out the link.

       Reply

33. **Violet** says:

    June 19, 2020 at 2:13 pm

    Must watch video.

    https://youtu.be/Q6FEYAunaTs

    Reply

34. **Angel** says:

    July 8, 2020 at 6:48 am

    1918 Armstrong invents the superhet – Although thermionic valves (tubes) enabled far greater performance to be gained in radio receivers, the performance of the devices was still very poor and receivers of the day

suffered from insensitivity and poor selectivity. During the First World War a considerable amount of effort was devoted into resolving these problems. An intermediate solution was developed by a Frenchman named Lucien Levy, but in 1918, Edwin Armstrong developed a receiver where the incoming signal was converted down to a fixed intermediate frequency. Here it could be satisfactorily amplified and filtered. Unfortunately the idea did not gain much acceptance at first because the war ended, and superhet receivers were very expensive because of the numbers of valves they used. It took until the late 1920s before the number of transmitting stations rose to a level that the performance of the superhet was required and further developments meant they could be made more cheaply.

https://www.electronics-notes.com/articles/history/radio-receivers/radio-history-timeline.php

High exposure to radio frequency radiation associated with cancer in male rats

Future cancers after 5G?
developed cancerous heart tumors, according to final reports released today. There was also some evidence of tumors in the brain and adrenal gland of exposed male rats. For female rats, and male and female mice, the evidence was equivocal as to whether cancers observed were associated with exposure to RFR.

https://www.nih.gov/news-events/news-releases/high-exposure-radio-frequency-radiation-associated-cancer-male-rats

Cancers caused by infections are also expected to increase. New cases of liver cancer are expected to go up more than 50%, likely the result of the increase in hepatitis infections, particularly in people born between 1945 and 1965. Oral cancers in white men are expected to increase by about 30%, likely the result of more human papillomavirus (HPV) infections.

https://www.cdc.gov/cancer/dcpc/research/articles/cancer_2020.htm

1952 Sony, a brand new Japanese company, introduces the first pocket-sized transistor radio and by 1957 Sony came up with the 13,800 yen “pocketable” TR-63 radio, which had a speaker and became a huge best-seller.

The 1957–1958 influenza pandemic, also known as Asian flu, was a global pandemic of influenza A virus subtype H2N2 which originated in Guizhou, China and killed at least one million people worldwide.

By June 1957 it reached the United States, where it initially caused few infections.[2] Some of the first affected were United States Navypersonnel at destroyers docked at Newport Naval Station, as well as new military recruits elsewhere.[9]The first wave peaked in October principally affecting children who recently returned to school after summer break; the second wave in January and February 1958 was more pronounced among elderly people, and consequently was more fatal.[2][10] Microbiologist Maurice Hilleman was alarmed by pictures of those affected by the virus in Hong Kong published in The New York Times. He obtained samples of the virus from a United States Navy doctor in Japan. The Public Health Service released the virus cultures to vaccine manufacturers on 12 May 1957, and a vaccine entered trials at Fort Ord on 26 July and Lowry Air Force Base on 29 July.[9] The number of deaths peaked the week ending 17 October with 600 reported in England and Wales. The vaccine was available in the same month in the United Kingdom.[3]Although it was available initially only in limited quantities,[10][3] its rapid deployment helped contain the pandemic.[2]

H2N2 influenza virus continued to transmit until 1968, when it transformed via antigenic shift into influenza A virus subtype H3N2, the cause of the 1968 influenza pandemic.[2][11]

Reply

1.  **admin** says:

July 8, 2020 at 4:45 pm

Fantastic info! Thank you for sharing this.

Reply

1.  **Angel** says:

   July 8, 2020 at 10:22 pm

   For Pandemic years search new frequency related inventions prior to the pandemic and look for its applications and wide acceptance or use causing the radiation poisoning that is sold as a pandemic.

   God Bless

   Reply

35.  **Donald WHITE** says:

August 21, 2020 at 9:02 pm

□ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □

" **TOP 26 MOST CENSURED PRO-WHITE NATIONALIST SITES WORLD** " by White Only Network ©

☒ http://www.ribinad.com/forum/viewtopic.php?id=278

☒ http://whiteeuropeonly.canalblog.com/archives/2020/02/11/38015829.html

☒ http://make-europe-white-again.over-blog.com/2020/08/top-26-sites-nationalistes-pro-blanc-les-censures-au-monde-by-white-only-network.html

Reply

36.  **Kenneth Lee** says:

September 25, 2020 at 9:27 pm

thank you so much for telling the truth about radiation dangers. The onslaught is worse for us victims who have been covertly implanted with neurotoxins as part of the C.I.A. Mk-ultra and other programs.

Reply

1.  **admin** says:

   September 26, 2020 at 1:45 am

   You're welcome Kenneth. To some extent, we've all been implanted with neurotoxins through the chemtrails, GMO foods, mercury in our dental fillings, pharmaceutical poisons (especially vaccines), and the list goes on. But I am sure it is much worse for the victims of MK-ultra and other

mind control programs. The creatures responsible for all this evil need to exported back to hell pronto. We all deserve to live in a world without evil.

Reply

37. **Dez** says:

October 30, 2020 at 2:45 am

Thank you for all the hard work you have done on putting this all together. I have spent a couple of hours reading it from top to bottom including reading through all the comments.

I have a fairly good understanding of what is going on in the world surrounding the ruling classes and their lies, deceit, dirty agendas and media brainwashing techniques but had never truly understood the implications of 5G or even EMF radiation until today after visiting a few other well researched websites and then finding yours.

The mainstream propaganda always say things like “5G is totally safe – it uses non-ionizing radiation, so don’t worry about a thing, those conspiracy nuts are crazy right??!!” yet they fail to mention any of the other implications – especially the 60GHZ and the effects on the electrons in oxygen molecules and the hemoglobin uptake. I tried to find a link to a single study on the bbc news site to any page relating to 5g, absolutely nothing whatsoever to back anything up other than slinging the conspiracy theory mud.

I’d actually class that as a crime against humanity and the directors of these organizations should be strung up as well with the rest of their psychopathic buddies in some Nuremberg style trials when this is all over.

Thanks again,
Dez

Reply

1.  **admin** says:

November 1, 2020 at 3:14 am

So well said Dez, and I agree 100%. It is time for them to be held responsible for what they have done and are doing. Many living things have died already as a result of this radiation. With 5G, it will be worse. And they are covering it up by saying the symptoms are from a virus. It’s a disgusting deception.

Reply

38. **zdb** says:

November 14, 2020 at 10:20 pm

Thank you for doing this. Please keep on.

Reply

39. **zdb** says:

November 14, 2020 at 10:45 pm

The last item on this list is the point that I remembered after reading here. Thank you for posting this and please keep on.

https://gizadeathstar.com/2020/08/news-and-views-from-the-nefarium-august-6-2020/
Joseph begins by mentioning a video with reference to the Beirut explosion, and then gets down to main story, shared by M.W., about Blackstone's acquisition of a controlling stake in Ancestry.com, and an unusual patent:
1) The youtube video in Beirut: https://www.youtube.com/watch?v=Tz3zaSQCETE&feature=youtu.be
2) Blackstone and ancestry.com: https://www.oann.com/blackstone-to-acquire-ancestry-com-for-4-7-billion/
and
3) A google patent on chloroquine compounds as radiation sickness therapy and DNA repairer: https://patents.google.com/patent/US20050014785A1/en

Reply

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DIRECTORY

- Family Fighting 5G Transmitter Next to their Child's Bedroom Has Their Youtube Account Deleted
- FCC Provides $9 Billion to Telecoms for Rural 5G Rollout
- Former US Presidential advisor Ron Powell PhD on 5G threat to public health
- French NGOs Demand Moratorium on 5G Due to Its "Out of Control" Consequences On Society
- Glastonbury Concert Goers Who Paid $315 Per Ticket Were Used as 'Guinea Pigs' in 5G Trial
- International Appeal to Stop 5G – Your Help is Needed Now
- Israel is Behind 5G Technology and the Attempt to Destroy All Life on Earth (VIDEO)
- Locating 5G Cell Towers Near You
- Long Island Guinea Pigs – 5G Roll-out Tested Without Warning in Woodbury
- Manhole Covers Serve as Antennas Expanding Wireless Network Coverage
- Mill Valley, California Blocks 5G Roll-Out – HOORAY!
- Millimeter Waves Travel More Than 10 Kilometers in Rural Virginia 5G Experiment – So Why Do We Need Small Cell Antennas Every Few Feet?
- More 5G tower victories across Australia
- More than 80 cities and counties have filed lawsuits challenging the new FCC rules
- MUST LISTEN! 5G Could Wipe Out Humans, Plants, Animals – Dr. Martin Pall
- New Hampshire Report Concludes 5G is a Health Threat to Humans, Animals, and the Environment
- New York City Saturated with 5G Radiation – People/Pets Becoming Ill – Naomi Wolf Reports Her Illness
- New York Congressman Thomas Suozzi Calls On FCC For Documentation That 5G Is Safe
- New York Times Says 5G Phones Won't Hurt You – Attacks Russia for Putting Out "False" Information Warning People About the Dangers of 5G
- OOKLA 5G MAP – See if You Will be Zapped Where you Live by 5G
- Radiation from Cell Phones, Wifi, 5G a Threat to Birds and Bees (and all of life)
- Reasons to Halt 5G
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ORAL ARGUMENT REQUESTED
20-1025 (Lead); 20-1138 (Consolidated)

UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

ENVIRONMENTAL HEALTH TRUST; CONSUMERS FOR SAFE CELL PHONES; ELIZABETH BARRIS; THEODORA SCARATO

CHILDREN'S HEALTH DEFENSE; MICHELE HERTZ; PETRA BROKKEN; DR. DAVID O. CARPENTER; DR. PAUL DART; DR. TORIL H. JELTER; DR. ANN LEE; VIRGINIA FARVER, JENNIFER BARAN; PAUL STANLEY, M.Ed.

Petitioners

v.

FEDERAL COMMUNICATIONS COMMISSION;
UNITED STATES OF AMERICA

Respondents

Petition for Review of Order Issued by the
Federal Communications Commission

PETITIONERS' JOINT OPENING BRIEF

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CERTIFICATE AS TO PARTIES, RULINGS, AND RELATED CASES

Pursuant to Circuit Rule 28(a), Petitioners, through their undersigned counsel, submit this Certificate as to Parties, Rulings, and Related Cases.

I. Parties, Amici, and Intervenors

A. Petitioners

"EHT Petitioners" 20-1025 (lead)
Environmental Health Trust
Consumers for Safe Cell Phones
Elizabeth Barris
Theodora Scarato

"CHD Petitioners" 20-1138 (consolidated)
Children's Health Defense
Michele Hertz
Petra Brokken
Dr. David O. Carpenter
Dr. Paul Dart
Dr. Toril H. Jelter
Dr. Ann Lee
Virginia Farver
Jennifer Baran
Paul Stanley, M.Ed.

B. Respondents

Federal Communications Commission
United States of America

II. Decision Under Review

FCC, *Resolution of Notice of Inquiry, Second Report and Order* and the *Memorandum Opinion and Order*, addressing *Proposed Changes in the*

Commission's Rules Regarding Human Exposure to Radiofrequency Electromagnetic Fields, ET Docket No. 03-137, and *Reassessment of Federal Communications Commission Radiofrequency Exposure Limits and Policies,* ET Docket No. 13-84, in FCC 19-126; 85 Fed. Reg. 18131 (Ap. 1, 2020).

III. Related Cases

None.

RULE 26.1 DISCLOSURE STATEMENT

Pursuant to Circuit Rule 26.1, Petitioner associations respectfully submit this Corporate Disclosure Statement as follows:

1. Environmental Health Trust ("EHT") is a non-profit 501(c)(3) scientific and educational organization whose mission is to safeguard human health and the environment by publishing scientific research, empowering people with state-of-the-art information, and working directly with various constituencies to mitigate health and environmental risks. EHT has no parent corporation, and no publicly-held company has a 10% or greater ownership interest in the organization.

2. Consumers for Safe Cell Phones ("CSCP") is a non-profit 501(c)(3) that promotes the safe use of cellular technology, including cell phones. CSCP has no parent corporation, and no publicly-held company has a 10% or greater ownership interest in the organization.

3. Children's Health Defense ("CHD") is a national non-profit 501(c)(3) organization whose mission is to end the epidemic of children's chronic health conditions by working aggressively to eliminate harmful exposures to environmental toxins via education, obtaining justice for those already injured and promoting protective safeguards. CHD has no parent corporation, and no publicly-held company has a 10% or greater ownership interest in the organization.

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GLOSSARY

ADA-Americans with Disabilities Act

APA-Administrative Procedures Act

BIR-BioInitiative Report

CDC-Centers for Disease Control and Prevention

CHD-Children's Health Defense

EA-Environmental Assessment

EHT-Environmental Health Trust

EIS-Environmental Impact Statement

EMF-Electromagnetic Field

FDA-Food and Drug Administration

FHA-Fair Housing Act

FONSI-Finding of No Significant Impact

GAO-Government Accountability Office

IARC-International Agency for Research on Cancer

IEEE-Institute of Electrical and Electronics Engineers

MMW-Millimeter Wave

NEPA-National Environmental Policy Act

NTP-National Toxicology Program RF-Radio Frequency

RFR-Radio Frequency Radiation

TCA-Telecommunications Act

STATEMENT OF JURISDICTION

This Court has jurisdiction under 47 U.S.C. §402(a) and 28 U.S.C. §2342(1) to review the Federal Communication Commission's ("FCC" or "Commission") *Resolution of Notice of Inquiry* ("*Inquiry*")*, Second Report and Order* and the *Memorandum Opinion and Order*, addressing *Proposed Changes in the Commission's Rules Regarding Human Exposure to Radiofrequency Electromagnetic Fields*, ET Docket No. 03-137, and *Reassessment of Federal Communications Commission Radiofrequency Exposure Limits and Policies*, ET Docket No. 13-84, in FCC 19-126 ("*Order*").[1] The *Order*, released on December 4, 2019, was published in the Federal Register on April 1, 2020 at 85 Fed. Reg. 18131. The FCC's claimed basis for the *Order*, and in particular the resolution of the *Inquiry*, includes 47 U.S.C. §§154(i)-(j).

Petitioners in 20-1025 timely filed their Petition For Review in this Court on January 31, 2020 (Doc. #1827096), and a Protective Petition For Review on April 9, 2020 (Doc. #1837472). Petitioners in 20-1138 timely filed their Petition for Review in the United States Court of Appeals for the Ninth Circuit on February 3, 2020 (20-70297; ID #11582294), and a Supplemental Petition For Review on April

[1] 34 FCC Rcd 11687.

2, 2020 (ID #11650275). The petitions in 20-70297 were transferred to this Court on April 24, 2020, with 20-1138 then consolidated with 20-1025 (lead case) on April 30, 2020 (Doc. #1840768).

STATEMENT OF ISSUES

Petitioners and others submitted well over one thousand peer-reviewed studies, science and medical reviews, and comments, including over 250 reports of sickness, during the FCC's reassessment of its 1996 safety regulations which limit consumers' and the general public's exposure levels to radiofrequency and electromagnetic fields ("RF/EMF") emitted from wireless devices and infrastructure. Those submissions, largely containing research completed since 1996, focused on significant health and environmental risks of RF/EMF that the FCC's now outdated regulations did not take into account. In the *Order*, the FCC decided not to amend the RF exposure regulations or related procedures it relies upon to test and certify cellphones for marketing and sale. This case raises the following issues:

1. Did the FCC violate the Administrative Procedure Act ("APA") when it failed to: (i) consider any evidence demonstrating that the 1996 RF/EMF regulations do not protect against numerous health and environmental risks; or (ii)

explain why such evidence did not warrant amending the exposure regulations and cellphone testing procedures to better protect human health and the environment?

2. Did the FCC violate the National Environmental Policy Act ("NEPA") when it failed to: (i) explain why NEPA does not apply to the *Order* and its reassessment of the 1996 RF/EMF exposure regulations and the cellphone testing protocols; or (ii) conduct an environmental analysis regarding its decision not to amend the exposure limits or testing procedures?

3. Did the FCC violate the APA when it failed to: (i) recognize and make some provision for those who have or will develop Radiation Sickness from RF/EMF exposure; (ii) resolve or establish some process to resolve case-by-case accommodations under the Americans With Disabilities Act ("ADA") and/or Fair Housing Act ("FHA"); or (iii) resolve or establish some process to resolve case-by-case individual objections to nonconsensual RF/EMF exposure or uninvited RF/EMF property instruction?

STATEMENT OF THE CASE

I. Background

This case involves the FCC's health and safety regulations for existing and new telecommunications technologies. The petitioners submit that the FCC's failure to update those regulations in the Order on appeal violates the

Telecommunications Act of 1996 ("TCA"),[2] the APA,[3] and NEPA.[4] There are also implications regarding the ADA[5] and FHA,[6] as well as constitutional issues.

A. Radiofrequency Basics

Wireless technology uses electromagnetic[7] waves to carry information. A wave "frequency" is the number of wave cycles per second. Each cycle per second equals a "Hertz" ("Hz").[8] The Radio-Frequency ("RF") signal is the "carrier wave." But communications require carrier wave manipulation to "encode" the data on the carrier wave. Two main techniques are used: "pulsation" and

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[2] Pub. L. No. 104-104, 110 Stat. 56 (1996).

[3] 5 U.S.C. §701, *et seq.*

[4] 42 U.S.C. §4321, *et seq.*

[5] 42 U.S.C. §12101, *et seq.*

[6] 42 U.S.C. §3601, *et seq.*

[7] An electromagnetic field ("EMF") is a field created by electric and magnetic components emitted by moving charges. The interaction between the electric and magnetic fields creates "energy" or "radiation" which is propagated by waves moving through space at the speed of light. Electromagnetic waves/frequencies differ by the number of wave-cycles per second and are generally grouped by frequency ranges, which include, Extra Low Frequencies ("ELF"), radio waves (frequencies), microwave, infrared, visible light, ultraviolet, X-rays and gamma rays. Radio frequencies ("RF") have a wave-cycle between 3 kilohertz and 300 gigahertz. The FCC has direct statutory authority over RF, and indirect authority over EMFs outside the radio portion to the extent it impacts authorized RF use.

[8] 1,000 Hz is a kilohertz ("KHz"). 1,000,000 Hz is a megahertz ("MHz"). 1,000,000,000 is a gigahertz ("GHz"). For example, one Wi-Fi carrier wave frequency is 2,450,000,000 Hz, or 2.45 GHz.

"modulation." Modulation places additional "mini"-waves on the RF carrier wave. Pulsation injects "bursts" or turns the signal on/off. Different technologies have their own protocols or "code." Two devices using the same code can "communicate" and exchange information. These manipulations of the RF carrier wave result in complex and versatile signals that are biologically active.

RFs emit "non-ionizing" radiation ("RFR") because they lack sufficient energy to pull electrons from atoms and molecules. Each RF wave, however, still radiates energy that is absorbed by biological tissue. The FCC's safety regulations protect only from emissions that are so high they create a heating or "thermal effect" because of "the body's inability to cope with or dissipate the excessive heat."[9] However, the Commission's regulations do not recognize or prevent any biological responses to non-thermal pulsed and modulated RF/EMF emissions.[10] This failure to account for non-thermal impacts can lead or contribute to health problems and diseases.

The FCC regulations use the Specific Absorption Rate to measure thermal responses to devices located within 20 cm from the body, like cell phones ("near

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[9] *Id.* FCC, OET Bulletin 56, at 6-7 (August 1999) ("OET 56"), https://tinyurl.com/y5mbsymn.

[10] *Id.* at 8.

field"). Specific Absorption Rate measures the absorption of RF energy in tissue (measured in grams) over a specified duration (minutes). Exposure is averaged over 30 minutes. 47 C.F.R. §1.1310. The Specific Absorption Rate limits for "general population" are 0.08 W/kg, averaged over the whole body; a peak spatial Specific Absorption Rate of 1.6 W/kg, averaged over any 1 gram; of tissue and 4 W/kg for extremities. Maximum Permitted Exposure is used for whole-body exposure from sources located farther than 20 cm, like cell towers ("far field"). Maximum Permitted Exposure is derived from Specific Absorption Rate and measures power per area. It is frequency dependent and ranges between 200-1,000 $\mu W/cm^2$ (microwatts per square centimeter). 47 C.F.R. §1.1310(b).

The health regulations only prevent thermal effects from short term exposures to one source, and they use extensive averaging. They do not protect against the biological effects of long-term exposure or exposure from multiple sources. They do not protect against pulsation or modulation. They do not provide for sensitive or vulnerable populations.

B. Governing Statutes and Regulations

1. Communications Act

The United States controls "all the channels of radio transmission." 47 U.S.C. §301. The FCC oversees spectral assignments, approves devices and

facilities, and prevents interference. 47 U.S.C. §§302a, 303, 305, 306, 307, 321. The FCC is charged with "promoting safety of life and property" and the environment, and these responsibilities stand on equal ground with utility. *See* §§151, 154(n), 254(c)(1)(A), 324, 332(a)(1), 336(h)(4)(B), 925(b)(2)(C), 1455(a)(3). Section 324 requires licensees to "use the minimum amount of power necessary to carry out the communication desired." The Commission's regulations must contain "adequate safeguards of the public health and safety." *See* H.R. Report No. 104-204, p. 94. The FCC must serve the "public interest," including consideration of utility and public health and safety. *KFKB Broad. Ass'n v. Fed. Radio Com*., 47 F.2d 670, 671-672 (D.C. Cir. 1931); *see also Banzhaf v. FCC*, 405 F.2d 1082, 1096 (D.C. Cir. 1968) (public interest indisputably includes public health).

2. FCC's Safety Regulations

The FCC initially adopted safety regulations in 1985 as part of the FCC's efforts to fulfill its obligations under NEPA. Section 704(b) of the Telecommunications Act of 1996 ("TCA") required the FCC to update the exposure limits to provide nationwide, uniform regulations, while protecting

human health and the environment.[11] The regulations were to provide "adequate safeguards of the public health and safety"[12] *Farina v. Nokia, Inc.*, 625 F.3d 97, 130 (3d Cir. 2010) (*citing* TCA legislative history demonstrating that "[p]rotecting public safety is clearly within the [FCC's] mandate"). Only then would the future provision of wireless services be "compatible with legitimate public health, safety and property protections."[13]

The *Inquiry*[14] noted that the FCC's "authority to adopt and enforce [RF/EMF] exposure limits beyond the prospective limitations of NEPA is well established" and cited various statutory bases for developing and updating the RF regulations. According to the FCC, these include TCA §704(b), its legislative history and 47 U.S.C. §151.[15] The FCC applies the RF/EMF limits just like any other public health and safety regulation. *Farina*, 625 F.3d at 107.

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[11] Pub. L. No. 104-104, 110 Stat. 56, 152 (1996). The FCC had opened proceedings in 1993 to update those regulations. FCC, *In the Matter of Guidelines for Evaluating the Environmental Effects of Radiofrequency Radiation*, Report and Order, 11 FCC Rcd 15123, at 15125-15127 (Aug. 1, 1996).

[12] See H.R. Report No. 104-204, pp. 94-95.

[13] *Id.* at 95.

[14] In the Matter of Reassessment of Federal Communications Commission Radiofrequency Exposure Limits, 28 FCC Rcd 3498, at 3531 n.176 (March 29, 2013).

[15] *Id.*

The 1996 regulations,[16] promulgated in response to the congressional directive, protect against thermal effects. Even though non-thermal emissions have biological effects, the FCC did not account for them.[17] Nor do the regulations consider effects from long-term and/or peak exposure, or modulation and pulsation. They do not provide for individual susceptibility and vulnerable populations.

II. Administrative Record

A. 2013 Inquiry

In 2013, the FCC opened the *Inquiry*:

> [G]iven the fact that much time has passed since the Commission last sought comment on exposure limits, as a matter of good government, we wish to develop a current record by opening a new docket.[18]

The FCC noted that much had changed since 1996, both in terms of RF/EMF science and wireless technology:

> We recognize that a great deal of scientific research has been completed in recent years and new research is currently underway, warranting a comprehensive examination of this and any other relevant information. Moreover, the ubiquity of device adoption as well as advancements in technology…warrant an inquiry to gather

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[16] In the Matter of Guidelines for Evaluating the Environmental Effects of Radio Frequency Radiation, Report and Order, 11 FCC Rcd 15123 (1996).

[17] OET 56, at 8, https://tinyurl.com/y5mbsymn.

[18] 28 FCC Rcd at 3570.

> information to determine whether our general regulations and policies limiting human exposure to [RF/EMF] are still appropriately drawn.[19]

The FCC conceded that there were "considerable differences of opinion about the biological effects of low level (*i.e.*, non-thermal or athermal) and long-term (chronic) exposure to [RF/EMF]."[20] The FCC also noted a "lack of scientific consensus about the possibility of adverse health effects at exposure levels at or below our existing limits."[21] Recognizing its "fundamental responsibility to provide for the appropriate protection of consumers, workers, and other members of the public," the FCC stated that the *Inquiry* "open[ed] a science-based examination of the efficacy, currency, and adequacy of the" RF/EMF limits.[22] The FCC invited public comment on a host of issues.[23]

B. Overview of Administrative Record

The Commission was deluged with submissions over the next six years. Hundreds of expert scientists, doctors, and public health experts submitted

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[19] *Id.*; *see Id.* at 3574-3575 (seeking comment on currently available research and noting an "increase in numbers and usage of fixed transmitters and portable and mobile devices, as well as changes in usage and consequent exposure patterns").

[20] *Id.* at 3571.

[21] *Id.* at 3502.

[22] *Id.* at 3571.

[23] *Id.* at 3574, 3577-3578, 3585.

thousands of peer-reviewed studies and medical reviews indicating the 1996 regulations are based on obsolete assumptions, do not protect the public in general, and are particularly harmful to sensitive sub-populations. In addition, commenters submitted over 250 individual reports of sickness from FCC-authorized RF/EMF levels. Some supplied documentary support, including medical diagnoses. These individuals detailed devastating personal and financial harm and disruption to their lives from RF/EMF and their inability to live or participate in today's society.

C. Major Peer-Reviewed Scientific Studies, Reports and Appeals

The comments submitted in the FCC proceeding identify several peer-reviewed scientific studies and reports bearing on the effects of RF/EMF:

1. Monograph by the International Agency for Research on Cancer (IARC)

The *Inquiry* invited comments on a Monograph by the International Agency for Research on Cancer (IARC), an intergovernmental agency within the World Health Organization (WHO).[24] The IARC Monograph, published in 2013, was prepared by a working group of 31 scientists from 14 countries.[25] The Monograph

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[24] *Id.* at 3575; IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, *Non-Ionizing Radiation, Part 2, Electromagnetic Fields*, Volume 102 (2013) ["the Monograph"]. JA_.

[25] JA_.

reviewed many scientific studies concerning the carcinogenicity of RFR.[26] It found that children are significantly more susceptible to RFR exposure than adults[27] and that "[p]ositive associations have been observed between exposure to radiofrequency radiation from wireless phones and glioma, and acoustic neuroma."[28] It reclassified RF/EMF as "possibly" carcinogenic to humans.[29] While IARC found sufficient epidemiological evidence, it did not at the time classify RF as a "probable" or "known" carcinogen because not enough animals studies existed to do so at the time.[30] The *Inquiry* invited comments on the Monograph and several parties responded but the *Order* never reviewed the findings in the IARC Monograph or addressed those comments.[31]

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[26] JA_@33-34.

[27] *Id.* at 406.

[28] *Id.* at 419.

[29] *Id.*

[30] JA_.

[31] 28 FCC Rcd at 3575.

2. National Toxicology Program (NTP) Study

A *National Toxicology Program (NTP) Study* from 2018 ("NTP Study")[32] found evidence of malignant tumors in rats after years of exposure to RFR[33] and concluded that the type of brain cancer observed is similar to a type of brain tumor linked to heavy cellphone use in some human studies, specifically citing to the IARC Monograph.[34] Another animal study published by the Ramazzini Institute in 2018 further supports the NTP findings.[35] Thus, the NTP and Ramazzini studies provided the information IARC previously lacked. As numerous commentators have noted, if these and other results had been available in 2011, IARC would likely have classified RF/EMF as a probable or definite human carcinogen.[36] In rejecting the relevance of animal testing for humans, which constitutes the foundation for drug and chemical evaluation, the FDA discounted the relevance of the NTP experiments to humans.

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[32] 34 FCC Rcd at 11692 n.30 (*citing* https://www.niehs.nih.gov/health/materials/cell_phone_radiofrequency_radiation_studies_508.pdf).

[33] *Id.*

[34] *Id.*

[35] 34 FCC Rcd at 11693 n.33.

[36] JA_; JA_@527; JA_.

3. The BioInitiative Report ("BIR")

The BioInitiative Report ("BIR") is an extensive analysis of the scientific evidence of RF/EMF by the BioInitiative Working Group —29 independent world-leading RF/EMF scientists and public health experts. The BIR reviewed over 3,800 studies and concluded that non-thermal pulsed/modulated RF/EMF has a panoply of adverse effects at levels well below the FCC's exposure limits. The 2007 version was the basis for a 2009 European Parliament Resolution[37] on "[h]ealth concerns associated with EMF." Numerous commenters referred to BIR and the work of several members of the BIWG submitted individual work in the record.[38] BIR was updated in 2012, 2014, and 2017. Petitioner Professor David Carpenter, MD, is a co-editor of the BIR.

4. Other Appeals

The Commission also received appeals and recommendations to reduce RF/EMF exposure from at least 30 scientific, medical, and health organizations and groups,[39] including:

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[37] JA_@22.

[38] JA_.

[39] JA_.

i. The 2002 Frieburger Appeal,[40] signed by 1,000 doctors, asserted that RF/EMF is a "fundamental trigger" for "a dramatic rise in severe and chronic diseases." "[T]herapeutic efforts" are becoming "less effective" and its growing uniqueness "prevents the patient's thorough recovery."

ii. The California Medical Association , in a 2014 Resolution,[41] highlighted conditions consistent with Radiation Sickness[42] and asserted that current limits are outdated and inadequate.

iii. The American Academy of Environmental Medicine stated in 2013 that "there has been an "exponential increase" in "radiofrequency induced disease and hypersensitivity."[43]

iv. Over 200 scientists from 42 countries who collectively published over 2,000 peer-reviewed RF/EMF studies sent an appeal letter to the United Nations and WHO in 2015, stating: "Based upon peer reviewed,

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[40] JA_.

[41] JA_.

[42] Radiation Sickness is also sometimes called "Microwave Sickness," "Electro-sensitivity", or "Electromagnetic Hyper-Sensitivity" ("EHS"). All these describe a syndrome where the injured develop symptoms as a result of RF/EMF exposure. This brief predominantly uses "Radiation Sickness," which is the Centers for Disease Control's usage.

[43] JA_.

published research, we have serious concerns regarding the ubiquitous and increasing exposure to…wireless devices." They listed several adverse health effects, called for biologically-based RF/EMF guidelines, and urged that "medical professionals be educated about the biological effects of electromagnetic energy and electromagnetic sensitivity."[44]

v. In 2017, 190 doctors and scientists presented a similar appeal. They wrote that thermally based regulations are "obsolete" and "new safety standards are necessary."[45]

vi. A Council of Europe report concluded that guidelines should cover non-thermal effects.[46] Numerous other organizations, scientific conferences, appeals and medical groups support this position.[47]

The *Order* did not address or acknowledge any of these significant materials.

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[44] JA_.

[45] JA_.

[46] JA_.

[47] JA_.

D. Non-Thermal Causal Mechanism

The *Order* states "no scientific evidence establishes a causal link between wireless device use and cancer or other illnesses."[48] The BIR noted this claim was "patently false."[49] Over fifty scientists and professors directly refuted this contention. It "reflects a lack of…understanding of the scientific literature. More than a thousand studies…show biological mechanisms of effect that do not involve heat."[50]

E. Oxidative Stress

Oxidative Stress is a known causal "mechanism of harm" that can lead to cancer, non-cancer illnesses, and DNA damage. Oxidative Stress occurs when the body is unable to counteract or detoxify free radicals through neutralizing antioxidants. A "meta-analysis" of 100 studies showed that 93 found non-thermal RF/EMF induces Oxidative Stress. Oxidative Stress "should be recognized as one of the primary mechanisms" of RF/EMF injury."[51] The 2019 BIR collected 203 RF/EMF studies showing Oxidative Stress.[52] BIR also provided evidence of

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[48] 34 FCC Rcd at 11695.

[49] JA_, p. 14.

[50] JA_.

[51] JA_.

[52] JA_; JA_.

RF/EMF Oxidative Stress-induced downstream mechanisms, including damage to the mitochondria,[53] the energy producer for cells, and the Blood-Brain-Barrier ("BBB").

The BBB prevents toxins in the blood from entering the brain and causing neurological damage. A Navy-funded study by Dr. Alan Frey was the first to show RF/EMF can damage the BBB.[54] Dozens of studies confirmed his findings, including studies by Dr. Professor Leif Salford, Professor of Neurosurgery and the author of the BIR section on BBB.[55] BIR concluded that BBB leakage can occur with exposures 1,000 times lower than FCC limits, at levels similar to holding a mobile phone at arm's length.[56] BBB damage can explain the headaches suffered by many from wireless exposure.[57] A 2015 study revealed that 13%-28% of Radiation Sickness subjects had BBB leakage biomarkers.[58]

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[53] JA_; JA_@26, 84, 85, 103, 140, 189, 190, 206, 232, 256, 307, 379, 397, 452, 454, 525.

[54] JA_.

[55] JA_.

[56] JA_@10.

[57] JA_@14

[58] JA_@4.

F. Modulation/Pulsation, Peak, Simultaneous and Cumulative Exposure Risks

EPA-retired scientist and BIR author Dr. Carl Blackman concluded that modulation may be more important for guidelines than RF levels.[59] BIR Section 15[60] analyzes 250 studies and shows that the exclusive focus on radiation levels is inadequate because it does not take frequency, modulation, duration or dose into account. Dr. Frey, whose own studies on auditory effects and BBB damage showed the effects of pulsation, concurs: "[t]he issue is not whether cell phones are safe; it is whether the particular frequencies and modulations that the FCC assigned to cell phones, based on faulty assumptions, are safe."[61]

A meta-analysis showed that almost 100% of studies that use actual pulsed/modulated mobile exposures showed effects. The authors observed that "[l]iving organisms seem to have decreased defense against environmental stressors of high variability."[62] BIR and other scientists also noted that frequency-specific, amplitude-modulated and pulsed EMFs have long been used for medical

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[59] JA_@36, 522.

[60] JA_.

[61] JA_.

[62] JA_.

purposes to treat bone fractures, advanced carcinoma,[63]and chronic pain.[64] These treatments would not work if human bodies were unaffected by non-thermal pulsed and modulated emissions.

The *Order* did not address this issue.

G. Exposure→Mechanism→Disease

RF/EMF exposure affects human biology and negatively impacts important bodily mechanisms. This can cause multiple diseases.

1. Cancer

Consistent with the NTP and Ramazzini studies, many commenters submitted extensive evidence demonstrating an increased risk of several forms of cancer from RF/EMF exposure. IARC classified RF/EMF as a 2B (possible) carcinogen in 2011. In 2018, Professor of Oncology and Cancer Epidemiology Lennart Hardell, MD PhD, a BIR author and a past IARC committee member, noted that, based on the NTP findings "there is clear evidence that RF radiation is a human carcinogen, causing glioma and vestibular schwannoma (acoustic neuroma)."[65]

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[63] JA_.

[64] JA_.

[65] JA__@171, 366.

A literature survey by Petitioner Dr. Paul Dart in 2013 concluded that "epidemiological research shows that greater than 10 years of cell phone use" significantly increases risk of ipsilateral brain tumors (glioma) and that the risk is greater in individuals who started cell phone use as children.[66] Dr. Dart also reviewed studies showing increased cancer risk from exposures to cellular towers, with proximity a key factor.[67] And a 2011 review of almost one-hundred studies on long-term exposure to RF/EMF, including from cell phones and cellular towers, found it "promote[s] cancer development."[68]

These authors also reviewed studies investigating potential mechanisms that could lead to cancer. This research demonstrates that RF/EMF exposures below thermal levels lead to DNA breakage and chronic inflammation that increases the activity of free radicals (oxidative stress).[69] Accordingly, all three submissions concluded that current regulations based on thermal heating should be re-assessed for non-thermal effects.[70]

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[66] JA_@61.

[67] *Id.* at 38-41.

[68] JA_@66-67.

[69] JA_@31-35; JA_@67-68.

[70] BioInitiative Working Group, *Use of Wireless Phones and Evidence for Increased Risk of Brain Tumors*, 2017 Supplement (Hardell),

Aside from the NTP study, the *Order* does not address any cancer-related submissions.

2. Reproductive

The BIR documents that "[s]everal international laboratories have replicated studies showing adverse effects on sperm quality, motility, and pathology in men who use and particularly those who wear a cell phone, PDA, or pager on their belt or in a pocket."[71] "[O]ther studies conclude that usage of cell phones, exposure to cell phone radiation, or storage of a mobile phone close to the testes of human males affect sperm counts, motility, viability and structure."[72] In addition, "animal studies have demonstrated oxidative and DNA damage, pathological changes in the testes of animals, decreased sperm mobility and viability, and other deleterious damage to the male germ line."[73]

Commenters raised these concerns in the *Inquiry.* EHT noted there is strong evidence that exposure to RFR reduces fertility in males and females." Increased usage of "mobile phones and increased exposure coming from WiFi, smart meters

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https://bioinitiative.org/wp-content/uploads/2017/11/Hardell-2017-Sec11-Update-Use_of_Wireless_Phones.pdf.; JA_@62; JA_@67-68.

[71] BIR, *Conclusions Table 1-1*, https://bioinitiative.org/conclusions/

[72] *Id.*

[73] *Id.*

and other wireless devices has been paralleled in time with male hypofertility and sperm abnormalities in semen." As shown by some studies "these effects may be related to holding an active wireless laptop in a man's lap or having an active mobile phone on their belt."[74]

3. Neurological

RF/EMFs, especially when pulsed and modulated, generate neurological responses. BIR analysis involving 222 studies [75] and another detailed science review [76] confirmed this phenomenon and showed effects on sleep, memory, learning, perception, visual, auditory, and motor abilities. Hippocampus studies explain the memory and learning effects.[77] Swiss government and University of California, Berkeley, studies on adolescents showed adverse effects on memory and cognitive functions and cumulative effects.[78] Human EEG studies record effects on brain physiology, alpha brain waves, cortical activity, brain

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[74] JA_@646.

[75] JA_; JA_; JA_.

[76] JA_.

[77] JA_@19.

[78] JA_.

synchronization, sleep and epileptic seizures.[79] Forty studies indicate Oxidative Stress is a causal mechanism for some of these effects.[80]

The *Order* did not mention any of this information.

4. Prenatal and Perinatal Complications and Children

The submissions in the record demonstrate adverse effects from RF/EMF during the prenatal period, through childhood, including teenage years. Both animal and human studies identify prenatal RF/EMF exposure as a risk factor for subsequent ADHD and attention/behavioral problems.[81]

Professor Hugh Taylor, MD, Chair of Obstetrics at Yale School of Medicine, performed a 2012 study showing that fetal exposure to RF/EMF permanently affects brain neurodevelopment, memory and behavior in mice, and can lead to ADHD.[82] The prenatal exposure resulted in brain electrical signaling changes throughout their lifetime.[83] This filing cites to 27 other studies.[84]

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[79] JA_@63. JA_.

[80] JA_@6, 20.

[81] JA_.

[82] JA_.

[83] JA_@4.

[84] JA_.

Professor Suleyman Kaplan, Editor of the *Journal of Experimental and Clinical Medicine*, wrote the FCC that chronic exposure can have long-term brain morphology effects. He detailed four animal studies showing that one hour a day prenatal RF exposure decreased brain cells in regions responsible for memory, attention, and learning.[85] Twenty-six studies from 2008-2017 show perinatal exposure affects nervous system development and function. Five studies indicate the cerebellum is especially vulnerable because it contains embryonic neural stem cells that play a critical brain development role.[86]

The human evidence confirms these findings. UCLA studies on 13,159 women,[87] 28,745 children[88] and a cohort of 5 studies on 83,884 women[89] revealed that children whose mothers used cell phones during pregnancy had more emotional problems (25%), hyperactivity (35%), and conduct problems (49%). Clinical evidence shows that removing exposure to wireless RF reduces and/or eliminates behavioral problems in children.[90]

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[85] JA_.

[86] JA_@7.

[87] JA_@45.

[88] JA_.

[89] JA_@375.

[90] JA_.

Studies on 1,300 adolescents indicate 1 year of cell phone exposure adversely affects their memory.[91] Testimonies in the record discuss children that have developed Radiation Sickness.[92]

Dr. Kaplan explained that children are now exposed to RF/EMF radiation while *in utero*. They begin using RF-enabled devices earlier and will have longer lifetime and cumulative exposures than previous generations. Environmental insults during the early growth stages can have profound impacts later in life.[93] Children also have less ability to remove themselves from harmful environments.

John Wargo, Ph.D., Yale Professor of Environmental Risk and Policy wrote "[t]he scientific evidence is sufficiently robust." "The weight of the evidence supports stronger …regulation by the federal government."[94]

For these reasons, The American Academy of Pediatrics , an organization of 60,000 pediatricians, the Maryland State Children's Environmental Health And Protection Advisory Council[95] and numerous experts urged the FCC to develop

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[91] JA_; JA_@63.

[92] JA_; JA_.

[93] JA_.

[94] JA_.

[95] JA_@51; JA_.

regulations that reflect both the biological sensitivity of children and the changes in usage patterns that exacerbate susceptibility.[96]

The *Inquiry* invited comments on whether the RF/EMF regulations are appropriate for device use by children notwithstanding the representation in IEEE Std 1528–2003 that the standard adopted by the FCC "represents a conservative case for men, women, and children."[97] In response, commenters submitted scientific evidence that RF limits are not protective of children because children not only have more intense exposures than adults but more importantly that children are uniquely sensitive due to their developing brains[98] (vulnerabilities the FCC did not address).

H. The Human Evidence-Radiation Sickness

The *Order* ignores substantial evidence of human sickness from RF/EMF. Considerable evidence came directly from people who had developed Radiation Sickness.

The scientific and medical communities now understand more about the symptoms, physiological injuries, and the mechanisms of harm for Radiation

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[96] JA_; JA_.

[97] 28 FCC Rcd at 3575.

[98] JA_.

Sickness. There are diagnosis guidelines and government-approved classifications. Doctors and scientists warn that it is widespread, and the rates are growing. Courts and US agencies have recognized it.

More than 180 individuals directly advised the FCC that they[99] and/or other family members,[100] developed Radiation Sickness or described consistent symptoms. Advocacy groups supplied 72 additional individual cases[101] and referred to hundreds more.[102] Nine filings included physicians' diagnoses.[103]

Radiation Sickness describes a constellation of mainly neurological symptoms that manifest as a result of RF/EMF exposure. It is a "spectrum condition." Some experience discomfort while others are entirely debilitated.[104] The testimonies and the scientific literature recite a host of symptoms, including headaches, memory and cognitive problems, sleep problems, heart palpitations and/or increased heart rate, ringing in the ears, fatigue, skin rashes, tingling, nose

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[99] JA_.

[100] JA_; JA_; JA_.

[101] JA_; JA_; JA_;JA_; JA_.

[102] JA_

[103] JA_.

[104] JA_;JA_@6; JA_@3.

bleeds, unremitting flu like symptoms, dizziness, and burning sensations. Exposure avoidance is the only effective management treatment. *Id.*

The US uses a modified version of WHO's International Classification of Diseases Codes. The CDC uses Clinical Modification and Procedural Classification System Code T-66 for a diagnosis of "Radiation Sickness." Code W-90 recognizes that "Exposure to Other Nonionizing Radiation" can cause injury.[105]

The Austrian Medical Association issued diagnosis guidelines in 2011.[106] They were updated and improved by the European Academy of Environmental Medicine in 2016, citing 235 scientific references for symptoms, physiological damage, and mechanisms of harm.[107] These guidelines are used by doctors worldwide. Courts around the world recognize the condition.[108] *Yannon v. N.Y. Tel. Co*., 86 A.D.2d 241, 450 N.Y.S.2d 893 (App. Div. 3rd Dept. 1982) affirmed a Worker's Compensation Board finding that microwave emissions caused "microwave sickness" and death.

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[105] JA_@2; JA_@25.

[106] JA_.

[107] JA_.

[108] JA_@7-8.

California firefighters developed Radiation Sickness after a cell tower appeared on their station. They reported typical symptoms, including memory/concentration difficulties like getting lost in their hometown and forgetting basic CPR. Computer-tomography scans revealed pervasive neuron hyper-excitability.[109]

Additional studies reveal severe physiological injuries. A functional MRI[110] study and a 675-subject study both revealed impaired brain blood flow.[111] The latter identified biomarkers, and showed autoimmune antibodies (23%), BBB leakage (15-28%), Oxidative Stress (40%) and reduced melatonin (100%). Another study identified genetic predispositions.[112] Hundreds of studies show that FCC-authorized RF/EMF exposures can cause the symptoms, injuries, and mechanisms associated with Radiation Sickness.[113]

The *Order* did not address the scientific evidence on Radiation Sickness or the "human evidence." Other federal agencies, including the Navy, Army and

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[109] JA_; JA_; JA_.

[110] Magnetic Resonance Imaging scanners use RF/EMF to generate images of the organs in the body.

[111] JA_@4; JA_@437.

[112] *Id.* at 9.

[113] JA_.

NASA,[114] have. Military-declassified materials admit to "possible adverse effects on human health" and recognize modulation as a potential harm agent.[115]

In 2002, the "Access Board," an independent federal agency responsible for publishing ADA Accessibility Guidelines used by the Justice Department to enforce the ADA, recognized that "electromagnetic sensitivities may be considered disabilities under the ADA."[116] The Access Board contracted the National Institute of Building Sciences 2005 report, which concluded RF/EMF is an "access barrier" and can render buildings "inaccessible" to those with Radiation Sickness and recommended accessibility guidelines.[117]

Public exposure to RF/EMFs has exploded since 1996. Radiation Sickness is now prevalent, and it is getting worse. A 2002 survey by the State of California's Department of Health Services reported 3% are affected.[118] Surveys before 2005 found a 10% rate.[119] 190 Scientists wrote in 2017 that it may become a "worldwide

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[114] JA_; JA_@15.

[115] JA_.

[116] JA_@3.

[117] JA_.

[118] JA_@10.

[119] JA_.

pan-epidemic."[120] A European Parliament resolution found the problem is growing "exponentially."[121] Physicians also provided direct clinical evidence. Drs. Elliot and Jelter reported an increase in patients."[122]

I. Technological/Exposure Sources

1. Existing Cell Towers

Dozens of studies and individual testimonies reveal profound harms from existing cell towers.[123] A 2012 study of 1.5 years' exposure found hormonal and cell stress effects and evidence of dose-response at radiation levels 1,000,000 times lower than the FCC guidelines.[124] A telecom company study (Swisscom) found dose response and neurological effects.[125] Epidemiological studies revealed typical Radiation Sickness symptoms[126] along with negative effects on hormones, sperm,

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[120] JA_@2.

[121] JA_@2.

[122] JA_; JA_.

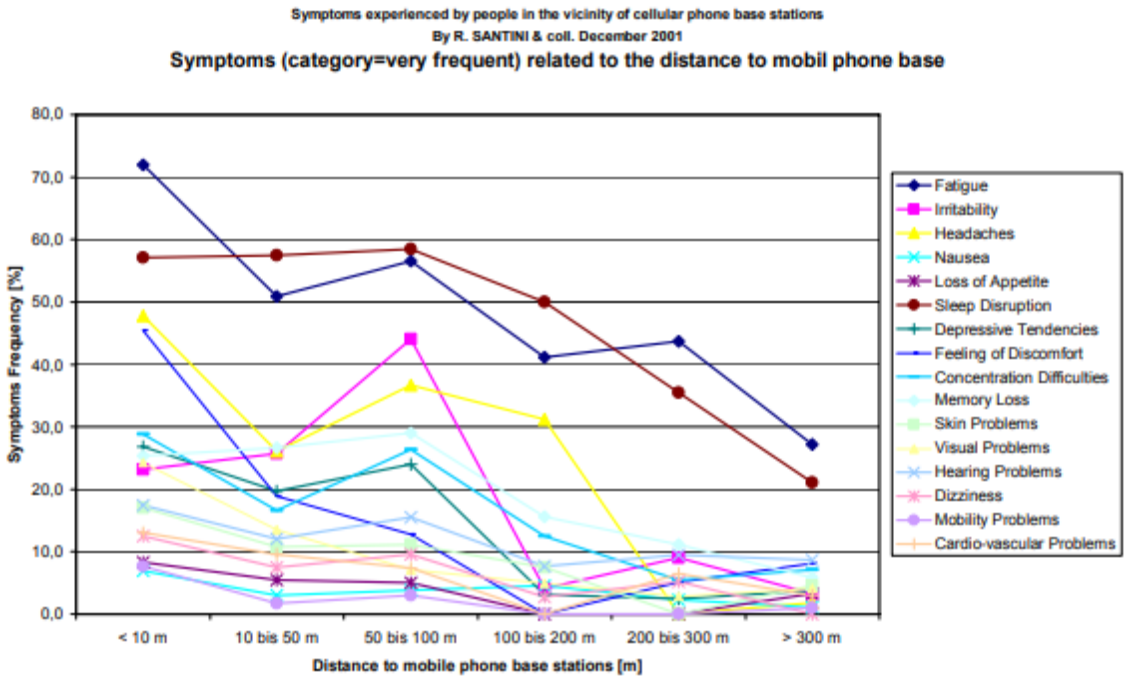
[123] JA_.

[124] JA_.

[125] JA_@9.

[126] JA_@30-34.

DNA and cancer.[127] Effects bore a direct relationship to distance from the cell tower:



Graph: Incidence (%) of Complaints by Respondents (n=530) Living in the Vicinity of Mobile Phone Base Stations as a Function of Distance

Another study indicates cell tower RF/EMF can cause antibiotic resistance, a major threat to public health.[128] A 2017 human study showed significantly higher DNA damage and Oxidative Stress. This study concluded: "[B]ase stations in the

[127] JA_.

[128] JA_@106.

residential areas…[are] silently creeping in the lives of residents"[129] BIR concurs.[130]

2. 5G Poles/Small Cells

5G (or Fifth Generation) completely changes the wireless environment and exponentially increases forced exposure to radiation. 5G is the infrastructure for the Internet of Things. It intends to wirelessly interconnect 50 billion more devices and requires at least a 1,000 times higher capacity than current infrastructure.[131] This involves a massive infrastructure intensification including 800,000 new cell towers.[132] When the 1996 RF regulations were finalized, cell towers were 50-200 feet high and often relatively far away from people.[133]

5G uses "small cells" with antenna heights limited to 50-feet.[134] They are usually installed on utility poles in public rights-of-way and are sometimes only a few feet from homes and bedrooms. Although small cells may use less power than

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[129] JA_.

[130] JA_.

[131] JA_; JA_.

[132] JA_; JA_; JA_.

[133] OET 56, at 20, https://tinyurl.com/y5mbsymn.

[134] 47 U.S.C. §1.6002(l)(1)(i).

big cell towers, they are closer to people. Radiation exposure is therefore exponentially higher.[135]

5G can operate in the lower (600 MHz), mid (2.5-4.2 GHz) and higher millimeter-wave bands (24-47 GHz) and have complex modulations. A growing body of evidence indicates 5G deployment and accompanying 4G densification can cause DNA damage, cancer, harm to bees, trees, cell membrane effects, antibacterial resistance, reduced immunity, neurological effects, reproductive effects, and interaction with sweat glands and the evidence leaves little doubt that adverse effects will ensue especially with more complex modulations.[136]

3. Cellphones

Over 95% of Americans own cellphones, with the share of smart phones at 81%, and other wireless devices, including laptops, also widely used.[137] The public "receives the highest exposure from transmitters close to the body."[138] Depending on design and positioning, a cellphone held close to the ear "can result in high

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[135] JA_@487; JA_@1; JA_@490; JA_@1; JA_@1.

[136] JA_; JA_@18, 27, 41, 72, 217.

[137] Pew Research Center, Mobile Fact Sheet, https://www.pewresearch.org/internet/fact-sheet/mobile/.

[138] JA_@34.

specific rates of absorption (SAR) of [RF] energy in the brain."[139] A hands-free device may lower exposure of the brain but "may increase exposure to other parts of the body."[140]

Specific Absorption Rate values reflected in the 1996 regulations are based on "a handful of animal studies that were used to determine the threshold values of Specific Absorption Rate for the setting of human exposure guidelines…."[141] These studies demonstrated disruption of behavior from thermal (or tissue heating) effects after short term exposure.[142]

Today's cellphones differ from the ones in use when the RF/EMF limits were adopted. They may contain several antennas including for the 2G, 3G, 4G frequency bands and Wi-Fi.[143] Modern technology also allows wireless devices to operate with 5G technology at much higher frequencies than when the 1996 regulations were adopted.[144]

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[139] *Id.*

[140] *Id.*

[141] JA_@373, 379.

[142] *Id.*

[143] NTP Technical Report on the Toxicology and Carcinogenesis Studies in Hsd: Sprague Dawley SD Rats Exposed to Whole-Body Radio Frequency Radiation at a Frequency (900 MHz) and Modulations (GSM and CDMA) Used by Cell Phones at 7 (November 2018), https://www.niehs.nih.gov/ntp-temp/tr595_508.pdf.

[144] *Id.* at 19.

The Commission failed to address either the change in technology or the available scientific data relating to wireless devices. The FCC failed to consider the BIR, IARC Monograph, the various international appeals from scientists, and numerous publications and studies relating to human health risks from wireless device use.

Petitioner EHT presented epidemiology studies published after the initial IARC 2011 categorization of RFR as a possible human carcinogen (Group 2B).[145] Based on studies in Sweden, France, the UK and other countries, these epidemiological studies found evidence sufficient to consider RFR as a *probable* human carcinogen (Group 2A) and, when supplemented with other studies including the Ramazzini and NTP studies, there was sufficient epidemiological evidence to "upgrade the IARC categorization of RFR to Group 1, carcinogenic to humans."[146]

Nasim and Kim examined the 5G downlink transmission to wireless devices and found human RFR exposure could "far exceed the Commission's SAR limit for frequencies under 6 GHz."[147] RFR safety concerns are raised by beam forming,

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[145] JA_.

[146] *Id.* at 9.

[147] JA_@1.

greater bandwidth, and closer proximity to transmitters delivering a signal that far exceeds 4G systems.[148]

A study by the Director of the National Institute on Drug Abuse shows through brain imaging that the glucose levels in the brain are significantly higher–especially in the areas closer to the antennae–after cellphone use.[149] A study of non-thermal effects of high frequency radiation from cellphones and wireless devices on the eyes finds reversible and irreversible ocular changes also went unaddressed.[150] Yet another unaddressed health concern was the *cumulative effects* of RFR exposures from multiple wireless devices, including wi-fi and smart meters.[151]

Numerous cell phones studies confirm neurological effects from cell phones as shown in a compilation of 700 cell phones studies' abstracts.[152] Fifteen EEG studies published between 2007-2017 found effects from 2G, 3G and 4G handset emissions.[153]

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[148] JA_@2.

[149] JA_@2.

[150] JA_@489.

[151] *See e.g.* JA_@7.

[152] JA_.

[153] JA_; JA_; JA_.

A 2013 functional MRI human study exposed 18 participants to a 4G cellphone located 1 centimeter away from the right ear for 30 minutes.[154] Brain images revealed human brain neural activity in both sides of the brain, even though the exposure was on one side, indicating a neural mechanism for the effects on the remote side of the brain. This can only be explained by non-thermal effects. None of the health issues raised in this and other studies were considered.

4. Wi-Fi

Wi-Fi is another example of effects from chronic exposure and pulsation/modulation. Human and animal studies confirmed profound effects from Wi-Fi and/or the 2.45 GHz frequency it uses as a carrier wave.[155] For example, a study observed deleterious effects on growing testes.[156] A 2019 meta-analysis[157] of 23 Wi-Fi studies, including 5 on humans, concluded Wi-Fi is hazardous to male sperm count, motility, and DNA integrity. Twenty-two studies published between 2016-2019 strengthen previous findings.[158]

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[154] JA_@98.

[155] JA_; JA_@181; JA_; JA_@6.

[156] JA_.

[157] JA_@6.

[158] JA_@6, 26, 167, 182, 190, 229, 235, 236, 246, 364, 293, 298, 371, 372, 375, 396, 420, 456, 482, 495, 500, 514.

Swisscom's US patent application for "safer" Wi-Fi admitted that "the influence of "electrosmog" on the human body is a known problem." "Non-thermal pathway" "impacts can be considerable" and "will continue to increase in the future for many people." RFR can cause DNA damage that "lead[s] to increased cancer risk."[159]

5. Smart Meters

The regulations' method of averaging the exposure during compliance testing obscures real exposure levels and pulsation effects. "Smart Meters" illustrate the problem. In a response to a comment, the FCC claimed that "the devices normally transmit for less than one second, a few times a day and consumers are normally tens of feet or more from the meter face…"[160] Many commenters corrected this assertion. Fifty experts in a letter "Correcting the Gross Misinformation"[161] explained that a single smart meter can emit up to 190,000 intense bursts (or pulses) each day. The bursts can be two and a half times above the FCC's limits. People can receive aggregate exposure greater than from a cell phone. These findings were confirmed by a technical report and other expert

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[159] JA_@89.

[160] JA_.

[161] JA_.

submissions.[162] People can sleep a foot away from a meter or be close to apartment complex meter banks.[163] The cumulative exposure is never measured.[164]

These erratic bursts/pulses create a bioactive on/off effect. One study of a physician with Radiation Sickness showed symptoms caused by the off-on, on-off rather than intensity and concluded that "chronic exposure to low RFR can cause even greater harm than an acute exposure to high levels."[165] The BIR pointed out the same issues.[166] Petitioner Paul Dart, MD, and 4 other MDs provided an 87-page review explaining why Smart Meters pose a significant risk to public health. He submitted additional supporting analyses addressing chronic exposure, electro-sensitivity, DNA damage, cancer, brain tumors, infertility and mechanisms of harm.[167] American Academy of Environmental Medicine referenced a peer-reviewed paper with 92 case studies[168] on smart meters' health effects.

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[162] . JA__; JA__; JA__; JA__.

[163] JA_.

[164] JA_; JA_.

[165] JA_.

[166]JA_.

[167] JA_.

[168] JA_.

Many individuals testified to horrible injuries by smart meters and the devastating impact on their lives.[169] The *Order* failed to mention any of this even though the *Inquiry* expressly asked about pulsation-related or other special issues.

J. Additional *Inquiry* Issues

1. Cell Phone and Wireless Device Testing

Cellphones and handheld wireless devices held close to the body must be tested and certified to ensure compliance with the FCC Specific Absorption Rate limits. The 1996 regulations stated that "portable devices shall be tested…based on 'standard' operating conditions or positions."[170]

Numerous submissions criticized the FCC compliance tests. First, the test does not reflect different physical characteristics based on age or size. Second, the test uses a separation distance and does not simulate the way people actually use phones and wireless devices—such as in positions against the body. Third, and most importantly, the testing regime's Specific Absorption Rate measurement is thermal-based, *i.e.* focused on heating only.

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[169] JA_.

[170] 11 FCC Rcd at 15149. In 1997, the FCC issued Bulletin 65, consisting of voluntary "guidelines and suggestions" for implementing the testing regime. 1997 FCC LEXIS 4631 at 1 (Bulletin 65).

In fact, the health hazards associated with mobile phone fields have nothing to do with heat, so Specific Absorption Rate is irrelevant to understanding health hazards. While the Commission at para. 15 of the Order maintains that Specific Absorption Rate testing is "conservative" for all ages, this has no bearing on whether RFR causes biological harm. The Specific Absorption Rate measurement also does not account for the unique characteristics of an information carrying wave that can moderate the biological impacts. In particular, the type of modulation, the pulse rate and polarization are not accounted for in Specific Absorption Rate or Maximum Permitted Exposure power density measurements.

While the 1996 regulations refer to testing of "human tissue," in practice, authorized testing facilities use a standardized anthropomorphic mannequin to test cellphones.[171] The standardized anthropomorphic mannequin models an adult male over six feet tall, weighing 220 pounds and transmits RF signals to a plastic shell containing a homogenous liquid with undifferentiated electrical properties (in lieu of actual human tissue).[172] A temperature probe measures the heat at various points in the liquid. The FCC has acknowledged other testing methodologies may be

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[171] 28 FCC Rcd at 3523.

[172] JA_@9.

more accurate for actual people of different sizes and ages and human tissue with non-uniform electrical properties but does not require their use.[173]

The agency-sanctioned testing procedures[174] require cellphones to be tested simulating use against the ear (not the skull) and "against" the body (torso), but with a separation distance up to 2.5 cm allowed when tested against the body. These procedures assume devices are carried and used away from the body in accessories such as "belt clips and holsters."[175] The FCC has recognized that these requirements may not identify the maximum exposure under *actual* use with zero separation (*e.g.,* in a pocket).[176]

Furthermore, the Commission maintains that the SAR Specific Absorption Rate limits provide a large margin of safety because they "are set at a level on the order of 50 times below the level at which adverse biological effects have been observed in laboratory animals as a result of tissue heating…"[177] Notwithstanding the presumed safety margin, the 2012 GAO Report recommended that the FCC

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[173] 28 FCC Rcd at 3523.

[174] In 2015, Bulletin 65 was superseded by FCC KDB publication 447498 "RF Exposure Procedures and Equipment Authorization Policies for Mobile and Portable Devices," https://tinyurl.com/jqxbklk.

[175] *Id.* at 10.

[176] 28 FCC Rcd at 3588.

[177] *Id.* at 3582.

reassess the testing requirements "in likely usage configurations, particularly when mobile phones are held against the body, and update testing requirements as appropriate."[178] The *Inquiry* acknowledged that "exposure in excess of our limits might result" in certain untested positions of use such as a phone in the pocket or in certain conditions such as in an area of low service.[179] Accordingly, the *Inquiry* asked the public to comment as to whether the body-worn separation distance should be changed or eliminated.

Subsequently, numerous parties submitted studies and comments identifying deficiencies in the certification and testing regime. Commenters demonstrated:

(a) The Specific Absorption Rate unit should be redesigned to capture non-thermal effects.[180]

(b) The standardized anthropomorphic mannequin model underestimates RF exposure in specific brain regions, especially for adults with heads smaller than the

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[178] GAO Report, Telecommunications- Exposure and Testing Requirements for Mobile Phones Should be Reassessed (July 2012) at 28, https://tinyurl.com/yyw2d8ea.

[179] 28 FCC Rcd at 3587.

[180] JA_@3 (Pong Letter); JA_@3-5 (CSCP Comments).

standardized anthropomorphic mannequin model and children,[181] and erroneously assumes all human tissue in the head contains uniform electrical properties.[182]

(c) The proximity requirements should be modified to include a "zero spacing" requirement[183] because many people today carry their devices at zero or near zero distance from their bodies.[184] Published analyses document that phones clearly exceed FCC Specific Absorption Rate limits when tested in body contact positions.[185] The FCC ignored evidence of a case study finding an association between breast cancer in women and the wearing of cellphones in bras, directly against the tissues of the breast with zero separation.[186]

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[181] JA_. For example, in 2019, Dr. Om P. Gandhi published the results of Specific Absorption Rate tests that he had conducted on 13 cellphones from different manufacturers. He found that none of the cellphones would pass the FCC's Specific Absorption Rate exposure limits when tested in positions that mimic actual use conditions, *i.e.* against the body. JA_.

[182] JA_@8.

[183] JA_@6 (Pong Reply Comments); JA_@9-10 (Environmental Working Group Reply Comments); CSCP JA_@5 (CSCP Comments); JA_@5 (CSCP Reply Comments).

[184] The Pong Research Corporation (Pong) submitted test results showing that the 1.6 W/kg standard was significantly exceeded when true "against-the-body" testing was conducted. JA_@2.

[185] JA_.

[186] JA_@4 (*quoting* West, *et al*., "Multifocal Breast Cancer in Young Women with Prolonged Contact between Their Breasts and Their Cellular Phones" 2013 *Case Reports in Medicine*).

(d) The FCC's assertion that the Specific Absorption Rate exposure limit has a 50 times safety margin for cell phone exposure limits is factually incorrect. In its Reply Comments, Pong Research Corporation demonstrates that the limit was selected arbitrarily from observations of lab rats conducted in 1980.[187] In their reply comments, EHT, Environmental Working Group and the CSCP also dispute the validity of the claimed 50-times safety margin.[188] CSCP challenged the supposed safety margin because many peer-reviewed, independently-funded studies show "negative biological effects at levels as much as 1,000 times below the current FCC exposure standard!"[189]

2. Environmental Harm

Substantial evidence in the administrative record concerns the impact of RFR on wild and domesticated animals, and therefore on the human environment. These submissions include:

(1) A July 14, 2016 "Briefing Memorandum"[190] by Dr. Albert M. Manville, II, former agency lead on avian-structural impacts — including from radiation—at

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[187] JA_@13-14.

[188] JA_@77.

[189] JA_@2.

[190] JA_.

the U.S. Fish and Wildlife Service. Dr. Manville addresses RFR impacts on wildlife, particularly migratory birds:

> There is an increasing body of published laboratory research that finds DNA damage at low intensity exposures— well below levels of thermal heating — …. This body of work would apply to all species, including migratory birds….[191]

(2) A 2010 report by an expert committee organized by the Government of India that analyzed 919 peer-reviewed studies.[192] The report found:

> Of the non-human species, impacts on birds and bees appear to be relatively more evident. Exposure to EMR field is shown to evoke diverse responses varying from aversive behavioural responses to developmental anomalies and mortality in…bees, amphibians, mammals and birds….Other wildlife such as amphibians and reptiles also appear to be at high risk with possible interference of EMF with metamorphosis and sex ratios where temperature dependent sex determination is operational.[193]

(3) A 2009 technical review of problems with reproduction, possible DNA damage, and behavioral changes in wild birds, domesticated chickens, bats, pigs,

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[191] *Id.* at 3.

[192] JA_.

[193] *Id.* at 6-7. Elsewhere, the report observes: "electromagnetic radiations are being associated with the observed decline in the population of sparrow in London and several other European cities (Balmori, 2002, Balmori, 2009, Balmori & Hallberg, 2007). In [the] case of bees, many recent studies have linked the electromagnetic radiations with an unusual phenomenon known as 'Colony Collapse Disorder'. *Id.* at 3.

mice, rats, and insects and arachnids when exposed to non-thermal RFR in various laboratory and field situations.[194]

Submissions also demonstrated adverse impacts on trees and other plant life.[195]

K. NEPA Public Comments

Commenters made clear that any re-evaluation of the 1996 RF/EMF regulations must comply with NEPA. *See infra* 74-76 (summarizing NEPA obligations). The FCC had indicated in the *Inquiry* that while NEPA may eventually apply, the FCC's obligations under the statute had not yet been triggered.[196]

Commenters disagreed with the FCC's statement and stressed the *Inquiry* required a full-blown environmental analysis (called an "Environmental Impact Statement" or "EIS").[197] Others noted an EIS is legally required where a "major

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[194] JA_ and JA_.

[195] JA_; JA_.

[196] JA_@6.

[197] JA_@2; JA_@2; JA_@4; JA_@2-3.

Federal action significantly affect[s] the quality of the human environment." *Id.* (*see* 42 U.S.C. §4332).[198]

The *Order* did not address these submissions or explain why an EA or EIS was not completed.

SUMMARY OF ARGUMENT

1. The fourteen Petitioners in this consolidated appeal have standing to challenge the *Order*. All four EHT Petitioners and all nine individual CHD Petitioners are a "party aggrieved" under the Hobbs Act. 28 U.S.C. §2344.

2. All fourteen Petitioners have standing under Article III of the U.S. Constitution because the *Order* caused each of them particularized and concrete injury-in-fact that would likely be redressed by a favorable decision. *Humane Soc'y of the U.S. v. Vilsack*, 797 F.3d 4, 8 (D.C. Cir. 2015). The Petitioners identify and describe numerous and varied negative professional and/or personal impacts of the *Order* in the declarations that accompany this Brief.

3. The *Order* closes an FCC *Inquiry* begun in 2013 into whether to revise and update regulations promulgated in 1996 to protect the public health and safety and to meet the FCC's obligations under NEPA. The FCC received an

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[198] JA_@2 and JA_@1; JA_@3.

enormous number of peer-reviewed scientific and medical studies, analyses, and reports demonstrating a consensus of the scientific community that radiofrequency radiation is harmful and sometimes lethal to individuals and the environment. The record also contains numerous statements from many individuals who must live day-by-day suffering these harms.

4. The factual record in this case is strong. Yet the *Order* gives no consideration to most of the evidence presented to it. By perpetuating a situation that is proven to constitute a threat to public health and safety, the FCC has failed to meet its statutory obligation under the Communications Act to protect public health and safety.

5. The FCC has also failed to engage in reasoned decision-making and to base its decision on substantial evidence and has acted in an arbitrary and capricious manner in violation of the Administrative Procedure Act. An agency cannot lawfully ignore material evidence simply because the evidence presents a position with which the agency may disagree.

6. The decision to terminate the *Inquiry* is a major federal action that could significantly affect the human environment and, therefore, the decision was subject to the procedural requirements of NEPA. Yet the FCC did not take the *hard look* at the range of possible adverse environmental effects of its decision required

by NEPA. Nor did it consider the relevant evidence in the record of likely environmental harm. As a consequence, the agency violated NEPA.

7. The FCC also erred because it did not consider the evidence in the record of many individuals suffering the effects of unavoidable exposure to radiofrequency radiation. The agency simply ignored the ills and challenges faced by individuals who have or will develop Radiation Sickness. In so doing, the FCC begged the question of whether the agency has a responsibility under the ADA, the FHA and the United States Constitution to develop a remedy that would address the ills being visited upon these people.

STANDARD OF REVIEW

Where an FCC order is challenged under the APA, this Court's review is limited to the administrative record. 5 U.S.C. §706; 47 U.S.C. §402(g). *AT&T Corp. v. FCC*, 86 F.3d 242, 245 (D.C. Cir. 1996). It must "hold unlawful and set aside agency action, findings, and conclusions" if they are found to be "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law" or "unsupported by substantial evidence." 5 U.S.C. §706(2)(A), (E); *AT&T Corp.*, 86 F.3d at 245. Further, this Court must vacate any order that is "contrary to constitutional right, power, privilege, or immunity" or "in excess of statutory jurisdiction, authority, or limitations." 5 U.S.C. §706(2)(B), (C). While judicial

review under the APA is deferential, the Court's inquiry must be "searching and careful." *Brookings Municipal Tel. Co. v. FCC*, 822 F.2d 1153, 1164 (D.C. Cir. 1987).[199]

Moreover, as there is no private cause of action under NEPA, courts apply the APA's arbitrary and capricious standard when reviewing factual findings underlying an agency's NEPA analysis. *Sierra Club v. U.S. Army Corps of Eng'rs*, 990 F. Supp. 2d 9, 22 (D.D.C. 2013) (citation omitted); 5 U.S.C. §706. But where an agency does not apply NEPA at all, as is the case here, this failure raises a question of law, and thus this Court reviews *de novo* the agency's decision not to comply with NEPA. *Citizens Against Rails-To-Trails v. Surface Transp. Bd.*, 267 F.3d 1144, 1150-51 (D.C. Cir. 2001); *Sierra Club*, 990 F. Supp. 2d at 22-23; *Sierra Club v. USDA*, 777 F. Supp. 2d 44, 54 (D.D.C. 2011) (citations omitted).

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[199] *See Fox TV Stations, Inc. v. FCC*, 280 F.3d 1027, 1045, 1049 (D.C. Cir. 2002) (applying APA and arbitrary and capricious standard to FCC decision to close Notice of Inquiry and retain (*i.e.*, not repeal or modify) certain rules).

ARGUMENT

I. Standing

A. Hobbs Act

All EHT Petitioners and all individual CHD Petitioners submitted comments to the *Inquiry* dockets. Hertz@¶3; Brokken @¶4; Lee@¶3; Stanley@¶2; Baran@¶3; Farver@¶3; Jelter@¶2; Carpenter@¶3; Dart@¶2; Tachover@¶¶34-36. Further, Dr. Erica Elliot MD, Angela Tsiang, and Mary Adkins, who are CHD members, filed comments and request that CHD advance their interests. Elliot@¶3; Tsiang@¶3; Adkins@¶3; Tachover@¶36. As the FCC did not adequately respond to their comments, and denied requested relief, each Petitioner is a "party aggrieved" under the Hobbs Act. 28 U.S.C. §2344. Hertz@¶24; Brokken@¶27; Lee@¶37; Stanley@¶23; Baran@¶41; Farver@¶41; Jelter@¶24; Carpenter@¶¶30-57, 58-63, 66; Dart@¶4; Tachover@¶¶34-36, 56-62.

B. Article III Standing

To establish Article III standing, each Petitioner must show particularized and concrete injuries-in-fact traceable to the *Order* that are likely to be redressed by a favorable decision. *Humane Soc'y of the U.S. v. Vilsack*, 797 F.3d 4, 8 (D.C. Cir. 2015). They must each suffer harms to a "legally protected interest." *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 560 (1992). An injury is particularized if it

"affect[s] the plaintiff in a personal and individual way." *Spokeo, Inc. v. Robins*, 136 S. Ct. 1540, 1548 (2016) (internal quotation marks omitted). It is concrete if it is "real," "actually exists," and is not "speculative." *Id.* at 1548-1549. Each Petitioner has standing based on one or more of the injuries addressed below.[200]

As for individual Petitioners, illness from toxic environmental agents provides standing. *NRDC v. EPA*, 464 F.3d 1, 7 (D.C. Cir. 2006) (illness "likely to occur"); *Mountain States Legal Found. v. Glickman*, 92 F.3d 1228, 1234-35 (D.C. Cir. 1996) (non-trivial increased risk). Many of the petitioners suffer from Radiation Sickness and RF/EMF related conditions. Hertz@¶¶18-23; Brokken@¶22; Lee@¶6; Stanley@¶7; Baran@¶5; Adkins@¶¶6-8; Elliott@¶12; McMahon@¶3; Gallo@¶18; Tachover@¶¶35, 37, 41. These injuries are clearly both particularized and concrete where petitioners have had to, *inter alia*, quit jobs and school, avoid public spaces, stop traveling by air, and spend money to shield themselves from nearby RF/EMF emissions. Scarato@¶¶9-42; Barris@¶¶5-26;

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[200] Petitioners also fall within the "zone of interests" protected by the substantive statutes in this case. *Mendoza*, 754 F.3d at 1016. The TCA obligates the FCC to guard against RF/EMF emissions that could harm human health and the environment. NEPA ensures that the FCC considers all relevant evidence regarding the human environment. *Gunpowder Riverkeeper v. FERC*, 807 F.3d 267, 274 (D.C. Cir. 2015). The ADA and FHA guarantee accommodations for a disability or handicap.

Hertz@¶¶20, 22; Brokken@¶¶8, 13-14, 17; Lee@¶20; Stanley@¶¶11-12, 16; Baran@¶¶6, 32-37; McMahon@¶¶5, 8; Gallo@¶¶15, 20; Dart@¶53; Elliott@¶11, 21; Tsiang@¶20; Adkins@¶11.

Individual petitioners also demonstrate standing when they allege exposure to harmful levels of hazardous materials due to an agency's failure to adopt more stringent safety limits. *Nuclear Energy Inst., Inc. v. EPA*, 373 F.3d 1251, 1265-66 (D.C. Cir. 2004) (EPA's failure to promulgate strong exposure limits for disposal of radionuclides). Here, the underlying basis of many Petitioners' claims is that the FCC failed to adopt necessarily stringent RF/EMF limits or cellphone testing procedures by not considering compelling evidence of non-thermal impacts. Scarato@¶¶44-45; Barris@¶¶27-30; Brokken@¶¶5-7; Lee@¶37; Stanley@¶22; Baran@¶38; Farver@¶15; Jelter@¶¶17, 20; Tachover@¶7; Dart@¶42; Carpenter@¶¶30-57, 63, 66; Hertz@¶14; Elliott@¶17; Tsiang@¶39-40; McMahon@¶13; Gallo@¶23-26.

Financial harm provides standing because money is property and requiring expenditure of personal funds injures a protected interest. *Czyzewski v. Jevic Holding Corp*., 137 S. Ct. 973, 983 (2017); *see also Twin Rivers Paper Co. LLC v. SEC*, 934 F.3d 607, 616 (D.C. Cir. 2019); *Carpenters Indus. Council v. Zinke*, 854 F.3d 1, 6 (D.C. Cir. 2017). Many Petitioners in this case have been required to

expend substantial sums to deal with past RF/EMF exposures and to minimize future exposures (*e.g.*, buying shielding to block radiation, moving homes). Scarato@¶¶9-42; Barris@¶¶5-26; Hertz@¶17; Brokken@¶16; Baran@¶35; McMahon@¶5; Gallo@¶15; Stanley@¶53; Adkins@¶13; Tachover@¶16.

Individuals may also show standing on based the violation of a procedural right provided such violation threatens a concrete interest of theirs. *City of Dania Beach v. FAA*, 485 F.3d 1181, 1185 (D.C. Cir. 2007) (discussing NEPA failures). They do not, however, need to show that "correcting the procedural right would necessarily alter the final outcome." *Mendoza v. Perez*, 754 F.3d 1002, 1010 (D.C. Cir. 2014). Here, the TCA requires the FCC to protect citizens from harmful RF/EMF exposures. And both the APA and NEPA obligate the FCC to consider relevant materials indicating that human health and environment may be adversely eaffected or that the FCC's cellphone testing procedures are inadequate. *Mendoza,* 754 F.3rd at 1010 (APA); *Scientists' Inst. for Public Info. v. AEC*, 481 F.2d 1079, 1086 n.29 (D.C. Cir. 1973) (NEPA).

All individual Petitioners have alleged that the FCC failed to consider and explain why it decided not to amend the RF/EMF regulations or testing protocols despite not having considered record evidence showing numerous potential non-thermal injuries at exposure levels allowed by the Commission. *Nat'l Wildlife*

Fed'n v. Hodel, 839 F.2d 694, 712 (D.C. Cir. 1988) (based on NEPA failures). Scarato@¶¶44-45; Barris@¶¶27-30; Hertz@¶24; Brokken@¶27; Lee@¶39; Stanley@¶23; Baran@¶41; Farver@¶41; Jelter@¶24; McMahon@¶13; Gallo@¶26; Tachover@¶56-63; Dart@¶63; Carpenter@60, 63; Adkins@¶4, 19-20; Elliot@¶17; Tsiang@¶40-41.

Scientists and physicians also have a legally-protected interest in the ability to engage in their chosen professions, in accordance with ethical and other duties imposed by law or custom. An agency action that significantly undercuts their ability to do so is a "professional injury." Courts recognize "professional injury" standing, but oftentimes the argument founders on the additional tests for concreteness, particularization, imminence, and redressability. *Animal Legal Defense Fund v. Espy*, 23 F.3d 496, 499 (D.C. Cir. 1994). By refusing to justify the decision to maintain the RF/EMF limits or consider non-thermal impacts, the FCC has frustrated the professional declarants' ability to effectively treat and heal their patients. Jelter@¶22; Elliot@¶¶19-20; Dart@¶60; Carpenter@¶¶47, 57-63.

Further, a non-profit organization has standing to pursue claims on its own behalf so long as it meets the same standing requirements as an individual plaintiff. *Equal Rights Ctr. v. Post Props., Inc*., 633 F.3d 1136, 1138 (D.C. Cir. 2011). Injury-in-fact has two parts: "first, whether the agency's action or omission to act injured

the organization's interest, and, second, whether the organization used its resources to counteract that harm." *Id*. (*quoting PETA v. U.S. Dep't of Agric*., 797 F.3d 1087, 1094 (D.C. Cir. 2015)). As part of the first inquiry, the organization must also demonstrate a "direct conflict between the defendant's conduct and the organization's mission." *Nat'l Treasury Emps. Union v. United States*, 101 F.3d 1423, 1430 (D.C. Cir. 1996).

Here, all three organizational Petitioners pursue missions of protecting consumers and citizens, including children, from harmful RF/EMF emissions. And the FCC's decision has "perceptibly impaired" the organizational Petitioners' ability to provide counseling, education, referral and other assistive services to members and/or followers, and the general public, including Radiation Sickness sufferers and others exposed to RF/EMF. *Havens Realty Corp. v. Coleman*, 455 U.S. 363, 379 (1982); *Spann v. Colonial Vill., Inc*., 899 F.2d 24, 27 (D.C. Cir. 1990). Davis@¶¶3-22; Franklin@¶¶3-12; Tachover@¶¶44-62.

Moreover, the FCC's failure to consider and explain its decision not to update the RF/EMF regulations and cellphone testing procedures, despite overwhelming evidence of non-thermal harms at FCC-approved levels, results in an informational injury. *Am. Anti-Vivisection Soc'y v. USDA*, 946 F.3d 615, 618-20 (D.C. Cir. 2020); *Scientists' Inst. for Public Info.*, 481 F.2d at 1086 n.29) (NEPA

organizational standing). Now, organizational Petitioners cannot provide evaluations and analyses regarding the FCC's purported justifications, whether to scientists looking for such advice or their members and followers asking for guidance, because the FCC has not disclosed its reasoning. Davis@¶¶3-22; Franklin@¶¶8-12; Elliot@¶17; Tsiang@¶¶40-41; Adkins@¶20; Carpenter@¶¶57, 60-63; Tachover@¶¶47-62.

Deprivation of or interference with personal rights or liberty interests is also an injury. Those rights/interests include the ADA, FHA, bodily autonomy, and property rights. The ADA and FHA each provide a private cause of action for refusal to accommodate a disability or handicap. 42 U.S.C §12133 (public services), §12188 (services by private entities).

Public and private service providers deny accommodations by claiming FCC-authorized emissions are "safe" and no accommodation is due and/or FCC rules pre-empt ADA and FHA remedies. The regulations authorize emissions that intrude on private property and invade the body. Harm to property or interference in property rights provides standing. *Scenic Am., Inc. v. United States DOT*, 836 F.3d 42, 55 (D.C. Cir. 2016); *Idaho, By & Through Idaho Pub. Utils. Comm'n v. ICC*, 35 F.3d 585, 591 (D.C. Cir. 1994). Multiple record comments expressed personal objections to involuntary RF/EMF exposures and noted the FCC's failure

to clarify whether the exposure limits preempt these constitutional and statutory rights. *Anti-Vivisection Soc'y*, 946 F.3d at 619. Elliot@¶¶11, 15; Tsiang¶¶35, 38; Adkins@¶¶11, 18-19; Tachover@5, 35, 37, 41, 46-47, 51, 60; Carpenter@39, 45, 60.

Finally, CHD has standing to represent its interests and its members, all of whom have common relevant interests. *Equal Rights Ctr. v. Post Props., Inc*., 633 F.3d 1136, 1138 (D.C. Cir. 2011). To secure "associational standing" an organization must show that (a) its members would otherwise have standing to sue in their own right; (b) the interests it seeks to protect are germane to its purpose; and (c) neither the claim asserted nor the relief requested requires the participation of individual members in the lawsuit. *International Union, UAW v. Brock*, 477 U.S. 274, 282 (1986). As cited above, CHD members Elliot, Tsiang and Adkins have standing to sue in their own right and CHD seeks to protect their interests which are germane to its purpose. No Petitioner is required to participate individually in this litigation for relief to be granted.

By vacating and remanding the *Inquiry*, this Court would provide the FCC another chance to fully consider the mountains of evidence regarding non-thermal impacts of RF/EMF exposures, as well as address constitutional and statutory

rights implicated by the *Order*, and to adequately explain and justify any decision to retain or amend its RF/EMF-related regulations.

II. APA/Reasoned Decisionmaking

Agency action is arbitrary and capricious if it "entirely failed to consider an important aspect of the problem" or "offered an explanation for its decision that runs counter to the evidence before the agency." *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983). The agency must instead show a "rational connection between the facts found and the choice made." *Brookings Mun. Tel. Co.*, 822 F.2d at 1165 (D.C. Cir. 1987). It must take a "hard look" at "all relevant issues" and engage in "reasoned decisionmaking." *Neighborhood TV. Co. v. FCC*, 742 F.2d 629, 639 (D.C. Cir. 1984).

The *Order* fails several fundamental principles. First, an agency cannot completely ignore evidence that it does not like. It must review the "whole record," including "whatever in the record fairly detracts from the evidence supporting the agency's decision" and "it may not minimize such evidence without adequate explanation." *Genuine Parts Co. v. EPA*, 890 F.3d 304, 312 (D.C. Cir. 2018).

Second, the agency must adequately respond to all material public comments, especially those "relevant to the agency's decision and which, if adopted, would require a change in an agency's proposed rule [because they] cast

doubt on the reasonableness of a position taken by the agency." *Home Box Office, Inc. v. FCC*, 567 F.2d 9, 35 n.58 (D.C. Cir. 1977). "Conclusory explanations for matters involving a central factual dispute where there is considerable evidence in conflict do not suffice to meet the [Court's] deferential standards." *Genuine Parts*, 890 F.3d at 312. Rather, the agency has to "respond in a reasoned manner to the comments received, to explain how the agency resolved any significant problems raised by the comments, and to show how that resolution led the agency to the ultimate rule." *Action on Smoking & Health v. Civil Aeronautics Bd.*, 699 F.2d 1209, 1216 (D.C. Cir. 1983) ("*ASH*").

Third, an agency's decision must be supported by "substantial evidence" in the record. *Nat'l Lifeline Ass'n v. FCC*, 921 F.3d 1102, 1111 (D.C. Cir. 2019). "Evidence that is substantial viewed in isolation may become insubstantial when contradictory evidence is taken into account." *Genuine Parts*, 890 F.3d at 312.

III. FCC Completely Ignored Evidence/Conclusory Treatment

A. No Mention of Non-Thermal Modulated/Pulsed/Peak or Long-Term Exposure

The *Order* did not acknowledge or respond to most of the material, peer-reviewed scientific and medical evidence demonstrating adverse biological responses to currently-authorized RF/EMF exposures. It has no response to the significant scientific and medical evidence that modulation, pulsation and peak

exposures may be even more important than mere carrier wave radiation. The *Order* says nothing about cumulative or long-term effects. It did not provide any reasoning to justify the conclusion that the current regulations protect public health and safety. Instead, it rejected the science because the scientific/medical experts did not also solve the engineering problem of being able to provide "viable" service within safe limits.[201]

The failure to respond to material comments was fatal. The evidence of harm was substantial, yet the FCC refused to meaningfully address it. The refusal to contend with these issues was arbitrary and capricious.

B. No Mention of Radiation Sickness

The *Order* did not acknowledge or respond to any of the scientific, medical or individual evidence regarding Radiation Sickness. This was plainly material and well-documented. The refusal to recognize that real people—those the FCC is required to protect—are suffering, and the withholding of any promise of relief clearly violated its responsibilities under the Communications Act and was an abuse of discretion. The Commission owed an apology but delivered a gut-punch.

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[201] 34 FCC Rcd at 11694.

C. Environmental Harm

The Order failed to address any of the evidence of substantive impacts of RFR on the non-human environment. The FCC violated its obligations under the APA to consider all relevant evidence and under NEPA to take a "hard look" at environmental impacts.

D. RF/EMF Effects

The FCC violated the APA because it failed to consider whether the RF/EMF regulations for wireless devices adopted almost a quarter century ago and based on the outdated technology of that era will fully protect the health and safety of the public in the modern wireless telecommunications environment. In rubber-stamping its decades-old emission regulations and finding no adverse health effects, the *Order* failed to address such critical issues as the use of 5G wireless devices, the multiple antennas on today's mobile phones, the growing use of Wi-Fi, and the cumulative effect of radiation from multiple wireless sources. The Commission's attempt to overlay emission regulations created for the 1990s on today's complex telecommunications environment without any analysis of associated health risks–or even a recognition of the underlying differences in wireless devices and technology–is a breach of its duty under the Telecommunications Act and the APA.

The FCC also violated the APA because it did not even reference–much less evaluate–the multitude of studies and research papers that supported a link between wireless devices and infrastructure health risks. Scientific research of the past 20 years showing health effects, including cancer, neurological impacts, reproduction, and immune system deficiencies, from the use of wireless sources were simply ignored in the seven paragraphs terminating the seven-year *Inquiry.*

The Commission's summation of the record containing many thousands of pages of significant and detailed scientific research and studies, including health studies relating to wireless devices, as being "brief comments or submissions of redundantly filed studies, reports and other publications" without naming a single commenter or study evidences a lack of any serious review or analysis of the record by the Commission in violation of the APA.

The Commission's violation of the APA is highlighted by its failure to fairly evaluate non-thermal health risks to humans from long term usage of cellphones–which were not protected by the 1996 emission regulations. A glaring omission from the *Order* is the IARC Monograph which addressed numerous health risks including its finding of a link between cellphone usage and brain cancer in humans. Although the Commission *specifically* requested comments on this important worldwide

scientific research in the *Inquiry*, it did not address any of these comments or even reference the Monograph in the *Order*.

Moreover, in its one-sided review of the NTP Study, the FCC failed to provide any analysis–or even a recognition–of voluminous research in the IARC Monograph, the BIR, and other significant scientific findings highlighted throughout the comments that linked the use of mobile devices to negative health effects, including cancer. The *Order's* failure to discuss the Monograph is particularly egregious in that the NTP Study specifically found that the type of brain cancer observed in its animal studies was "similar to a type of brain tumor linked to heavy cellphone use in some human studies." The Monograph found that "there is an increased risk for glioma, a malignant type of brain cancer associated with wireless phone use."

The evidence does not support the claim at ¶¶2, 10, 11, and 13 of the *Order* that "sister agencies" support the decision. OSHA indicated that this issue is "not on OSHA's regulatory agenda"[202] and advised the FCC to contact the National Institute for Occupational Safety and Health ("NIOSH") and NTP.[203] The NTP is an FDA "sister agency" since both are DHHS divisions. Its report does not agree

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[202] JA_.

[203] *Id.*

the regulations are adequate.[204] The CDC (another DHHS division) uses a classification system that recognizes that non-ionizing radiation can cause injury.[205] The EPA noted in 2002 that the 1996 regulations' premises are "not justified."[206] The Interior Department[207] contended in 2014 they are "out of date and inapplicable today."[208] The federal Access Board recognizes Radiation Sickness as a disability.[209] The relevant federal agencies do not, in fact, all agree current regulations are adequate.

An FDA department director (Dr. Jeff Shuren) did provide specific input in response to the FCC's request. *Order* ¶¶11-12. There were apparently non-public, off-the-record discussions between FCC and FDA staff.[210] Mr. Shuren's letter basically parroted back what the FCC wrote to FDA when it claimed the NTP conclusions do not support adverse health effects from cell phones.[211] This directly conflicts with NTP findings and National Institute of Environmental Health

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[204] *See* Part I.D.c.2 (NTP Study topic).

[205] *See* Part I.D. (Human Evidence – Radiation Sickness).

[206] JA_.

[207] JA_.

[208] JA_@45.

[209] JA_.

[210] JA_.

[211] JA_.

Sciences ("NIEHS")-appointed scientist evaluations, and does not address the studies finding reproductive and nervous system damage.[212] Neither the FCC letter nor the "cut and paste" response from the FDA employee cite *any* scientific evidence or health data to support rejection of the NTP Study and other findings.[213]

The Commission violated the APA by relying on off-the-record meetings and the summary conclusions of an FDA employee letter made public on the eve of the *Order's* release. The public had no meaningful opportunity to supply comments explaining why the FCC should not rely on the late-filed FDA employee letter.

Accordingly, the *Order* constitutes arbitrary and capricious rulemaking and must be set aside.

E. Limited Discussion Re Children

The numerous studies and comments on the *Inquiry* consistently demonstrate children's special situation while *in utero* and in their early years, and the inadequacies in the FCC's current approach—the standardized anthropomorphic mannequin model—to protecting children. The FCC, at para. 15 of the *Order*, seems to acknowledge these age-related differences. Yet, without analyzing any of the studies or comments, the *Order* declines to adjust the

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[212] JA_; JA_ (both papers finding criticism of NTP to be unfounded).

[213] *Id.*

regulations to better protect children. The FCC's decision not to act when the agency recognizes that physiological differences mean greater RFR exposure for children raises a serious question as to whether the FCC is serious about protecting the public health.

The FCC seeks to defend its inaction by maintaining that the existing cellphone testing method was designed to test for effects on children as well as adults and already appropriately takes into account children's physical differences. The *Order* at n. 50 predicates this statement on the same statement from IEEE Std 1528-2003 that was discussed seven years ago in para. 53 of the *Inquiry* that the cellphone test setup currently in effect represents a conservative case "for men, women, and children" alike.

The *Order* provides no discussion of the many scientific studies of the issue in the intervening years that demonstrate the deleterious, sometimes life-threatening effects of RFR and the inadequacies of the standardized anthropomorphic mannequin model with respect to the special vulnerabilities of children. Nor, as requested by the American Academy of Pediatrics, does the agency consider changes in technology and the pattern of cellphone use, especially by children, that increase risks from RFR. It is difficult to understand why the

agency would rely on the plainly outdated and false statement from IEEE Std 1528-2003.

Seemingly, as if to gild its decision with the patina of scientific reasoning, the *Order* at n. 54 refers to three studies—two from 2010 and one from 2006—that appear by their titles to relate to the issue of the differential in RFR for children's heads versus adult heads. But the *Order* does not explain why it refers to the cited studies or explain how the cited studies, all of which tested for thermal effects, have any bearing over concerns about non-thermal biological effects.

Lacking any support in the record for its failure to address human vulnerabilities during the prenatal period and childhood, including teenage years, the FCC in para. 15 of the *Order* turns to the FDA for support: "Similarly, the FDA maintains that '[t]he scientific evidence does not show a danger to any users of cell phones from RF exposure, including children and teenagers.'" But the quoted statement is nothing more than a conclusion bereft of any analysis. The *Order* refers at n. 51 to an FDA webpage that, at the time the FCC released its *Order*, contained a very similar conclusory statement. The webpage at the time also lacked any analysis or explanation to support the agency's decision.

Thus, the FCC has not supported its decision to not to revise its safety regulations to account for the needs of fetuses and children through the teenage

years. Indeed, the FCC displayed a cavalier approach to protecting those needing protection the most. This refusal violates the FCC's statutory duty to protect the public and is arbitrary, capricious, and unlawful.[214]

F. Cell Phone Testing

The administrative record contains substantial evidence that (a) the FCC's cellphone certification and testing procedures and policies underestimate Specific Absorption Rate exposures, and (b) do not test for RFR's harmful biological effects. The Commission does not contest these facts but seems to acknowledge their validity.[215]

Notwithstanding these uncontested facts, the *Order* briefly concludes that the existing cellphone testing procedures are adequate. This conclusion is particularly difficult to understand because the *Order* does not address the evidence showing otherwise. That is, the *Order* does not even attempt to explain why or how to adjust testing procedures and policies to correct for their admitted

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[214] 7 U.S.C. §706(2)(A).

[215] In the *Inquiry*, for example, the FCC acknowledged some of the limitations of the standardized anthropomorphic mannequin model ("The standardized anthropomorphic mannequin does not model children, tissue layers, or a hand holding the device….") and invited comments on alternative methodologies that "can in principle more realistically model a range of variables not present using mannequins." 28 FCC Rcd at 3586.

inaccuracies. For example, the *Order* recognizes inaccuracies in the standardized anthropomorphic mannequin model but does not attempt to resolve them. Similarly, the *Order* does not explain why it will not modify testing procedures to examine how cellphones are actually used today.

Instead of addressing any of this substantial evidence, the *Order* simply concludes that against-the-body testing is unnecessary because tests are conducted against-the-head with no separation; these against-the-head tests are performed at the cellphone's maximum power setting; and testing separation distances are less than 2.5 cm. for "many devices." With regard to the last point, the *Order* refers to only one type of cellphone—those with "tethering" capabilities, i.e. "hotspot mode." Finally, the *Order* seeks to assure the public that the testing procedures and policies adequately protect against heating from RFR by recalling the supposed 50-times safety margin, discussed in the comments summarized above.

The *Order's* defense of the current certification and testing procedures and policies, by ignoring virtually all of the relevant evidence demonstrating the need to revise and update those procedures and policies, violates the APA. An agency has a legal responsibility to address the relevant evidence placed before it and to explain how that evidence bears on the agency's handling of the matter.

Furthermore, the reasoning that the agency did offer is deeply flawed to the point of being arbitrary and capricious. The *Order* attempts to equate Specific Absorption Rate testing against the head with SAR testing against the body so that the failure to require Specific Absorption Rate testing against the body should be excused because Specific Absorption Rate testing against the head is conducted. Yet no scientific or other factual evidence is offered to show that the Specific Absorption Rate results would be the same.[216] Such reasoning is fantastical, arbitrary and capricious, and a clear violation of the APA.

Moreover, the statement made in the *Order* that the health effects from cellphones against the body need not concern people because there is a 50-times safety margin completely ignores the substantial evidence showing that the supposed safety margin is a completely arbitrarily derived number. Nor does the *Order* offer any new reason to conclude otherwise. In short, the *Order* did not engage in reasoned decision-making to support its assumption that the supposed

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[216] It is, however, oddly consistent with the Commission's history of not recognizing that human tissue in and among different bodily organs has different electrical properties and, therefore, different susceptibilities to RFR. Indeed, this failure to appreciate the proven different characteristics of differently placed human tissue resulted in adoption of the standardized anthropomorphic mannequin model despite the proven fact that standardized anthropomorphic mannequin produces inaccurate Specific Absorption Rate readings and should be replaced.

50-times margin of safety is real. The *Order's* reliance on the supposed margin of safety is arbitrary, capricious, and unlawful.

Given all of these circumstances, the FCC's refusal to act to revise and improve its cellphone certification and testing procedures is plainly unreasonable, arbitrary and capricious, and unlawful in violation of the APA and the Telecommunications Act.

IV. NEPA

A. Statutory/Legal Background

Congress recognized in NEPA the "profound influences" of "new and expanding technological advances" and declared a "policy of the Federal Government" to promote beneficial uses of the environment "without…risk to health or safety." 42 U.S.C. §4331.

For "major Federal actions significantly affecting the quality of the human environment," a federal agency must prepare a "detailed statement" on the "environmental impact of the proposed action." 42 U.S.C. §4332. While NEPA does not impose any substantive environmental mandates, it requires agencies to follow procedures for assessing environmental impacts of their decisions. *Am. Bird Conservancy, Inc. v. FCC*, 516 F.3d 1027, 1032 (D.C. Cir. 2008). These include preparing an Environmental Assessment ("EA") or, if necessary, a more

comprehensive Environmental Impact Statement ("EIS"), assuming the agency action has not been categorically excluded. *Id.*; 40 C.F.R. §§1508.9, .11. If an EA is prepared, and no significant impact is found, the agency issues a Finding of No Significant Impact ("FONSI"). 40 C.F.R. §1508.13.

These procedures serve two important "action-forcing" goals. First, they "ensure[] that the agency, in reaching its decision, will have available, and will carefully consider, detailed information concerning significant environmental impacts." *Robertson v. Methow Valley Citizens Council*, 490 U.S. 332, 349 (1989). Second, they "guarantee[] that the relevant information will be made available to the larger audience that may also play a role in both the decisionmaking process and the implementation of that decision." *Id.*; 40 C.F.R. §1500.1.

An agency also cannot simply state in conclusory fashion that an action will not have a significant effect on the human environment. Rather, the agency must, at a minimum, conduct an EA. *Found. On Economic Trends v. Heckler*, 756 F.2d 143, 146-47 (D.C. Cir. 1985). "The Court may not substitute its own findings of no significant environmental impact on the basis of arguments of the parties, when the agency has failed to prepare" an EA "in the first instance." *Anacostia Watershed Soc'y v. Babbitt*, 871 F. Supp. 475, 482 (D.D.C. 1994).

B. *Inquiry* Triggered NEPA

NEPA clearly applies to this *Order*. The *Order* constitutes a "major Federal action." 42 U.S.C. §4332. The CEQ defines that term to include: (i) "actions with effects that may be major and which are potentially subject to Federal control and responsibility" and (ii) "new or revised agency rules, regulations, plans, policies, or procedures." 47 C.F.R. §1508.18. Here, the RF/EMF regulations were adopted, in part, pursuant to Section 704 of the TCA. By issuing the *Order*, the FCC exercised its exclusive authority granted by Congress to set and enforce RF/EMF exposure limits. The *Order* will also have major effects. It determines the radiation levels that U.S. consumers and citizens will be continuously exposed to in and outside their homes, and whether they have been placed at risk of non-thermal injuries. Finally, the *Order* essentially establishes new RF/EMF limitations as they are based on an entirely new administrative record that did not exist in 1996.

Further, the *Order* may "significantly affect[] the quality of the human environment." 42 U.S.C. §4332. Whether this factor is met depends on "both context and intensity." 40 C.F.R. §1508.27.[217] Among the relevant considerations, "intensity" refers to the "severity of impact," including the "degree to which the

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[217] "Context" requires the action to be analyzed in several contexts, such as "society as a whole (human, national), the affected region, the affected interests, and the locality." *Id.* All of these are implicated by the RF/EMF regulations.

proposed action affects public health or safety." *Id.*; *see City of Dania Beach v. FAA*, 485 F.3d 1181, 1189 (D.C. Cir. 2007). An agency must also analyze whether possible effects are "highly uncertain," "unique" or "unknown," and if they are "likely to be highly controversial." 40 C.F.R. §1508.27; *see Found. on Economic Trends v. Weinberger*, 610 F. Supp. 829, 837 (D.D.C. 1985). Each of these elements is satisfied here.

RF/EMF obviously affect public health and safety. Under the TCA, one of the driving factors behind the 1996 limitations was protecting consumers and citizens from harmful RF/EMF.

In addition, the FCC's assertions that the science underlying non-thermal impacts of RF/EMF is of "variable quality" or fails to make a "persuasive case" only further supports the need for a NEPA analysis.[218] No scientific certainty or consensus is required to constitute a significant effect. *Am. Bird Conservancy*, 516 F.3d at 1033.

The decision whether to maintain the 1996 regulations is also highly controversial. "The term 'controversial" refers to cases where a substantial dispute exists as to the size, nature, or effect of the major federal action rather than to the

[218] 34 FCC Rcd at 11694.

existence of opposition to a use." *Town of Creek Cave v. FAA*, 325 F.3d 320, 331 (D.C. Cir. 2003). Here, commenters referenced well over a thousand peer-reviewed studies indicating that RF/EMF can have devastating non-thermal effects. This directly placed into question the purported evidence underpinning the FCC's decision not to strengthen RF/EMF protections.

C. FCC Failed To Apply NEPA

Accordingly, this Court, in applying a *de novo* standard of review, must find that the FCC failed to satisfy its NEPA obligations and vacate the *Order* so that the FCC can, at a minimum, conduct an EA. The FCC did not issue an EA or EIS. The *Order* also fails to explain why the *Inquiry* did not trigger the FCC's NEPA obligations and never even mentions NEPA in this context.

Moreover, even if the *Order* is viewed as having considered health and environmental impacts, the FCC's decision to maintain the 1996 exposure limits still fails under the APA's arbitrary and capricious standard of review. 5 U.S.C. §706. When this Court reviews agency compliance with NEPA, it must determine, at a minimum, whether the agency took a "hard look" at the environmental consequences. *Robertson*, 490 U.S. at 350 (citation omitted). "An agency has taken a hard look…if the statement contains sufficient discussion of the relevant issues *and opposing viewpoints*, and the agency's decision is fully informed and well-

considered." *Myersville Citizens for a Rural Cmty., Inc. v. FERC*, 783 F.3d 1301, 1324-25 (D.C. Cir. 2015) (emphasis added).

As such, mere conclusory statements regarding potential effects are insufficient. *Heckler*, 756 F.2d at 154.

Thus, for the same reasons the *Order* fails under the APA, it also falls short of complying with NEPA.

V. Additional Legal Considerations

A. Personal Objection to Involuntary Exposure

The *Inquiry* ¶232[219] recognized that "exposures due to fixed RF sources are both involuntary and long-term." At least 29 individuals advised the FCC they objected to involuntary exposure.[220] Others contended that involuntary exposure was a trespass, nuisance, assault, battery, or torture.[221] All asserted their statutory, constitutional, and/or common law individual rights. The *Order* wrongly failed to acknowledge these comments or even address this topic.

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[219] 28 FCC Rcd at 3581

[220] JA_.

[221] JA_.

B. ADA/FHA

Petitioners strongly contest the notion current regulations adequately protect the general population. But assuming, *arguendo*, they are generally protective that cannot end the inquiry. Radiation Sickness is real, many have it, and more will soon. The CDC and Access Board agree it is, respectively, a source of injury and disability.[222] We know its cause. The only way to treat the disease is through exposure-avoidance. The issue is how that can be accomplished in today's wireless-infested world. Those with Radiation Sickness require consideration and accommodation on a case-by-case basis. FCC did nothing about them.

A large number of comments asked the FCC to clarify its regulations do not pre-empt ADA or FHA rights and remedies or prevent accommodations to those disabled by Radiation Sickness.[223] For example, Chris Nubbe contended that "[t]he Telecommunications Act should not be interpreted…to allow them no remedy under City, State or Federal laws or constitutions."[224] The Cities of Boston and Philadelphia specifically flagged this issue and sought clarification.[225]

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[222] *See* Part I.D. *supra*. [Human Evidence – Radiation Sickness]

[223] JA_.

[224] JA_.

[225] JA_@7-8.

Sufferers must surmount tremendous difficulties, mistreatment, and discrimination. They face a dismal future: progressive worsening from unavoidable, ever-increasing and more intense exposure from multiple sources using a variety of pulsation/modulation schemes.[226] Some have died or committed suicide because constant RF/EMF was torturing them beyond their ability to survive or cope.[227]

The regulations provide "color of law" to wireless provider activities that inflict injuries on innocent people and children who just want to enjoy life, peace, and security. They cannot go into public spaces, access medical care, obtain public services, use public transportation, drive on the road, fly, stay at a hotel or have a job. Children are ridiculed, forced out of schools and into social isolation. Finding a home has become almost impossible.[228]

The question is whether the Commission's regulations concerning RF environmental effects preempt ADA/FHA accommodation obligations for those afflicted by Radiation Sickness. The Commission erred by not addressing these material comments.

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[226] JA_.

[227] JA_@4.

[228] JA_.

C. Balancing and Public Interest

The Commission opened the *Inquiry* because GAO recommended it assess the costs and benefits associated with keeping the current limits. *Inquiry* ¶¶205-210.[229]

Six years later, the *Order* summarily rejected requests for reduced limits because the scientists and medical experts did not venture outside their expertise and provide a full engineering analysis of how biologically-based limits "might affect the viability or performance of wireless services and devices." *Order* ¶12. The FCC did not address the costs and benefits *associated with keeping the current limits* even though that was a primary purpose of the *Inquiry*. The FCC made no findings regarding the human or environmental impact under current limits, despite all the evidence of immense societal and personal costs.

D. Burden of Proof

The *Inquiry* ¶210[230] promised a "science-based examination" and assured the FCC would be "responsive to the public's interest…in RF exposure guidelines…based on the most current information, analysis, and expertise available." Many commenters were not convinced. These concerns proved valid: the Commission discounted the scientific and medical evidence on specious

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[229] 28 FCC Rcd at 3570-3571.

[230] 28 FCC Rcd at 3571.

grounds without meaningful analysis, examination, or explanation. The Commission elevated the *industry's* health over *people's* lives. This was arbitrary, irrational, and inconsistent with the balancing required by law.[231]

Inquiry ¶¶6, 236-243[232] inquired whether the FCC should embrace "prudent avoidance" under the "precautionary principle." Paragraph 237 asked if the Commission should adjust its regulations to protect against "non-thermal" effects. These were, in part, "burden" questions: do those advocating more protective limits have to prove the existing limits are inadequate, or does the FCC or industry have the burden to prove current thresholds are adequate?

This subject generated enormous discussion: 54 commenters strongly supported use of the precautionary principle and/or prudent avoidance.[233] The scientific/medical submissions uniformly urged the precautionary principle and a finding of current inadequacy due to lack of any protection against non-thermal effects.[234] Many drew comparisons to prior instances where regulatory action came far too late, as was the case with asbestos, leaded petrol, and tobacco.[235]

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[231] See Part I.B.I.

[232] 28 FCC Rcd at 3501, 3582-3585.

[233] JA_.

[234] JA_.

[235] JA_.

This issue was clearly important and material to everyone. The *Order*, however, failed to mention, much less resolve its a questions at *Inquiry* ¶¶6, 236-243 or all the comments addressing them. Nor did the Commission elucidate any balancing factors between "safety" and "efficient service." That is because there were none. Service viability and reliability concerns under hypothetical lower limits outweighed any consideration of current risk. *Order* ¶12.[236]

There is no meaningful explanation why the scientific and medical evidence regarding harms and risks from current limits was not valid. The public still has no idea why the FCC decided thousands of studies and hundreds of individual assertions of harm were unworthy of serious discussion. There is no hint of the risk level that must be proven before the FCC will even consider lower limits, or what evidentiary standard applies at the agency level.

The *Order* ¶¶2, 10-16[237] lack any independent analysis, but do reveal the FCC imposed a conjunctive burden on those advocating change: they had to prove undue risk under current regulations and propose alternative limits that would still allow viable wireless service. Submission without replacement "viable" limits were rejected out of hand, without any evaluation of the science showing undue

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[236] 34 FCC Rcd at 11694.

[237] 34 FCC Rcd at 11688, 11697.

risk under current regulations. The *Inquiry* was about whether current limits are appropriate. The rulemaking to follow would establish "viable" replacements.

This sleight-of-hand allowed the FCC to avoid independent and searching evaluation and disposition of the scientific/medical evidence or the testimony by those who claimed current limits are inadequate. The *Inquiry* ¶6[238] acknowledged the Commission had the ultimate burden and responsibility for "safe" regulations and limits but it did not even try. The *Order* does not explain how or why its current thresholds are indeed safe based on the evidence.

The FCC assigned impossible proof and persuasion burdens on those advocating change, even though the FCC is the one that has the burden at all times. Advocates did not have to prove the regulations are unsafe; the FCC has to conclude based on substantial scientific and medical evidence that its existing regulations *are safe*. More important, the Commission had the legal and moral duty to acknowledge the unchallenged human evidence of present actual sickness and provide some answers and respite to those who are clearly already sick.

The Commission is the "agency engaged in rulemaking" and is responsible for "solicit[ing] expert opinions and marshal[ing] the scientific data to ensure it's

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[238] 28 FCC Rcd at 3501.

both protects the public and provide for an efficient wireless network." *Farina v. Nokia, Inc*., 625 F.3d at 126. Public health and safety is a statutorily mandated factor, 47 U.S.C. §§151, 154(n), 254(c)(1)(A), 324, 332(a)(1), 336(h)(4)(B), 925(b)(2)(C), 1455(a)(3), so they are by definition an important issue. The FCC's decisions must consider its duty to protect the public. *Mozilla Corp. v. FCC*, 940 F.3d 1, 60 (D.C. Cir. 2019). If and to the extent FCC-adopted emissions regulations override any other legal requirements, whether state, federal or even constitutional, the Commission had a much higher analytical and transparency burden because it alone is responsible for getting it right. "Making that difficult decision was the agency's job, but the agency failed to do it." *Dep't of Homeland Sec. v. Regents of the Univ. of Cal.*, N 18-587, 18-588, 18-589, 2020 U.S. LEXIS 3254 *43 (June 18, 2020).

The *Inquiry* was entirely about current levels. When it does open a rulemaking for new limits, the FCC will have to determine a standard that adequately protects health while still allowing effective service. But the Commission refused to even consider whether some reduction could occur, so there could be a better balance between *both* ends (health and effective service).

The FCC did not articulate a satisfactory explanation for the action. There is no rational connection between the facts found and the choice made. It failed to

consider important aspect[s] of the problem. *State Farm,* 463 U. S. at 43. The *Order* also fails the test for reasoned decision-making. It did not adequately respond to material issues raised by the *Inquiry* and extensively addressed by the comments. The reader has no idea what "proof" will suffice and what it will take for individuals claiming harm to obtain relief. The FCC is obviously committed to widespread non-thermal irradiation that exposes people as much as possible, without any regard to risk or objection, but it must follow the law to achieve that goal.

E. *Order* Ignored Express Invocations of Constitutional, Statutory and Common Law Based Individual Rights

1. Property Rights

FCC-authorized emissions intrude on private property against the owner's will. "The hallmark of a protected property interest is the right to exclude others. That is 'one of the most essential sticks in the bundle of rights that are commonly characterized as property.'" *Coll. Sav. Bank v. Fla. Prepaid Postsecondary Educ. Expense Bd*., 527 U.S. 666, 673, 119 S. Ct. 2219, 2224 (1999).

Government-authorized interference with enjoyment and use of the land is a compensable taking. *United States v. Causby*, 328 U.S. 256, 66 S. Ct. 1062 (1946)

(non-physical intrusion of airport noise).[239] *Kyllo v. United States*, 533 U.S. 27, 32 (2001) involved government agents that directed RF energy at the defendant's home. The energy waves intruded on the defendant's property and violated the owner's property-based right to exclude others. 533 U.S. at 34-40.

2. Bodily Autonomy and Informed Consent

Non-consensual RF emissions violate individuals' right to bodily autonomy. The FCC's current regulations authorize interference with human biological processes

"Bodily autonomy" and "autonomy privacy" derive from the "negative" individual liberty rights embodied in the Bill of Rights. *United States v. Rumely*, 345 U.S. 41 (1953); *NAACP v. Patterson*, 357 U.S. 449 (1958); *Griswold v. Connecticut*, 381 U.S. 479 (1965); *Stanley v. Georgia*, 394 U.S. 557 (1969); *Eisenstadt v. Baird*, 405 U.S. 438 (1972); *Roe v. Wade*, 410 U.S. 113 (1973). *Cruzan v. Dir. Mo. Dep't of Health*, 497 U.S. 261, 269-273 (1990) expressly recognized and reaffirmed the right to self-determination and bodily integrity. FCC-authorized emissions violate non-consenting citizens' "right to be let alone."

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[239] RF/EMF property intrusions are similar to loud noises. They, among other things, cause a reduction in melatonin production, which reduces sleep quality. See Part I.C.3. (neurological). Preventing someone from getting a good night's rest is classic nuisance.

In common law and most state statutes, non-consensual irradiation is a "battery." "A battery is an intentional act that causes harmful or offensive bodily contact." *Doe v. District of Columbia*, 796 F.3d 96, 107 (D.C. Cir. 2015). RF/EMF radiation "contacts" and penetrates the body. People who suffer contact and penetration after expressing non-consent will be both harmed and offended. The wireless provider is intentionally unleashing radiation and knows there will be contact.

Jacobson v. Massachusetts, 197 U.S. 11, 25 S. Ct. 358 (1905) held a state may generally mandate vaccines. The Court closed its opinion, however, with an important caveat: if the individual can show a *special sensitivity due to a medical condition*, there **must** be some process for case-by-case exceptions. This is necessary to avoid the ultimate liberty deprivations–denial of life itself or cruelty. 197 U.S. at 38-39.

Government-sanctioned and virtually mandatory exposure to RF/EMF can rise to the level of cruelty and inhumane treatment described in *Jacobson.* The FCC's disregard for this situation has caused a sub-population to lose hope of ever being able to meaningfully participate in society.[240] Reasoned decision-making

[240] JA_.

requires that the FCC at least acknowledge the situation and provide some rational justification for the incredible costs it is imposing on a significant segment of the population.

Jacobson also flatly requires that the Commission allow for some remedy for those who suffer from exposure. This is necessary to "'protect the health and life' of susceptible individuals." *In re Abbott*, 954 F.3d 772, 789 (5th Cir. 2020) (*citing Jacobson*, 197 U.S. at 37). Many participants requested that the FCC provide a remedy. It could have, at least, noted that those with individual health conditions related to or worsened by exposure can seek and obtain accommodations on a case-by-case basis or through an as-applied challenge. *See Gonzales v. Carhart*, 550 U.S. 124, 167 (2007). The Commission wrongly avoided the entire issue.

3. Preemption/Implied Repeal

The Communications Act does not expressly repeal ADA/FHA rights and remedies, which are specific and operate case-by-case. Unless there is "clear intention otherwise, a specific statute will not be controlled or nullified by a general one, regardless of the priority of enactment." *Telecomms. Research & Action Ctr. v. FCC*, 836 F.2d 1349, 1361, n.25 (D.C. Cir. 1988). Similarly, there was no repeal by implication. There is no clear and manifest evidence of

congressional intent to displace the ADA or FHA through the Communications Act. The earlier and later statutes can be reconciled and coexist. *In re Grand Jury Subpoena*, 912 F.3d 623, 628 (D.C. Cir. 2019). Case-by-case accommodation does not disrupt the FCC's authority to promulgate general standards. *G v. Fay Sch., Inc.*, 282 F. Supp. 3d 381, 395 (D. Mass. 2017).

An agency cannot repeal a statute. *Merritt v. Cameron*, 137 U.S. 542, 551-52 (1890). There is no evidence Congress intended to delegate its legislative repealer power to the Commission, especially since the ADA and FHA are administered by other federal agencies and enforced through the courts. *Hunter v. FERC*, 711 F.3d 155, 160 (D.C. Cir. 2013). In any event, neither Congress nor the FCC can suspend or override constitutional rights.

The FCC had a duty to clarify, especially since courts are rendering mixed decisions. Two federal district courts held local authorities cannot consider individual citizens' health issues as part of the zoning process. *Santa Fe All. for Health & Safety v. City of Santa Fe*, 2020 U.S. Dist. LEXIS 80196, at *35 (D.N.M. May 6, 2020); *Firstenberg v. City of Santa Fe, N.M.*, 782 F.Supp.2d 1262, 1271-1274 (D.N.M. 2011), vacated jurisdictional grounds, 696 F.3d 1018 (10th Cir.

2012).[241] *Santa Fe*, 2020 U.S. Dist. LEXIS 80196, *29-31, *33-34 held the FCC was the exclusive venue for health and safety issues. On the other hand, *G v. Fay,* 282 F. Supp. at 395 ruled that requests to schools for ADA accommodation are not preempted.

Commenters "plead[], and offer[ed] factual material in support of, a non-frivolous [legal] contention" that the FCC ignored or dismissed with no individual analysis. *WAIT I*, 418 F.2d at 1156. The *Order* pertained to the population in general; there was no recognition that discrete individuals might have one or more conditions that made them uniquely or especially harmed by RF/EMF. The FCC did not consider, or state, what could or should be done when an individual demonstrates injury and/or a violation of the individual's constitutional, common law, or statutory rights on an "as-applied" basis.

The *Order* at notes 5, 306 and 308 indirectly imply FCC RF regulations overrule, pre-empt or impliedly repeal all individual rights and remedies granted by other federal statutes like ADA/FHA and even constitutionally-protected liberty/property interests, in the context of individual, as-applied to the challenges

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[241] There is a circuit split on whether state tort damages actions seeking damages for cancer caused by wireless devices are preempted. *Pinney v. Nokia, Inc*., 402 F.3d 430 (4th Cir. 2005); *Farina v. Nokia, Inc*., 625 F.3d 97 (3d Cir. 2010); *Robbins v. New Cingular Wireless PCS, LLC*, 854 F.3d 315 (6th Cir. 2017).

outside the context of local zoning. Yet nothing in the Communications Act or §332(c)(7) expressly repeals the ADA or FHA. Neither ADA nor FHA explicitly exempt covered entities from accommodation requirements. *Little Sisters of the Poor et al v. Pennsylvania, et al*, No. 19-431, slip op. at 20-22 (May 6, 2020); *see also* Alito and Gorsuch concurrence.

Section 332(c)(7) addresses only state and local government action and has nothing to do with other federal statutes. The Act's savings clauses clearly disfavor implied preemption, even as to state law. *See* 47 U.S.C. §§152 (notes), 253(b), 414, 601(c)(1). They say nothing of as-applied challenges. *See NRDC v. NRC*, 666 F.2d 595, 602 (D.C.Cir.1981); *Geller v. FCC*, 610 F.2d 973, 978 (D.C.Cir.1979) (*per curiam*); *Network Project v. FCC*, 511 F.2d 786, 789 n.1 (D.C. Cir. 1975); *Functional Music, Inc. v. FCC*, 274 F.2d 543, 546 (D.C.Cir.1958), *cert. den*., 361 U.S. 813 (1959). If there is conflict between the Act and the Constitution, then the former falls, not the latter.

These individual rights/liberties issues were squarely before the Commission. Aside from its opaque comment in n.5, the *Order* failed to deal with them, even though all the FCC's cited cases base their holdings on the proposition the Commission has exclusive original jurisdiction to resolve them. It failed to do so, leaving the Petitioners' rights and remedies in limbo. The Commission was not

just "tolerably terse" in this respect; it was "intolerably mute." *WAIT Radio v. FCC*. 418 F.2d 1153, 1157 (D.C. Cir. 1969).

The Commission could have solved the "individual rights" issues in several ways. The easiest would be to include them in a rulemaking. It could have immediately closed the issue by stating the individual case-by-case claims are not preempted but are also outside its jurisdiction and should be pursued in a proper forum. The courts and some other regulators dealing with RF emissions issues arising from smart meters have so ruled. *White v. PPL Electric Utilities Corp.,* 2020 PA. PUC LEXIS 77 *12 (May 21, 2020); *In re Whitaker*, 2020 N.C. App. LEXIS 364 (Ct. App. May 5, 2020); *Metallo v. Orlando Utils. Comm'n*, 2015 U.S. Dist. LEXIS 116269 (M.D. Fla. Sep. 1, 2015).

When "human lives are at stake" an agency "must press forward with energy and perseverance in adopting regulatory protections." *Pub. Citizen Health Research Grp. v. Brock*, 823 F.2d 626, 629 (D.C. Cir. 1987); *Pub. Citizen Health Research Grp. v. Auchter*, 702 F.2d 1150, 1157-1158 (D.C. Cir. 1983). The failure to address individual rights and accommodations issues by reconciling the Commission's rules with other statutes like ADA/FHA and the Constitution was arbitrary, capricious, an abuse of discretion, and a failure to engage in reasoned decision-making. *Little Sisters of the Poor et al v. Pennsylvania, et al*, No. 19-431,

slip op. at 20-22 (May 6, 2020); *see also* Kagan concurrence in judgment slip op. at 7 ("Even in an area of broad statutory authority–maybe especially there–agencies must rationally account for their judgments.")

CONCLUSION

The Court must vacate the order closing the *Inquiry* and remand for proper disposition.

Respectfully submitted,

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14	38	Numerous commenters referred to BIR and the work of several members of the BIWG submitted individual work in the record.		
			https://ecfsapi.fcc.gov/file/1092820574235/5%20-%20Attachment%205%20-%20Martin%20Blank%20PhD%20-%20Opposition%20Statement%20-%20File%2013-0953.pdf	
			https://ecfsapi.fcc.gov/file/10916151357910/RFR%20DNA%20comet-assay-studies%20Henry%20Lai%202017.pdf	
			https://ecfsapi.fcc.gov/file/10920151427784/Henry%20Lai-ELF%20static%20fields%20free%20radicals%20supplementary%20material%207-2019.pdf	
			https://ecfsapi.fcc.gov/file/10916151357910/RF-Free-Radical-oxidative-effect%20Henry%20Lai%204-19-2019.pdf	
			https://ecfsapi.fcc.gov/file/10916020933093/Neurological%20effects%20of%20RF%20Henry%20Lai%20chapter%20Markov%202018.pdf	
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			https://ecfsapi.fcc.gov/file/10916020933093/RFR%20ResearchSummary%20Henry%20Lai%202017.pdf	
			https://ecfsapi.fcc.gov/file/1091330786203/Wireless%20radiation%20and%20EMF%20abstracts%20August%202016%20-%20August%202019%20Joel%20Moskowitz%209-13-2019.pdf, p.522	

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			https://ecfsapi.fcc.gov/file/1210030663890/HARDELL%20Environmental%20radiofrequency%20radiation%20at%20the%20J%C3%A4rntorget%20Square%20in%20Stockholm%20Old%20Town%2C%20Sweden%20in%20May%2C%202018%20compared%20with%20results%20on%20brain%20and%20heart%20tumour%20risks%20in%20rats%20exposed%20to%201.8%20GHz%20base%20station%20environmental%20emissions.pdf	
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			https://ecfsapi.fcc.gov/file/106070048305926/Doctor-Letters-on-Wi-Fi-In-School-Full-Compilation.pdf,	pp. 1-81
			https://ecfsapi.fcc.gov/file/12103008105187/World%20Health%20Organization%2C%20radiofrequency%20radiation%20and%20health%20-%20a%20hard%20nut%20to%20crack%20(Review)%20Lennart%20Hardell%20.pdf	
			https://ecfsapi.fcc.gov/file/1091330786203/Wireless%20radiation%20and%20EMF%20abstracts%20August%202016%20-%20August%202019%20Joel%20Moskowitz%209-13-2019.pdf, pp. 161, 171, 228, 290, 318, 361, 366, 394	
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			https://ecfsapi.fcc.gov/file/7520941958.pdf	
			https://ecfsapi.fcc.gov/file/1001669617135/sec15_2012_Evidence_Disruption_Modulation.pdf	

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			https://www.fcc.gov/ecfs/filing/6017464211	
28	103	Nine filings included physicians' diagnoses.		
			https://ecfsapi.fcc.gov/file/7520941839.pdf	
			https://ecfsapi.fcc.gov/file/7520920972.pdf	
			https://ecfsapi.fcc.gov/file/7520941349.pdf	p. 6
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			https://ecfsapi.fcc.gov/file/7520940956.pdf	p. 58
			https://ecfsapi.fcc.gov/file/109281319517547/17-Attachment%2017-%20Testimony-Wireless%20Health%20Effects.pdf	p.27
			https://ecfsapi.fcc.gov/file/109281319517547/17-Attachment%2017-%20Testimony-Wireless%20Health%20Effects.pdf	p. 53
30	113	Hundreds of studies show that FCC-authorized RF/EMF exposures can cause the symptoms, injuries, and mechanisms associated with Radiation Sickness.		
			https://ecfsapi.fcc.gov/file/10709642227609/Belyaev%20et%20al%202015.pdf	
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			https://ecfsapi.fcc.gov/file/1092820574235/12c%20-%20WiFi%20and%20Device%20Studies-%20(Attachment%2012%20-%20900%2B%20Studies-%20General%20Opposition%20Statement%20-%20File%2013-0953).pdf	

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32	123	Dozens of studies and individual testimonies reveal profound harms from existing cell towers		
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42	169	Many individuals testified to horrible injuries by smart meters and the devastating impact on their lives		
			https://ecfsapi.fcc.gov/file/109281319517547/17-Attachment%2017-%20Testimony-Wireless%20Health%20Effects.pdf	
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			https://www.fcc.gov/ecfs/filing/10713174822422	
			https://ecfsapi.fcc.gov/file/7520937675.pdf	
80	220	At least 29 individuals advised the FCC they objected to involuntary exposure.		
			https://ecfsapi.fcc.gov/file/7520958155.pdf	
			https://ecfsapi.fcc.gov/file/7520943747.pdf	
			https://ecfsapi.fcc.gov/file/7520943196.pdf	
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			https://ecfsapi.fcc.gov/file/7022311282.pdf	
			https://ecfsapi.fcc.gov/file/107140107208853/Chris%20Nubbe%20Comments%20on%20FCC%205G%207-12-16.doc	
			https://ecfsapi.fcc.gov/file/7520937524.pdf	
80	221	Others contended that involuntary exposure was a trespass, nuisance, assault, battery, or torture.		
			https://ecfsapi.fcc.gov/file/7520931789.pdf	
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81	223	A large number of comments asked the FCC to clarify its regulations do not pre-empt ADA or FHA rights and remedies or prevent accommodations to those disabled by Radiation Sickness.		
			https://ecfsapi.fcc.gov/file/1093087536094/FCC%20Testimony%20Patricia%20Burke.pdf	
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			https://ecfsapi.fcc.gov/file/107140107208853/Chris%20Nubbe%20Comments%20on%20FCC%205G%207-12-16.doc	
			https://ecfsapi.fcc.gov/file/1070795887708/Dr_Erica_Mallery-Blythe_EHS_A_Summary_Working_Draft_Version_1_Dec_2014_for_EESC_Brussels_(3)%20(1).pdf	
			https://ecfsapi.fcc.gov/file/1070795887708/Federal%20Wifi%20in%20schools%20complaint%20of%20X%20vFay.pdf	
			https://ecfsapi.fcc.gov/file/7520958706.pdf	
			https://ecfsapi.fcc.gov/file/7520945311.pdf	
			https://ecfsapi.fcc.gov/file/1093087536094/ENG_EUROPEAN_MANIFESTO_IN_SUPPORT_THE_ECI.pdf	
			https://ecfsapi.fcc.gov/file/1093087536094/FCC%20Testimony%20Patricia%20Burke.pdf	
			https://ecfsapi.fcc.gov/file/7520958046.pdf	
			https://ecfsapi.fcc.gov/file/7520943196.pdf	

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			https://ecfsapi.fcc.gov/file/7520941197.pdf	
			https://ecfsapi.fcc.gov/file/1071413202273/SubmissionsbythePublictotheFCC%20(1).pdf	
			https://ecfsapi.fcc.gov/file/10712158797276/NO-SAFE-PLACE-Letter-to-Gregor-Robertson-040716.pdf	
			https://ecfsapi.fcc.gov/file/1070795887708/Federal%20Wifi%20in%20schools%20complaint%20of%20X%20vFay.pdf	
			https://ecfsapi.fcc.gov/file/7520958011.pdf	
			https://ecfsapi.fcc.gov/file/7520950200.pdf	
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			https://ecfsapi.fcc.gov/file/7022311536.pdf	
			https://ecfsapi.fcc.gov/file/109281319517547/Statement%202.pdf	
82	226	They face a dismal future: progressive worsening from unavoidable, ever-increasing and more intense exposure from multiple sources using a variety of pulsation/modulation schemes		
			https://www.fcc.gov/ecfs/filing/10929002344399	
			https://www.fcc.gov/ecfs/filing/6017465527	
			https://ecfsapi.fcc.gov/file/7520940272.pdf	
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			https://ecfsapi.fcc.gov/file/7022311189.pdf	
84	233	This subject generated enormous discussion: 54 commenters strongly supported use of the precautionary principle and/or prudent avoidance		
			https://ecfsapi.fcc.gov/file/1001669617135/final_mobile_towers_report.pdf	
			https://ecfsapi.fcc.gov/file/1070786836035/False%20Statements%20Made%20on%20MCPS%20Webpage%20Feb%202016%20Letter%20to%20MCPS.pdf	
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			https://ecfsapi.fcc.gov/file/7520942896.pdf	pp. 1, 6
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			https://www.fcc.gov/ecfs/filing/6017339057	
			https://ecfsapi.fcc.gov/file/7022311272.pdf	
			https://ecfsapi.fcc.gov/file/107140107208853/Chris%20Nubbe%20Comments%20on%20FCC%205G%207-12-16.doc	
			https://ecfsapi.fcc.gov/file/7022311196.pdf	
			https://www.fcc.gov/ecfs/filing/6017465552	
			https://ecfsapi.fcc.gov/file/7520938713.pdf	
84	234	The scientific/medical submissions uniformly urged the precautionary principle and a finding of current inadequacy due to lack of any protection against non-thermal effects.		
			https://ecfsapi.fcc.gov/file/1001669617135/RF-Radiation%20injures%20trees%202016.pdf	
			https://ecfsapi.fcc.gov/file/1082378196122/mobile-phone2869e7ae8d79d01d84b5e9e2938fe2c4.pdf	
			https://ecfsapi.fcc.gov/file/10718080685516/Porto_Alegre_Resolution.pdf	
			https://ecfsapi.fcc.gov/file/10709642227609/Renewal45_Koetzsch%20(4).pdf	
			https://ecfsapi.fcc.gov/file/10709642227609/Yakymenko%20Long-term%20MW%20Rad%20Provokes%20Cancer%206-11.pdf	

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			https://ecfsapi.fcc.gov/file/12103008105187/nonionizing%20radiation%20international%20perspective%20Belpomme%20Hardell%20Carpenter%202018.pdf	
			https://ecfsapi.fcc.gov/file/10607967426295/International-Policy-Precautionary-Actions-on-Wireless-Radiation.pdf	
			https://ecfsapi.fcc.gov/file/109303096909269/Carpenter.2010.Human%20health%20effects%20of%20EMFs.Cost%20of%20doing%20nothing.pdf	
			https://ecfsapi.fcc.gov/file/1070795887708/WireleassDevices_GaryBrown.pdf	
			https://ecfsapi.fcc.gov/file/7520958480.pdf	
			https://ecfsapi.fcc.gov/file/7520940927.pdf	
			https://ecfsapi.fcc.gov/file/7520939955.pdf	
			https://ecfsapi.fcc.gov/file/106070048305926/Doctor-Letters-on-Wi-Fi-In-School-Full-Compilation.pdf	pp. 2, 15, 17, 28, 35, 41, 43 46, 53, 54, 61, 62 69, 83, 85, 95
90	240	The FCC's disregard for this situation has caused a sub-population to lose hope of ever being able to meaningfully participate in society.		
			https://ecfsapi.fcc.gov/file/7520943747.pdf	

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			https://ecfsapi.fcc.gov/file/7520923462.pdf	
			https://www.fcc.gov/ecfs/filing/107212194427601	
			https://ecfsapi.fcc.gov/file/7520939739.pdf	
			https://ecfsapi.fcc.gov/file/7520940277.pdf	
			https://www.fcc.gov/ecfs/filing/10713174822422	
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			https://ecfsapi.fcc.gov/file/7520943725.pdf	
			https://www.fcc.gov/ecfs/filing/10912513712220	
			https://ecfsapi.fcc.gov/file/7520940591.pdf	
82	228	The regulations provide "color of law" to wireless provider activities that inflict injuries on innocent people and children who just want to enjoy life, peace, and security. They cannot go into public spaces, access medical care, obtain public services, use public transportation, drive on the road, fly, stay at a hotel or have a job. Children are ridiculed, forced out of schools and into social isolation. Finding a home has become almost impossible		
			https://ecfsapi.fcc.gov/file/7520940954.pdf	pp. 32-36

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			https://ecfsapi.fcc.gov/file/7520941681.pdf	
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			https://ecfsapi.fcc.gov/file/7520960309.pdf	
			https://ecfsapi.fcc.gov/file/7022311640.pdf	
			https://ecfsapi.fcc.gov/file/7520941898.pdf	
			https://ecfsapi.fcc.gov/file/7520941165.pdf	
			https://ecfsapi.fcc.gov/file/7520941369.pdf	
			https://ecfsapi.fcc.gov/file/7520941099.pdf	
			https://ecfsapi.fcc.gov/file/7022311483.pdf	
			https://ecfsapi.fcc.gov/file/7022311292.pdf	
16	47	Numerous other organizations, scientific conferences, appeals and medical groups support this position		
			https://ecfsapi.fcc.gov/file/7022311506.pdf	
			https://ecfsapi.fcc.gov/file/10929811111664/41-	
			https://ecfsapi.fcc.gov/file/7022311383.pdf	pp. 2-8
			https://ecfsapi.fcc.gov/file/7520942173.pdf	
			https://ecfsapi.fcc.gov/file/109281319517547/20-	
			https://ecfsapi.fcc.gov/file/7022311420.pdf	
			https://ecfsapi.fcc.gov/file/7520958408.pdf	
28	99	More than 180 individuals directly advised the FCC that they		
			https://ecfsapi.fcc.gov/file/7520943725.pdf	
			https://ecfsapi.fcc.gov/file/7520939735.pdf	
			https://ecfsapi.fcc.gov/file/7022311262.pdf	
			https://ecfsapi.fcc.gov/file/7022311189.pdf	
			https://ecfsapi.fcc.gov/file/1090341911619/Personal%20health%20impacts%20of%205G.txt	

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			https://www.fcc.gov/ecfs/filing/10912513712220	
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			https://ecfsapi.fcc.gov/file/7520943194.pdf	
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			https://ecfsapi.fcc.gov/file/7520940272.pdf	
			https://ecfsapi.fcc.gov/file/107131064028084/Dear%20Commissioners.docx	
			https://ecfsapi.fcc.gov/file/7520939713.pdf	
			https://ecfsapi.fcc.gov/file/7520938799.pdf	
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			https://ecfsapi.fcc.gov/file/7520941309.pdf	
			https://ecfsapi.fcc.gov/file/7520938471.pdf	
			https://ecfsapi.fcc.gov/file/7520937354.pdf	

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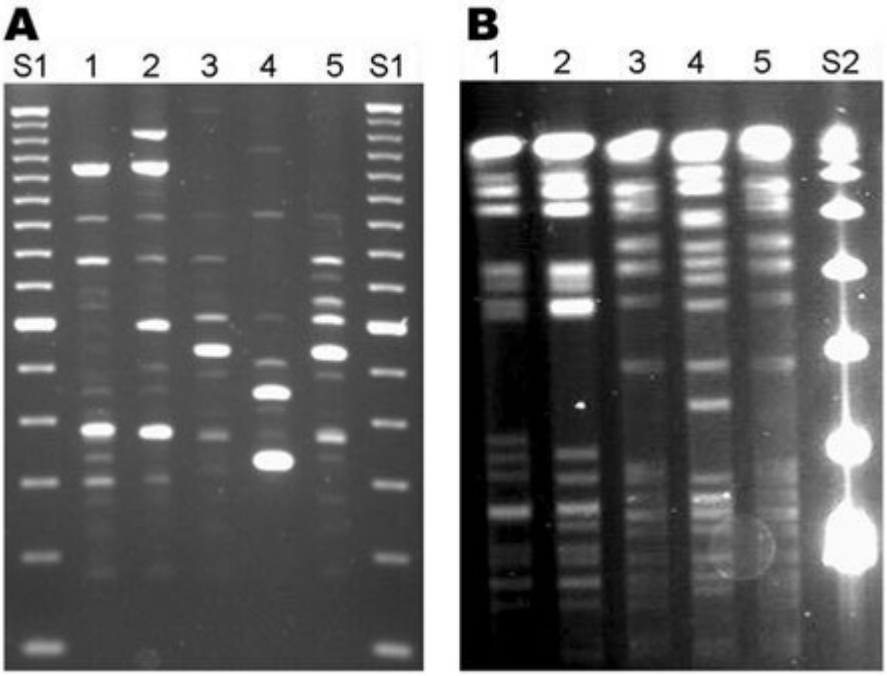
https://www.youtube.com/watch?v=GWRbIIaPV78&feature=youtu.be

Covid 19

https://uncoverdc.com/2020/04/07/was-the-covid-19-test-meant-to-detect-a-virus/

Was the COVID-19 Test Meant to Detect a Virus?

By Celia Farber April 7, 2020



The Corona Simulation Machine: Why the Inventor of The "Corona Test" Would Have Warned Us Not To Use It To Detect A Virus

"Scientists are doing an awful lot of damage to the world in the name of helping it. I don't mind attacking my own fraternity because I am ashamed of it." –Kary Mullis, Inventor of Polymerase Chain Reaction

What do we mean when we say somebody has 'tested positive' for the Corona Virus? The answer would astound you. But getting this "answer" is like getting to a very rare mushroom that only grows above 200 feet on a Sequoia tree in the forbidden forest.

I say that for dramatic effect, but also because I wound up, against all odds, finding it.

Every day I wake up and work at shedding one more layer of ignorance —by listening carefully. I got lucky with scientists many years ago; Epic, incredible scientists, happening to cross my path when nobody else wanted to talk to them. Now their names are emerging, their warnings and corrections crystallizing. True "science" (the nature of the natural world) is never bad news. Globalist science is nothing but bad news.

The reason Bill Gates wants you to believe a Corona Virus will exterminate over 450 million people is that he hates nature, God, and you. (A subjective interpretation.)

Why is that? You'd have to ask his psychiatrist.

But let's talk about the latest terror bomb detonated by Global Atheist PC Creeps upon your perfectly good, free life as a US citizen in 2020, governed by a President who does not think backwards.

How many of us are "infected" with this novel Corona virus, and how scared should we be?

First, a spiritual law: Anything that tries to frighten you comes from "opposition," in spiritual battle. It's not the Holy Spirit, period. Ignore its threats and keep your wits about you. You don't have to shout, "Stay safe!' to your neighbors. We *are* safe. We have an immune system that is a miracle like The Sistine Chapel. It withstands toxic, microbial inundation on a grand scale at all times, while operating a super-highway of adaptive life-sustaining genetic information, on cellular bridges, emitting telegrams of vital evolutionary code, slandered as "viruses" or "retroviruses."

People die—yes. But people don't die the way Bill Gates would have you believe, at the mercy of malicious, predatory pathogens, "lurking" on every surface, and especially other humans. That's not "science." That's social engineering. Terrorism.

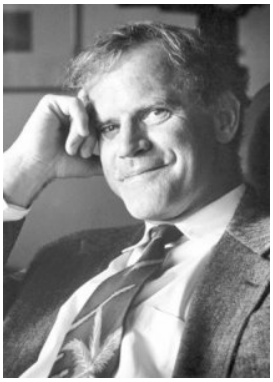
Let's proceed.

What do we mean when we say a person "tests positive" for Covid-19?

We don't actually mean they have been found to "have" it.

We've been hijacked by our technologies, but left illiterate about what they actually mean. In this case, I am in the rare position of having known, spent time with, and interviewed the inventor of the method used in the presently available Covid-19 tests, which is called PCR, (Polymerase Chain Reaction.)

His name was Kary B. Mullis, and he was one of the warmest, funniest, most eclectic-minded people I ever met, in addition to being a staunch critic of HIV "science," and an unlikely Nobel Laureate, i.e. a "genius."

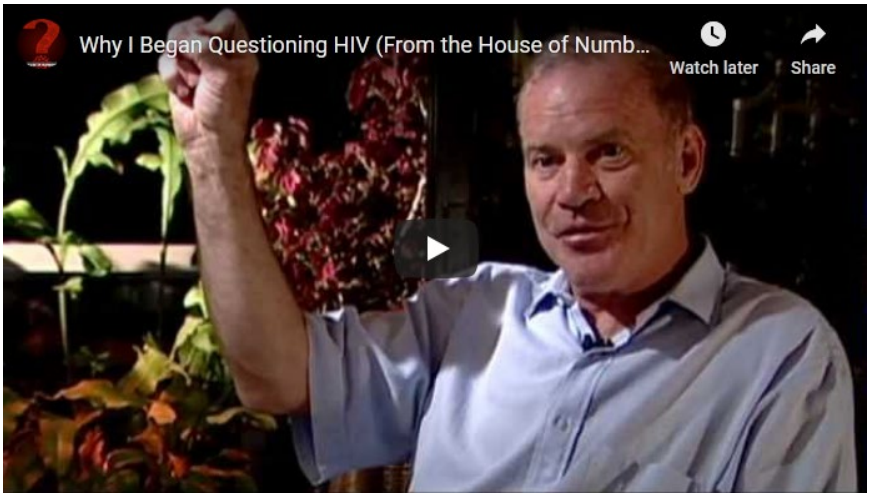


One time, in 1994, when I called to talk to him about how PCR was being weaponized to "prove," almost a decade after it was asserted, that HIV caused AIDS, he actually came to tears.

The people who have taken *all* your freedoms away in recent weeks, they're social engineers, politicians, globalist thought leaders, bankers, WHO fanatics, and the like. Their army is composed of "mainstream media," which is now literally a round-the-clock perfect propaganda machine for the Gates-led Pandemic Reich.

Kary Mullis was a *scientist.* He never spoke like a globalist, and said once, memorably, when accused of making statements about HIV that could endanger lives: "I'm a scientist. I'm not a lifeguard." That's a very important line in the sand. Somebody who goes around claiming they are "saving lives," is a very dangerous animal, and you should run in the opposite direction when you encounter them. Their weapon is fear, and their favorite word is "could." They entrap you with a form of bio-debt, creating simulations of every imaginable thing that "could"

happen, yet hasn't. Bill Gates has been waiting a long time for a virus with this much, as he put it, "pandemic potential." But Gates has a problem, and it's called PCR.



Of Mullis' invention, Polymerase Chain Reaction, the *London Observer* wrote:

"Not since James Watt walked across Glasgow Green in 1765 and realized that the secondary steam condenser would transform steam power, an inspiration that set loose the industrial revolution, has a single, momentous idea been so well recorded in time and place."

What does HIV have to do with Covid-19?

PCR played a central role in the HIV war (a war you don't know about, that lasted 22 years, between Globalist post-modern HIV scientists and classical scientists.) The latter lost the war. Unless you count being correct as winning. The relentless violence finally silenced the opposition, and it seemed nobody would ever learn who these scientists were, or why they fought this thing so adamantly and passionately.

And PCR, though its inventor died last year, and isn't here to address it, plays a central role in Corona terrorism.

Here is an outtake from an article I published in SPIN, in 1994, about Kary Mullis, PCR, HIV and…Tony Fauci:

"PCR has also had a great impact on the field of AIDS, or rather, HIV research. PCR can, among other things, detect HIV in people who test negative to the HIV antibody test.

The word "eccentric" seems to come up often in connection with Mullis' name: His first published scientific paper, in the premier scientific journal Nature in 1986, described how he viewed the universe while on LSD – pocked with black holes containing antimatter, for which time runs backward. He has been known to show photographs of nude girlfriends during his lectures, their bodies traced with Mandelbrot fractal patterns. And as a side project, he is developing a company which sells lockets containing the DNA of rock stars. But it is his views on AIDS that have really set the scientific establishment fuming.

Mullis, like his friend and colleague Dr. Peter Duesberg, does not believe that AIDS is caused by the retrovirus HIV. He is a long-standing member of the Group for the Reappraisal of the HIV-AIDS Hypothesis, the 500-member protest organization pushing for a re-examination of the cause of AIDS.

One of Duesberg's strongest arguments in the debate has been that the HIV virus is barely detectable in people who suffer from AIDS. Ironically, when PCR was applied to HIV research, around 1989, researchers claimed to have put this complaint to rest. Using the new technology, they were suddenly able to see viral particles in the quantities they couldn't see before. Scientific articles poured forth stating that HIV was now 100 times more prevalent than was previously thought. But Mullis himself was unimpressed. "PCR made it easier to see that certain people are infected with HIV," he told Spin in 1992, "and some of those people came down with symptoms of AIDS. But that doesn't begin even to answer the question, 'Does HIV cause it?'"

Mullis then went on to echo one of Duesberg's most controversial claims. "Human beings are full of retroviruses," he said, "We don't know if it is hundreds or thousands or hundreds of thousands. We've only recently started to look for them. But they've never killed anybody before. People have always survived retroviruses."

Mullis challenged the popular wisdom that the disease-causing mechanisms of HIV are simply too "mysterious" to comprehend. "The mystery of that damn virus," he said at the time, "has been generated by the $2 billion a year they spend on it. You take any other virus, and you spend $2 billion, and you can make up some great mysteries about it too."

Like so many great scientific discoveries, the idea for PCR came suddenly, as if by direct transmission from another realm. It was during a late-night drive in 1984, the same year, ironically, that HIV was announced to be the "probable" cause of AIDS.

"I was just driving and thinking about ideas and suddenly I saw it," Mullis recalls. "I saw the polymerase chain reaction as clear as if it were up on a blackboard in my head, so I pulled over and started scribbling." A chemist friend of his was asleep in the car, and, as Mullis described in a recent special edition of Scientific American: "Jennifer objected groggily to the delay and the light, but I exclaimed I had discovered something fantastic. Unimpressed, she went back to sleep."

Mullis kept scribbling calculations, right there in the car, until the formula for DNA amplification was complete. The calculation was based on the concept of "reiterative exponential growth processes," which Mullis had picked up from working with computer programs. After much table-pounding, he convinced the small California biotech company he was working for, Cetus, that he was on to something. Good thing they finally listened: They sold the patent for PCR to Hoffman-LaRoche for the staggering sum of $300 million – the most money ever paid for a patent. Mullis meanwhile received a $10,000 bonus.

Mullis's mother reports that as a child, her lively son got into all kinds of trouble – shutting down the house's electricity, building rockets, and blasting small frogs hundreds of feet into the air. These days, he likes to surf, rollerblade, take pictures, party with his friends – most of whom are not scientists – and above all, he loves to write.

Mullis is notoriously difficult to track down and interview. I had left several messages on his answering machine at home but had gotten no response. Finally, I called him in the late evening, and he picked up, in the middle of bidding farewell to some dinner guests. He insisted he would not give me an interview, but after a while, a conversation was underway, and I asked if I couldn't just please turn my tape recorder on. "Oh, what the hell," he gruffed. "Turn the fucker on."

Our talk focused on AIDS. Though Mullis has not been particularly vocal about his HIV skepticism, his convictions have not, to his credit, been muddled or softened by his recent success and mainstream acceptability. He seems to revel in his newly acquired power. "They can't pooh-pooh me now, because of who I am," he says with a chuckle – and by all accounts, he's using that power effectively.

When ABC's "Nightline" approached Mullis about participating in a documentary on himself, he instead urged them to focus their attention on the HIV debate. "That's a much more important story," he told the producers, who up to that point had never acknowledged the controversy. In the end, "Nightline" ran a two-part series, the first on Kary Mullis, the second on the HIV debate. Mullis was hired by ABC for a two-week period, to act as their scientific consultant and direct them to sources.

The show was superb, and represented a historic turning point, possibly even the end of the seven-year media blackout on the HIV debate. But it still didn't fulfill Mullis' ultimate fantasy. "What ABC needs to do," says Mullis, "is talk to [Chairman of the National Institutes of Allergy and Infectious Diseases (NIAID) Dr. Anthony] Fauci and [Dr. Robert] Gallo [one of the discoverers of HIV] and show that they're assholes, which I could do in ten minutes."

But I point out, Gallo will refuse to discuss the HIV debate, just as he's always done.

"I know he will," Mullis shoots back, anger rising in his voice. "But you know what? I would be willing to chase the little bastard from his car to his office and say, 'This is Kary Mullis trying to ask you a goddamn simple question,' and let the cameras follow. If people think I'm a crazy person, that's okay. But here's a Nobel Prize-winner trying to ask a simple question from those who spent $22 billion and killed 100,000 people. It has to be on TV. It's a visual thing. I'm not unwilling to do something like that."

He pauses, then continues. "And I don't care about making an ass of myself because most people realize I am one."

While many people, even within the ranks of the HIV dissidents, have of late tried to distance themselves from the controversial Duesberg, Mullis defends him passionately and seems genuinely concerned about his fate. "I was trying to stress this point to the ABC people" he says, "that Peter has been abused seriously by the scientific establishment, to the point where he can't even do any research. Not only that, but his whole life is pretty much in disarray because of this, and it is only because he has refused to compromise his scientific moral standards. There ought to be some goddamn private foundation in the country, that would say, 'Well, we'll move in where the NIH [National Institutes of Health] dropped off. We'll take care of it. You just keep right on saying what you're saying, Peter. We think you're an asshole, and we think you are wrong, but you're the only dissenter, and we need one, because it's science, it's not religion.' And that was one of the reasons why I cooperated with ABC."

"I am waiting to be convinced that we're wrong," Mullis continues. "I know it ain't going to happen. But if it does, I will tell you this much – I will be the first person to admit it. A lot of people studying this disease are looking for the clever little pathways they can piece together, that will show how this works. Like, 'What if this molecule was produced by this one and then this one by this one, and then what if this one and that one induces this one' – that stuff becomes, after two molecules, conjecture of the rankest kind. People who sit there and talk about it don't realize that molecules themselves are somewhat hypothetical, and that their interactions are more so, and that the biological reactions are even more so. You don't need to look that far. You don't discover the cause of something like AIDS by dealing with incredibly obscure things. You just look at what the hell is going on. Well, here's a bunch of people that are practicing a new set of behavioral norms. Apparently, it didn't work because a lot of them got sick. That's the conclusion. You don't necessarily know why it happened. But you start there."

http://aidswiki.net/index.php?title=Document:Farber_interviews_Mullis

That was a historical detour, shared in hopes of rooting this conversation historically.

When you see the word "cases" on your TV screen, in this world that has now been hijacked by one single event, one dread, one Idol, you will be forgiven for thinking those are *cases* of Covid-19.

The number of “cases” is often a very big number, back-lit in red. Today for example, the number of “total cases,” in the US, according to Worldometer, is 309,728. The total death figure is 8,441. “Active cases,” is 286,546, of which 8,206 are “Serious, Critical.” The number of “new deaths” is 1,037, and the number of “total recovered” is 14,741.

I’m not clear what an “active” case is. Does that mean fully symptomatic? Partially symptomatic? If the latter, it surely encompasses influenza/pneumonia, which has magically, as many have observed, dropped off a cliff for 2020.

In China, generally, they diagnose ‘Corona’ with CT scans and one or two positive PCR tests. In the US, it’s difficult to find out what makes a “case,” ie what the case definition is. Absent CT scans, we are in a bio-tech free-fall. One website offers this distressingly unclear definition: “The novel coronavirus, or COVID-19, has been spreading worldwide, resulting in growing numbers of infected individuals since late 2019 and increased mortality numbers since early 2020. So far, experts have seen that while there are severe cases, the infection is usually mild with non-specific symptoms. And there are no trademark clinical features of COVID-19 infection.”

There are no trademark clinical features? What then, collapsed the world? I sure hope this isn’t all riding on a “test,” as bio-tech Oracle.

A few graphs down, my fears are confirmed: “Diagnosis of COVID-19 involves laboratory tests. Once someone has been diagnosed with the coronavirus, additional diagnostic tests may be done to determine the severity of the infection.”

I accept that “something is going on” that overlaps with flu, but reportedly worse than a normal flu. That’s what we’re hearing. It involves an acute lack of oxygen, for reasons unclear. People can’t breathe. Intubation is a serious, potentially dangerous procedure that begs many questions—but that’s for a future article.

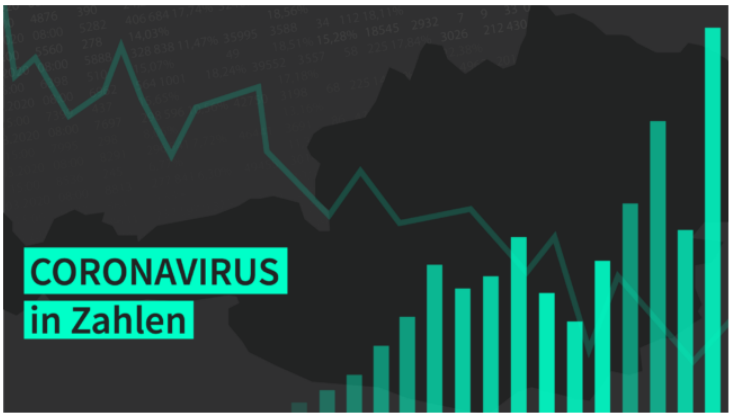
What is the relationship between the spread of testing and the “spread” of a new virus? How do we know what we are experiencing, in comparison to what we are assuming we are experiencing? One study in Austria found that increased testing correlated with, no surprise, increased “cases.”

In an email discussion between a group of international scientists, academics and MD’s, the question was posed whether the daily number of new cases would track with the daily number of tests.

“Yes, they do,” wrote Austrian MD Christian Fiala. “Here are the data from Austria. In other words if they want to further increase the number of ‘infected‘ people, they have to also increase the number of tests. However, that is physically impossible.

Another aspect: during the first weeks most tests were done on sick people. Therefore, the percentage of positive tests was relatively high. But there are not so many sick people and with the general roll out of tests, the vast majority of those tested will be healthy. Consequently, the percentage of positive tests will be low, and most will be false positive.

In other words, it is impossible to continue the increase of positive test results.”



▷ Coronavirus [18. November]: 7091 Neuinfektionen in Österreich

Die Ausbreitung des Erregers SARS-CoV-2 (die Erkrankung heißt COVID-2019) hält die [...]

In the US, we have all but abandoned classical diagnostic medicine in favor of biotech, or lab result medicine. This has been going on for a long time and is a dangerous turning. The "Corona test" is named with characteristic tech-tedium: "CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel." That means it is a needle in a DNA haystack test. A PCR test.

It finds fragments, nucleic acids. From an email from Kary Mullis, to the widow of boxer Tommy Morrison, whose career and life were destroyed by an "HIV test," and who litigated ferociously for years, against test manufacturers, Dr. Mullis wrote, on May 7, 2013:

"PCR detects a very small segment of the nucleic acid which is part of a virus itself. The specific fragment detected is determined by the somewhat arbitrary choice of DNA primers used which become the ends of the amplified fragment. "

If things were done right, "infection" would be a far cry from a positive PCR test.

"You have to have a whopping amount of any organism to cause symptoms. Huge amounts of it," Dr. David Rasnick, bio-chemist, protease developer, and former founder of an EM lab called Viral Forensics told me. "You don't start with testing; you start with listening to the lungs. I'm skeptical that a PRC test is ever true. It's a great scientific research tool. It's a horrible tool for clinical medicine. 30% of your infected cells have been killed before you show symptoms. By the time you show symptoms…the dead cells are *generating* the symptoms."

I asked Dr. Rasnick what advice he has for people who want to be tested for COVID-19.
"Don't do it, I say, when people ask me," he replies. "No healthy person should be tested. It means nothing but it can destroy your life, make you absolutely miserable."
One of the countless head-spinning mysteries of this whole Corona Situation has been the advent of famous people, from Tom Hanks and his wife, to Sophie Trudeau, to Prince Charles announcing they had "tested positive" for COVID-19 and were self-quarantining. In all these famous-powerful people cases, the symptoms were either non-existent or mild. Why, one wondered, did they make such hay about it? The British Royals, especially, seemed to contradict their ethos of secrecy in this case. So what did it mean? It signaled, if anything, that COVID-19 is not all that deadly. That the virus can be present without causing the disease. That host factors matter. And that being "positive" for COVID-19 is neither a PR death sentence nor an actual death sentence. Maybe in their elite and esoteric language, it means some kind of prestige, or sacrament to a Pagan Virus Deity. Who knows? In the case of the Trudeau, Sophie tested positive, and had symptoms, while her husband Justin, the Prime Minister, never got sick, and was never tested. (He didn't want to appear privileged; Not everybody can get tested in Canada, you must have symptoms.)

We do live now in a world dominated by a Corona virus, as my friend Kevin Corbett, a retired nurse in the UK puts it, "with knobs on it." Shrek-Green is the color that was chosen. We're lost in a simulation, seeking to grab hold of "truth" and reality. One way that I do that is to grab hold of words, slow them down, and analyze them. Globalists love to weaponize words and make spells out of them. Hypnotics. To this end, they invent new words, and force you to use them and live them. Words like "Corona Virus," and "Social Distancing." "COVID-19." "Tested Positive."

Whether we realize it or not, this phrase is an echo of HIV-think, which I swam through for most of my so-called career in journalism, choking and spitting all the way out. The globalists write *code.* They encode "viruses" and give them a weaponized, video-game identity. In this video game, you lose all your freedoms, and must display gratitude and servitude. Viral code trumps all other forms of politics. Nothing can counter it. Especially not "science." The virus is also a sweeping metaphor for the spread of "misinformation," which means anything outside their religious doctrines, not recognizable by classical virology.

The code, the potential scenarios, the mysticism and superstition about how the virus spreads, must not be questioned, If you wish to remain a person, as opposed to an un-person. It's a form of post-globalist environmental socialism gone malignant: Demand that all people submit to an equal chance to be killed by a virus. Act out the theatrics of worshiping the virus with fear as the measure of inverted faith. This is why celebrities love this kind of thing. It gives them a chance to debase themselves, to self-flagellate as fellow sufferers. As I write this, from my window in New York City, at 7 pm every evening, people are heard hollering, clapping, and blowing horns from their windows, to show solidarity to the health care workers on the front lines. Was any such thing ever devised for the mass deaths from opioids? No, they weren't significant deaths for the global elites. It's not "death," this play is about. It's socialist contagion theology. You can't go to the grocery store without encountering new displays of Corona Heroica. Only *viruses* interest these people, these haters of liberty. Yet they refuse to learn the first thing about the natural life of viruses and humans. If they did peer into this world, they would find beauty, truth, and wonder. They would find that viruses are rarely deadly, always misunderstood, and actually trying to protect us. The reason the globalists are obsessed with "spread" and "viruses" is because they want to shut down all forms of communication and information exchange that threatens their New World Order.

"Every time somebody takes a swab, a tissue sample of their DNA, it goes into a government database. It's to track us," says David Rasnick. "They're not just looking for the virus. Please put that in your article."

Technocracy

In HIV, the death spell (code) came to people in the form of two antibody tests called ELISA and Western Blot, initially. Not PCR tests—they came later, to measure "viral load," and were specifically *not* to be used for diagnosing HIV. Rather, to stress people out about their "surrogate markers," said to represent where they stood in their battle against HIV. (Did people really need to be in a "battle" against HIV? This was the trillion-dollar question.)

In any case, those tests were not built on a "gold standard" which means purification of an actual virus. Purification means the pathogen has been separated from all else. HIV co-discoverer and Nobel Laureate Luc Montagnier famously told journalist Djamel Tahi in an interview: "I repeat, we did not purify."

HIV was never "separated from everything else." It was and is a laboratory artifact, a set of lab-tortured antigens around which a "test" was built—a test which shattered countless millions of lives, because people watched TV and believed what they were told. They didn't get a chance to hear what Kary Mullis or dozens of other real scientists had to say about the supposedly deadly retrovirus, HIV.

Nothing was proven before it was asserted. This became the norm, paving the way for the situation we are in now. Global viral communism. We all dreaded this would happen, but we never dreamed they would choose a cold virus. A Corona virus.

In the early 1990's, PCR, (Polymerase Chain Reaction) came into popular use, and Kary Mullis was awarded the Nobel Prize for it in 1993. PCR, simply put, is a thermal cycling method used to make up to billions of copies of a specific DNA sample, making it large enough to study. As it correctly says on PCR's Wikipedia page, PCR is an "…indispensable technique" with a "broad variety" of applications, "…including biomedical *research* and criminal forensics." [Italics mine.] The page goes on to say, to my dismay, that one of the applications of PCR is "…for the diagnosis of infectious diseases."

PCR is a needle in a haystack technology that can be extremely misleading in "the diagnosis of infectious diseases." The first conflict between this revolutionary technology and human life happened on the battlefield of AIDS, and Mullis himself came to the front line arguing *against* PCR as diagnostic tool. In 1987, esteemed Berkeley cancer virologist Peter Duesberg had doomed his funding and "career" by issuing a broadside in a paper published in *Cancer Research* to the growing and promiscuous assertions made for cancer viruses, including at least one he stood to gain a Nobel Prize for had he not diffused its significance himself.

His main argument was that the Gallo/Montagnier fusion "virus" that came to be called 'HIV' was (like all viruses in its class) barely capable of infecting cells. It infected so few cells that Duesberg likened the pathogenic model to thinking you can conquer China by killing 3 soldiers a day. There was simply not enough "there-there" in the form of cell death. "It's a pussycat," he said. He even said he wouldn't mind being injected with it. (though not if it came from Gallo's lab.)

With PCR's rise, the HIV Industrial Complex weaponized it to assert that *now* they could see HIV more abundantly, hence their maligned foe Peter Duesberg was toast. And it was Kary Mullis, himself an HIV dissenter, who rose to Duesberg's defense and said, "No he isn't."

I conducted a two-hour interview with David Crowe– Canadian researcher, with a degree in biology and mathematics, host of *The Infectious Myth* podcast, and President of the think-tank *Rethinking AIDS.* He broke down the problems with the PCR based Corona test in great detail, revealing a world of unimaginable complexity, as well as trickery.

"The first thing to know is that the test is not binary," he said. "In fact, I don't think there are any tests for infectious disease that are positive or negative."

The next part of his explanation is lengthy and detailed, but let's push through:

"What they do is they take some kind of a continuum and they arbitrarily say this point is the difference between positive and negative."

“Wow,” I said. “That’s so important. I think people envision it as one of two things: Positive or negative, like a pregnancy test. You “have it” or you don’t.”

“PCR is really a manufacturing technique,” Crowe explained. “You start with one molecule. You start with a small amount of DNA and on each cycle the amount doubles, which doesn’t sound like that much, but if you, if you double 30 times, you get approximately a billion times more material than you started with. So as a manufacturing technique, it’s great. What they do is they attach a fluorescent molecule to the RNA as they produce it. You shine a light at one wavelength, and you get a response, you get light sent back at a different wavelength. So, they measure the amount of light that comes back and that’s their surrogate for how much DNA there is. I’m using the word DNA. There’s a step in RT- PCR test which is where you convert the RNA to DNA. So, the PCR test is actually not using the viral RNA. It’s using DNA, but it’s like the complimentary RNA. So logically it’s the same thing, but it can be confusing. Like why am I suddenly talking about DNA? Basically, there’s a certain number of cycles.”

This is where it gets wild.

“In one paper,” Crowe says, “I found 37 cycles. If you didn’t get enough fluorescence by 37 cycles, you are considered negative. In another, paper, the cutoff was 36. Thirty-seven to 40 were considered “indeterminate.” And if you got in that range, then you did more testing. I’ve only seen two papers that described what the limit was. So, it’s quite possible that different hospitals, different States, Canada versus the US, Italy versus France are all using different cutoff sensitivity standards of the Covid test. So, if you cut off at 20, everybody would be negative. If you cut off a 50, you might have everybody positive.”

I asked him to pause so I could exclaim my astonishment. And yet, it was Déjà vu all over again. Just like in the HIV battle—people were never told that the “HIV test” had different standards in different countries, and within countries, from lab to lab. The highest bar (the greatest number of HIV proteins) was in Australia: five. The Lowest was Africa: 2. In the US it is generally 3-4.

We used to joke that you could rid yourself of an “HIV diagnosis” by flying from either the US or Australia, to Africa. But for many years, “AIDS” in Africa was diagnosed without any tests whatsoever. Just a short list of symptoms that tracked precisely with symptoms of most tropical diseases, such as fever, cough, and shortness of breath.

David, in his quiet Canadian way, dropped a bombshell in his next statement:

“I think if a country said, “You know, we need to end this epidemic,” They could quietly send around a memo saying: “We shouldn’t be having the cutoff at 37. If we put it at 32, the number of positive tests drops dramatically. If it’s still not enough, well, you know, 30 or 28 or something like that. So, you can control the sensitivity.”

Yes, you read that right. Labs can manipulate how many “cases’ of Covid-19 their country has. Is this how the Chinese made their case load vanish all of a sudden?

“Another reason we know this is bogus,” Crowe continued, “is from a remarkable series of graphs published by some people from Singapore in JAMA. These graphs were published in the supplementary information, which is an indication that nobody’s supposed to read them. And I think the authors probably just threw them in because they were interesting graphs, but they didn’t realize what was in them. So, they were 18 graphs of 18 different people. And at this hospital in Singapore, they did daily coronavirus tests and they grasped the number of PCR cycles necessary to detect fluorescence. Or if they couldn’t detect florescence by…37 cycles, they put a dot on the bottom of the graph, signifying a negative.”

"So, in this group of 18 people, the majority of people went from positive, which is normally read as "infected," to negative, which is normally read as "uninfected" back to positive—infected again. So how do you interpret this? How do you have a test if a test act is actually, you know, 100% positive for detecting infection, then the negative results must've been wrong? And so, one way to solve that is to move the point from 37 to say 36 or 38. You can move this, this cycle of numbers. It's an arbitrary division up or down. But there's no guarantee that if you did that, you wouldn't still have the same thing. It would just, instead of going from, from 36 to undetectable and back to 36 or back to 45, it might go from 33 to undetectable to 30 or something like that. Right? So, you can't solve the problem by changing this arbitrary binary division. And so basically this says that the test is not detecting infection. Because if it was, like if you're infected, and then you're uninfected, and you're in a hospital with the best anti-infective precautions in the world, how did you get re-infected? And if you cured the infection, why didn't you have antibodies to stop you getting re-infected? So, there's no explanation within the mainstream that can explain these results. That's why I think they're so important."

I couldn't believe my ears. And yet I could. Have you ever tried to read the package insert for a "Corona" PCR test? You begin to feel after a while that the technobabble is some kind of spell, or bad dream. An alien language from another dimension, that could not possibly—whatever else it may do—help a single human being have a better life. It's not "English." I don't know what it is.

"I've been quoting, Alice in Wonderland a lot recently," David says, "because it's the only way I can wrap my head around it. Alice said: "Sometimes I can believe six impossible things before breakfast!"

One of the ways to distinguish truth from deception in contemporary "science" is to track what gets removed. For example, David tells me, there was apparently an English abstract online at PubMed out of China that rendered the entire COVID testing industrial complex baseless and absurd.

"There was a famous Chinese paper that estimated that if you're testing asymptomatic people, up to 80% of positives could be false positive. That was kind of shocking, so shocking that PubMed had to withdraw the abstract even though the Chinese paper appears to still be published and available. I actually have a translation with a friend. I translated it into English and it's a really, standard calculation of what they call positive predictive value. The abstract basically said that in asymptomatic populations, the chance of a positive coronavirus test being a true positive is only about 20%. 80% will be false positive."

"Doesn't that mean the test means nothing?" I asked.

"The Chinese analysis was a mathematical analysis, a standard, the standard analysis that's been done a million times before. There's no reason to withdraw the paper for any reason. There's nothing dramatic about the paper. It's a really boring analysis. It's just that they did the standard analysis and said, in some populations, like they estimated 1% of people are actually infected in the population. You could have 80% false positive. Uh, they couldn't do a real analysis of false positives in terms of determining whether a test is correct or not because that requires a gold standard and the only gold standard is purification of the virus. So, we get back to the fact that the virus is not being purified. If you could purify the virus, then you could take a hundred people who tested positive and you could search for the virus in them. And if you found the virus in 50 out of a hundred and not in the other 50, you could say that the test is only accurate 50% of the time. But we have no way to do that because we haven't yet purified the virus. And I don't think we ever will."

Dave Rasnick has had exchanges with David Crowe about this, and concurs, "To my knowledge, they have not yet purified this virus."

In a previous interview I did with him a few weeks ago, he said this, about PCR tests and the fallacies of thinking less is more, or smaller is better, or more "sensitive" means more accurate:

“It’s like fingerprints. With PCR you’re only looking at a small number of nucleotide. You’re looking at a tiny segment of gene, like a fingerprint. When you have regular human fingerprints, they have to have points of confirmation. There are parts that are common to almost all fingerprints, and it’s those generic parts in a Corona virus that the PCR test picks up. They can have partial loops but if you only took a few little samples of fingerprints you are going to come up with a lot of segments of RNA that we are not sure have anything to do with corona virus. They will still show up in PCR. You can get down to the levels where its biologically irrelevant and then amplify it a trillion-fold.”

“The primers are what you know. We already know the strings of RNA for the Corona family, the regions that are stable. That’s at one end. Then you look at the other end of the region, for all Corona viruses. The Chinese decided that there was a region in those stable areas that was unique to their Corona virus. You do PCR to see if that is true. If it is truly unique it would work. But they’re using the SARS test because they don’t really have one for the new virus.”

“SARS isn’t the virus that stopped the world,” I offer.

“That’s right.”

“PCR for diagnosis is a big problem,” he continues. “When you have to amplify it these huge numbers of time, it’s going to generate massive amounts of false positives. Again, I’m skeptical that a PCR test is ever true.”

Crowe described a case in the literature of a woman who had been in contact with a suspect case of Corona (in Wuhan) they believed was the index case. “She was important to the supposed chain of infection because of this. They tested her 18 times, different parts of the body, like nose, throat—different PCR tests. 18 different tests. And she tested negative every time. And then they—because of her epidemiological connection with the other cases, they said: “We consider her infected. So, they had 18 negative tests and they said she was infected.”

“Now why was she important? Well there was only one other person who could have theoretically transmitted the virus if the original patient, outside the family was who they thought it was. But secondly, she had the same exact symptoms as everybody else. Right? So, four people in his family came down with fever and cough and headaches, fatigue and all these kinds of big symptoms. So, if she could get those symptoms without the virus, then you, you’ve got to say, well, why couldn’t everybody else’s symptoms be explained by whatever she had? I mean, maybe they, they ate some bad seafood or something and so they all got sick, but it had nothing to do with the coronavirus. But because three out of the four, tested positive, then they were, they were all considered infected and out of the same paper.

Another interesting thing is that they did a lot of tests. The first person in the list of people tested, he was positive on three out of 11 tests. So again, they took nose and throat samples and you know, different methods and all this kind of stuff. And they got 11 separate tests and only three were positive. And of course, all you need to be considered infected is one positive test. They could test you 20 times and if you test positive once, then you’re infected. So, a positive test is meaningful. A negative test. It’s like, eh. Not so much.”

I asked Crowe what he thought Kary Mullis would say about this explosion of PCR insanity.

“I’m sad that he isn’t here to defend his manufacturing technique,” he said. “Kary did not invent a test. He invented a very powerful manufacturing technique that is being abused. What are the best applications for PCR? Not medical diagnostics. He knew that and he always said that.”

Our conversation went in many different directions and I plan to publish the entire audio interview. I asked David what he thought was happening here, at the most core level.

“I don’t think they understand what they’re doing,” he said. “I think it’s out of control. They don’t know how to end this. This is what I think what happened: They have built a pandemic machine over many years and, and as you know, there was a pandemic exercise not long before this whole thing started.”

“I just want to identify who sponsored that simulation conference, 6 weeks before the first news broke out of Wuhan,” I interjected. “It was the Bill and Melinda Gates foundation, Johns Hopkins Center For Health Security, and the World Economic Forum. Incidentally, all the stats, projections and modeling you see in the media are coming out of Johns Hopkins.”

“Right. So, this beautiful pandemic machine is a lot like…let’s use an example of an aircraft simulator. Okay. So, so pilots are tested on an aircraft simulator. So if you’re flying along in an airplane and there’s a loud bang and you see smoke coming from an engine on the right hand side, this is probably the first time a pilot has ever been in an airplane that had an engine failure. But he’s tested this scenario 25 times on an aircraft simulator. So, he knows exactly what to do without being told. He goes through the procedure. He doesn’t have to think, he just does the steps that he’s been taught through the, the aircraft simulator and he successfully lands the airplane with one engine. So, a pandemic simulator is just like that. You sit down at the computer, you see the virus going around the world, um, and you say, okay, so what we need to do is we need to dress everybody in protective clothing.” “We need to quarantine everybody who’s positive. Next step. We need to do social isolation. It’s a *mathematical* model. And at the end you always win, right? So, in the end, the good guys win, and the pandemic is defeated. But there’s, there’s never been like an actual real pandemic since they built this machine. So, there’s this huge machine, it’s got a red button on it and it’s like if you ever detect a pandemic starting, you press the red button. We don’t know exactly what happened, but I think the Chinese government was embarrassed cause they were being accused of covering up a pandemic. They said, okay, you know, we want Western approval for our medical system so we’re going to press the goddamn red button. Or they did. And then everything followed from that. The problem is that the simulation was never based on reality.”

In another part of our conversation, he said something unforgettable:

“So, we’ve essentially been taken over by the medical Taliban, if you like.”

I pressed him one last time:

“David, in conclusion, finish this sentence: “The PCR test for Corona is as good as…”

His reply made me laugh. I didn’t know I still could laugh.

“It’s as good as that Scientology test that detects your personality and then tells you need to give all your money to Scientology. “

Celia Farber is half Swedish, raised there, so she knows “socialism” from the inside. She has focused her writings on freedom and tyranny, with an early focus on the pharmaceutical industry and media abuses on human liberties. She has been under ferocious attack for her writings on HIV/AIDS, where she has worked to document the topic as a psychological operation, and rooted in fake science. She is a contributor to UncoverDC and The Epoch Times, and has in the past written for Harper’s, Esquire, Rolling Stone and more. Having been gravely injured in legacy media, she never wants to go back. She is the recipient of the Semmelweis International Society Clean Hands Award For Investigative Journalism, and was under such attack for her work, she briefly sought protection from the FBI and NYPD. She is the author of “Serious Adverse Events: An Uncensored History of AIDS,” and the editor of The Truth Barrier, an investigative and literary website. She co-hosts “The Whistleblower Newsroom” with Kristina Borjesson on PRN, Fridays at 10am.

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COVID-19 vaccine development and a potential nanomaterial path forward

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Abstract

The COVID-19 pandemic has infected millions of people with no clear signs of abatement owing to the high prevalence, long incubation period and lack of established treatments or vaccines. Vaccines are the most promising solution to mitigate new viral strains. The genome sequence and protein structure of the 2019-novel coronavirus (nCoV or SARS-CoV-2) were made available in record time, allowing the development of inactivated or attenuated viral vaccines along with subunit vaccines for prophylaxis and treatment. Nanotechnology benefits modern vaccine design since nanomaterials are ideal for antigen delivery, as adjuvants, and as mimics of viral structures. In fact, the first vaccine candidate launched into clinical trials is an mRNA vaccine delivered via lipid nanoparticles. To eradicate pandemics, present and future, a successful vaccine platform must enable rapid discovery, scalable manufacturing and global distribution. Here, we review current approaches to COVID-19 vaccine development and highlight the role of nanotechnology and advanced manufacturing.

Main

In December 2019, a novel coronavirus (nCoV or SARS-CoV-2) belonging to the betacoronavirus family emerged[1,2]. All human betacoronaviruses are unique from one another, however, they do share a certain degree of genetic and structural homology. SARS-CoV-2 genome sequence homology with SARS-CoV and MERS-CoV is 77% and 50%, respectively[3]. In contrast to the relatively smaller outbreaks of SARS-CoV in 2002 and MERS-CoV in 2012, SARS-CoV-2 is exhibiting an unprecedented scale of infection, resulting in a global pandemic declaration of Coronavirus Infectious Disease (COVID-19) on 11 March 2020 by the World Health Organization (WHO). On 1 June 2020, the World Health Organization reported >6 million confirmed cases and 371 thousand deaths globally.

Of note, during the 1918 influenza pandemic, more death was observed in the second phase of outbreak[4]. Similar to influenza, COVID-19 harbours the potential to become a seasonal disease[5]. The high infection rate, long incubation period, along with mild-to-moderate symptoms experienced by many, make COVID-19 a troubling disease. A vaccine is crucial, in particular because data indicate asymptomatic transmission of COVID-19[6,7,8]. More than 10 years ago, scientists predicted the pandemic potential of the coronaviruses[9].

And for the past 30 years, a once-per-decade novel coronavirus has pushed our public health system to the limit, with SARS-CoV-2 being the most severe. Despite the repeated warnings and discussion, the world was not prepared for this pandemic. The rapid development, distribution and administration of a vaccine to the global population is the most effective approach to quell this pandemic and the only one that will lead to a complete lifting of restrictions. Challenges include the vaccine design itself, but also its manufacture and global distribution; cold chain requirements present logistical and fiscal barriers to the availability of important, life-saving vaccines in resource-poor areas of the world. Innovating vaccine delivery platforms and devices to break cold chain limitations are therefore an efficient solution to safeguard potent vaccination for both wealthy and lower-income countries.

Box 1 Components and options in vaccine design

Antigen: a foreign material that can induce an immune response within the body—often derived from the pathogen one aims to immunize against. Based on how the antigen is presented, vaccines can be categorized as:

- Live-attenuated vaccine: weakened form of pathogens capable of replication, but not causing illness.
- Inactivated vaccine: killed form of pathogens incapable of replication or infection.
- Subunit vaccine: minimal antigenic element of a pathogen, for example, a protein, protein subunit or polysaccharides or VLPs self-assembled from these components. These antigens in purified forms are administered in combination with molecular adjuvants or expressed in vivo using RNA, DNA or viral vectors.
- Peptide-based vaccines: peptides are fundamental element of a protein subunit recognized by the immune system; all antigens described above contain peptide epitopes.

Adjuvant: a stimulatory agent designed to boost immune response toward a co-delivered antigen.

- Occurs as ‘independent entities’ in a mixture with antigens.
- Occurs as ‘conjugate-entities’ via chemical fusion directly to antigens.

Nanoparticle/nanocarrier: The live-attenuated and inactivated viral vaccines can be regarded as nanoparticles themselves. Rather than serving as the vaccine itself, a nanoparticle (viral or non-viral) can be employed as nanocarrier to encapsulate or present the antigen payload or nucleic acid encoding the antigen. Nanocarriers provide stability and targeting of these payloads to antigen presenting cells (APCs); nanocarriers can confer innate adjuvant behaviour (see Fig. 3). Nanocarriers synchronize delivery of both, antigen and adjuvant, to target immune cells.

- Viral vector: repurposed mammalian viruses engineered to deliver a gene encoding the antigen (examples include adenoviral vectors derived from chimpanzee and human).
- Proteinaceous nanoparticles: nanoscale biomaterial assemblies with atomic precision and complexity (examples include protein nanocages and non-infectious viruses such as plant viruses or bacteriophages) engineered to present a subunit vaccine or deliver a nucleic acid encoding the antigen.
- Synthetic nanoparticles: nanoscale assemblies of synthetic materials (examples include polymer, liposomal, or lipid nanoparticles) engineered to present a subunit vaccine or deliver a nucleic acid encoding the antigen.

Device: a piece of equipment designed to administer vaccine (Fig. 4).

- Syringe: hypodermic needle used for intramuscular, subcutaneous or intradermal delivery of vaccine by a healthcare professional (>10 mm length and 0.25–0.5 mm in outer diameter, somewhat invasive)
- Implant: slow-release device containing vaccine for sustained subcutaneous delivery, administered by a healthcare professional (<10 mm in length and <2 mm in width, more invasive)
- Microneedle patch: array of micrometre-scale needles containing vaccine for slow release, sustained intradermal delivery, administered by a healthcare professional or via self-administration (<1 mm in length and 0.1–0.5 mm in width, approximately 1 cm^2 patch, minimally invasive).

The vaccine strategies

When designing a vaccine, principally, one needs to define the antigen, the adjuvant, the manufacturing system and the delivery strategy (Box 1). The rapid development of vaccines is possible because the genome and structural information of SARS-CoV-2 was made available in record time[10,11,12,13,14]. These data, along with expedited communication of bioinformatic predictions and epitope mapping[15,16,17,18], has provided crucial knowledge enabling vaccine design beyond development of live-attenuated and inactivated vaccines[19,20,21,22,23]. Also, information available from prior development of SARS/MERS vaccine candidates aids in the development of SARS-CoV-2 vaccine candidates[24,25]. Nanotechnology platforms offer great utility in modern vaccine design and have helped catalyse novel candidate vaccines toward clinical testing at unprecedented speed. Along with inactivated vaccines, emerging nanotechnologies such as mRNA vaccines delivered by lipid nanoparticles and viral vector vaccines have already reached Phase II and III clinical trials (Fig. 1 and Table 1).

Fig. 1: Landscape of COVID-19 vaccine development.

a, As of 1 June 2020, 157 vaccine candidates are undergoing development by academic labs and industry (and partnerships thereof). COVID-19 vaccine candidates include live-attenuated vaccines, inactivated vaccines, subunit vaccines, virus-like particles (VLPs), viral vectors (replicating and non-replicating), DNA and RNA vaccines. **b**, 16 vaccine candidates have entered clinical testing (Table 1). The vaccine candidate data was compiled from searching vaccine trackers resources: Milken Institute (https://milkeninstitute.org/covid-19-tracker), Regulatory Affairs Professionals Society[104], BioCentury (https://www.biocentury.com/preclinical-vaccines-and-therapies), and World Health Organization (http://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus/en/).

Full size image

Table 1 COVID-19 vaccine candidates in the clinical development pipeline

Full size table

SARS-CoV-2 is an enveloped ssRNA virus with spike-like glycoproteins protruding from its exterior membrane surface forming a ‘corona’. The four major structural proteins of betacoronaviruses are spike (S) protein, envelope (E) protein, membrane (M) protein, and nucleocapsid (N) protein[26]. The S protein is an attractive target for vaccine design because it facilitates viral entry into the host cell during the infection process. The two spike protein subdomains, S1 and S2, are responsible for host cell angiotensin-converting enzyme 2 (ACE2) receptor binding and host cell membrane fusion, respectively[27]. S1 contains the receptor-binding domain (RBD) and S2 the fusion

machinery enabling virus entry (Fig. 2). While the S1 domain is divergent across the coronaviruses, the S2 domain is more conserved[12]. Combining SARS-CoV-2 structural information and knowledge gained from SARS/MERS vaccine candidates[28], researchers projected the full length S protein, as well as S1, RBD, and S2 subunit derivatives, to contain the prime target epitopes for the induction of neutralizing antibodies. Indeed, recent clinical data from a cohort of convalescent SARS-CoV-2 patients validates this approach—analysed patient sera indicates neutralizing antibodies targeting the different domains of S protein: S1, RBD and S2[29].

Fig. 2: The spike protein (S protein) protruding from the coronavirus SARS-CoV-2 is the primary target for various ongoing vaccine development efforts.

Assembled form three identical chains (depicted in orange, grey and white colours), the S protein is functionally subdivided in S1 (red) and S2 (green) domain; S1 contains the receptor binding domain (RBD). The SARS-CoV-2 structure was reproduced and adapted from the CDC Public Health Image Library. The S protein structure was prepared on the PyMol molecular graphics system (2.3.4) using the PDB file '6VSB'.

Full size image

SARS-CoV-2 S protein is also extensively glycosylated[30], and computational analysis indicates glycosylated SARS-CoV-2 S protein to have a more organized conformation versus its non-glycosylated counterpart[31]. Therefore, glycosylation of SARS-CoV-2 S vaccine candidates should be considered: DNA/RNA vaccines are produced in situ inside the patient and thus would carry native glycosylation; for recombinant subunit vaccines glycoengineering protocols may be applied. The hotspot of SARS-CoV-2, however, which is critical in binding to the ACE2 receptor, appears to be free from glycosylation[32]; therefore, it may not be required to glycosylate corresponding peptide epitopes.

Contemporary vaccines

Active immunization against viruses have traditionally relied on the usage of whole pathogen in a weakened or killed form through chemical or physical processes, and this has resulted in clinically-approved treatments. Further, several mammalian viral vectors such as oncolytic herpes simplex virus have been repurposed into clinically-approved treatments. Contemporary vaccines hold merit, and here, we highlight how live attenuated, inactivated, and viral vector vaccine development efforts are making the reality of a vaccine against SARS-CoV-2 palpable.

Live attenuated and inactivated vaccines

Live-attenuated vaccines (LAVs) are live, reproducing but avirulent viruses. LAV design intends single-dose immunity without illness. Because LAV technology is mature, LAVs are likely to emerge as one of the frontrunner vaccine candidates for the ongoing COVID-19 pandemic. Codagenix Incorporation's proprietary deoptimized SARS-CoV-2 vaccine candidate currently leads the charge. However, LAVs bear risks of transfer of the virus and/or reversion to the pathogenic form, reactivation in immune-compromised individuals or recombination with related viruses circulating in the population—especially for novel diseases where pathophysiology is not yet fully understood. LAVs generally require cold chain distribution. Furthermore, loss of efficacy and reproductive potential of progeny viruses during vaccine production poses a significant challenge. Preliminary studies of silent codon change indicate some positive effect on mitigating reversion events, however, these are not general to all viruses[33]. New technologies such as genetic code expansion are being applied to create highly reproductive but genetically stable LAVs[34]. More recently, synthetic genomics approaches have enabled the synthesis of recombinant SARS-CoV-2 viruses from fragments of viral DNAs[35,36]. These strategies could be employed towards rapid generation of SARS-CoV-2 LAVs.

Inactivated vaccines (IVs) are heat or chemically inactivated pathogens or fractions thereof. These vaccine formulations are incapable of replication and safer than LAVs, but their inactivation results in lowered immunogenicity and requirement for multiple-dose regimens to establish long-lasting immunity; also, these vaccine formulations often require adjuvants to immunize the aging population due to immune senescence[37]. While IVs have better stability profiles compared to LAVs, they still require a cold chain. Several COVID-19 IVs are in development, with the first clinical trial approved recently for Sinovac.

Viral vectors

Mammalian viruses have been engineered and repurposed for several vaccine applications. For COVID-19, there are several vaccine candidates in development that utilize non-replicating adenoviral vectors. Leading adenoviral vectors in SARS-CoV-2 clinical trials are adenovirus type 5 vector (Ad5-nCoV) as of 16 March 2020 and chimpanzee adenovirus vaccine vector (ChAdOx1) as of 31 March 2020 by CanSino Biological and the University of Oxford, respectively (Table 1). Advantages of adenoviral vectors include their broad tissue tropism, inherent adjuvant qualities and scalability. A challenge for adenoviral vector platforms is pre-existing immunity in humans, which may dampen efficacy of the adenoviral vector. While pre-existing immunity against Ad5 is reportedly widespread, its clinical application continues and moreover, alternative ChAdOx1 with low human seroprevalence have been derived for use as vaccine platforms[38,39].

Next-generation vaccines enabled through advances in nanotechnology

Viruses are nanoscale objects and therefore can be regarded as naturally occurring nanomaterials; per that definition, LAVs, IVs and viral vectors are nanotechnologies. Nanoparticles and viruses operate at the same length scale—this is what makes nanotechnology approaches in vaccine development and immunoengineering so powerful. Nanoparticles, natural or synthetic, mimic the structural features of viruses whereas chemical biology, biotechnology and nanochemistry enables the development of next-generation designer vaccine technologies. From a vaccine technology development point of view, this is an exciting time and novel technologies and approaches are poised to make a clinical impact for the first time.

Nucleic acid-based vaccines

Delivering the genetic code for in situ production of viral proteins is a promising alternative to conventional vaccine approaches. Both DNA and mRNA vaccines fall under this category and are being pursued in the context of the COVID-19 pandemic. While these platforms are attractive in terms of safety, speed, stability and scalability, they carry a significantly higher risk of failure in clinical development as seen previously with other novel technologies[40]. To date there is no licensed DNA or RNA vaccine. Nevertheless, a particular advantage of these vaccines is that in addition to antibody and $CD4^+$ T cell responses, DNA or RNA vaccine elicit $CD8^+$ cytotoxic T cell responses, which plays a key role for virus eradication[41,42]. For the DNA vaccines, the frontrunner in this space

is Inovio Pharmaceuticals with their Phase I clinical trial having commenced 6 April 2020. Another rising company on track for a Phase I clinical trial is Entos Pharmaceuticals, Inc. a company based in Alberta, Canada. mRNA vaccines can be produced through in vitro transcription, which precludes the need for cells and their associated regulatory hurdles[43]. Moderna's mRNA-based technology was the fastest to Phase I clinical trial in the US, which began on 16 March 2020 (see Table 1). Additionally, BioNTech-Pfizer recently announced regulatory approval in Germany for Phase I/II clinical trials to test four lead mRNA vaccine candidates[44].

While DNA vaccines offer higher stability over mRNA vaccines, the mRNA is non-integrating and therefore poses no risk of insertional mutagenesis. Additionally, the half-life, stability and immunogenicity of mRNA can be tuned through established modifications[45]. For example, researchers at the Imperial College of London and Arcturus Therapeutics are incorporating self-amplifying RNA technology to prolong the otherwise short half-life of the RNA and thereby boost S protein expression levels[46] (http://www.imperial.ac.uk/a-z-research/future-vaccine-hub/workstreams/rna-vaccine-manufacture). Nanotechnology-based approaches offer enabling solutions to the delivery challenge by trafficking the vaccine to appropriate cellular populations and subcellular locations. While synthetic nanocarriers including cationic liposomes and polymeric nanoparticles have been used for the delivery of DNA vaccines across cell membranes, targeted formulations could further enhance nuclear translocation of the plasmid DNA[47]. Moderna's mRNA vaccine is based on a lipid nanoparticle platform, but there are many other emerging nanotechnologies for delivery of nucleic acid vaccines (several structures are shown in Fig. 3). Nanotechnology platforms including cationic nanoemulsions, liposomes, dendrimers or polysaccharide particles have been employed for improving the stability and delivery of mRNA based vaccines[41,45].

Fig. 3: Nanoparticle platform vaccine technologies.

a, Protein nanoparticles and their size; sizes for the synthetic nanocarriers vary between 10–1000 nm. The protein nanoparticles were prepared using Chimera software using the PDB files (3IYI, 1FHA, 1NY7 for P22, ferritin and CPMV, respectively). **b**, Components of nanoparticle-based vaccines. **c**, Key steps involved in nanoparticles-based vaccine processing by APCs. The antigenic cargo is processed by the APC and epitopes are presented by MHC-I

and MHC-II leading to production of CD8+ cytotoxic T cells or CD4+ T helper cells required for antiviral antibody production (or a combination thereof).

Full size image

Subunit vaccines

Subunit vaccine candidates constitute minimal structural components of SARS-CoV-2 that can prime protective immune responses in the host when administered with molecular adjuvants for enhanced immunogenicity. For example, contemporary SARS-CoV-2 subunit vaccine candidates are formulations of full-length S protein or S1/S2 subunits with adjuvants. The frontrunner amongst developers is Novavax who initiated a Phase I/II trial on 25 May 2020. Also, Sanofi Pasteur/GSK, Vaxine, Johnson & Johnson and the University of Pittsburgh have announced that they expect to begin Phase I clinical trials within the next few months. Others, including Clover Biopharmaceuticals and the University of Queensland, are independently developing subunit vaccines engineered to present the prefusion trimer confirmation of S protein using the molecular clamp technology[48] and the Trimer-tag technology[49], respectively. Further, other groups are exploring subunit vaccines using only the RBD of the S protein[50].

Alternatively, subunit vaccines can also take the form of protein nanoparticles or virus-like particles (VLPs). VLP vaccines can be produced by recombinant expression and allows for genetic engineering to incorporate ligands, immunomodulators and targeting moieties. Both self-assembled protein nanoparticles and VLPs offer highly ordered, stable and monodisperse vaccine formulations as well as scalable production through fermentation or molecular farming (Table 2). For example, Medicago and iBio are using *Nicotiana benthamiana* to produce VLPs using the S protein, and AdaptVac/ExpreS2ion is using insect cell expression system to make VLPs from the S2 protein; clinical trials are expected as early as July 2020 (https://www.medicago.com/en/newsroom/; https://ir.ibioinc.com/press-releases; https://news.cision.com/expres2ion-biotechnologies). Besides generating protein nanoparticles from antigenic subunits, their expression and/or display on proteinaceous biomaterial scaffolds such as ferritin, encapsulin[51] and bacteriophage VLPs has also been utilized to achieve multivalent antigen display for enhanced immunogenicity[52,53,54].

Table 2 Features of production platforms for vaccine manufacture

Full size table

And finally, subunit vaccines can constitute viral proteins incorporated in synthetic nanomaterials, protein cages and VLPs, which serve as adjuvants and/or delivery vehicles, in addition to conferring other benefits inherent to each nanocarrier platform[55,56,57]. For example, the influenza virus vaccine Crucell (Janssen, Johnson & Johnson) is a liposomal formulation that incorporates influenza protein haemagglutinin[58]. Figure 3a, b highlights some nanotechnologies used in subunit vaccine design. Besides the aforementioned antigen multivalency, nanocarriers enable efficient co-delivery of antigen/adjuvant to secondary lymphoid organs[59], exhibit size-dependent lymphatic trafficking and preferential uptake by antigen presenting cells (APCs), create depot effects for sustained immune stimulus, and facilitate antigen cross presentation—enabling extracellular antigens to be presented via the MHC-I pathway for $CD8^+$ T cell engagement[60] (Fig. 3c).

Peptide-based vaccines

An important consideration for vaccine design is safety. Many vaccines rely on immunological presentation of whole structural motifs, for example, full-length S protein, which will present a large repertoire of potent epitopes leading to a broad spectrum of antibody and cellular responses. However, earlier studies on SARS and MERS vaccine candidates have pointed to risks of antibody-dependent enhancement (ADE) of infection[61,62,63]. In the former, presence of non-neutralizing antibodies contributes to increased infections whereas the latter can lead to life-threatening allergic inflammations[64,65]. While there is no clear evidence yet, immunological data from patients may point toward possible ADE for SARS-CoV-2, suggesting that high IgG titers correlate with worse outcomes[66,67]. Therefore, developing peptide epitope vaccine strategies targeting the SARS-CoV-2 S protein may yield a safer vaccine. Various B- and T-cell epitopes of the SARS-CoV-2 S protein have already been identified

and predicted in silico[15,16,17,18]. Importantly, when serum from convalescent COVID-19 patients is screened for neutralizing antibodies, experimentally-derived peptide epitopes will confirm useful epitope regions and inform more optimal antigens in second-generation SARS-CoV-2 peptide-vaccines; the National Institutes of Health (NIH) recently funded La Jolla Institute for Immunology (LJI) in this endeavour[68].

Peptide-based vaccines represent the simplest form of vaccines that are easily designed, readily validated and rapidly manufactured[69]. Peptide-based vaccines can be formulated as peptides plus adjuvant mixtures or peptides can be delivered by an appropriate nanocarrier or be encoded by nucleic acid vaccine formulations. Several peptide-based vaccines as well as peptide–nanoparticle conjugates targeting chronic diseases and cancer are in clinical testing and development[70,71]. In addition to the development of peptide-based COVID-19 vaccines, industry and academic efforts leverage predicted B- and T-cell epitopes in their subunit vaccines against SARS-CoV-2; for example OncoGen, and University of Cambridge/DIOSynVax are using immunoinformatics-derived peptide sequences of S protein in their vaccine formulations (https://oncogen.ro/oncogen-vaccine-design-for-coronavirus/; https://www.cam.ac.uk/research/news/cambridge-research-team-working-towards-vaccine-against-covid-19). Within the DNA vaccine domain, Immunonomic Therapeutics/EpiVax/PharmaJet are leveraging in silico T-cell epitope prediction[72]. The use of B-cells epitopes appears practical because of its universality compared to the HLA-restricted T-cell specific vaccines[16,18].

Peptide based vaccines are dependent on adjuvants and delivery systems for efficacy, and nanoparticles can serve both these roles. By incorporating emerging strategies for targeting lymph nodes (LNs) or cellular subsets and subcellular locations, nanoparticle vaccine efficacies can be improved and their immune profiles tailored to address specific diseases. For example, the innovative strategy of ‘albumin hitchhiking’ exploits the natural trafficking ability of albumin to LNs[73]. Recently, the intrinsic ability of nanoparticles to target specific subsets of LN-resident dendritic cells (DCs) and macrophages was utilized to design a dual targeting Hepatitis B virus (HBV) vaccine. The complementing immune responses generated by these cellular subsets resulted in an enhanced efficacy of viral clearance in a chronic HBV mouse model[74]. Subcellular localization of the antigen is also a critical determinant of the ensuing immune response. Vaccine design parameters such as encapsulated antigens versus surface displayed antigens govern the processing and presentation of the antigen. While the former requires degradation or disassembly of the nanocarrier and therefore mimic viral infection leading to cellular immune response, the latter leads primarily to humoral immune response generated by the externally displayed viral proteins[56]. However, nanocarriers such as polymeric micelles (PEG-PE) that transform antigenic peptides conformation to facilitate cytosolic delivery could be reliably used for LN targeting, APC uptake and antigen cross presentation[75].

VLPs from mammalian viruses, insect viruses, plant viruses and bacteriophages have been developed as peptide display nanotechnologies for various vaccine and immunotherapy applications[76] (Fig. 3a,b). While non-infectious toward mammals, VLPs mimic the molecular patterns associated with pathogens, making them highly visible to the immune system. Therefore, VLP display and delivery platforms also serve as adjuvants, making them efficient activators and amplifiers of antigen-specific immune response (Box 1). Several VLP platforms are in the development pipeline and some have entered clinical trials[70,77]. The beauty of the VLP display platform technology is the scalability and modularity; the peptides can be rapidly adapted as new information about SARS-CoV-2 and its immunogenicity is made available; it is also possible to rapidly adapt the technology should novel or mutated strains emerge. Over the past years, our laboratory has developed plant virus-based nanotechnologies for cancer vaccines and immunotherapy[78,79,80]. We are now putting this technology toward development of COVID-19 vaccines. An established delivery platform would ensure that the next wave of SARS-CoV-2 infections and other emerging viruses, potentially including novel betacoronaviruses, are met with a more efficient and rapid response.

Vaccine scalability and manufacturing

The rapid emergence of the COVID-19 pandemic has also raised concerns regarding critical deficiencies in manufacturing and distribution of vaccines. Even when an effective vaccine is developed, considerations of cost, formulation and scale-up manufacturing must be taken into account. Large-scale production and worldwide distribution of a potent COVID-19 vaccine(s) will be governed by economic disparities between nations. When demand exceeds supply, developing countries are in a disadvantaged position for the bidding contest to procure the highly sought after vaccine, a situation already seen with personal protective equipment and other critical goods

even between industrialized nations. Therefore, it is critical to also consider technologies and platforms suited for developing countries.

Recombinant protein production can be carried out in a variety of platforms, each coming with its own advantages and disadvantages regarding yields, regulatory compliance, cost, scalability, flexibility, speed and safety (Table 2)[81,82]. While traditional manufacturing processes using bioreactors and mammalian, bacterial or yeast cell cultures are well-established in the pharmaceutical sector, these platforms are expensive, and production can be hampered by human pathogen contamination. Innovative manufacturing technologies that can meet the required global demand and distribution in response to outbreak have recently been deployed with success.

Plant-based expression systems have emerged in the past decade and already made an appearance during the 2014 Ebola epidemic when patients were treated with ZMapp, an antibody cocktail manufactured through molecular farming[83,84]. Plant molecular farming approaches offer scalability: while in fermentation-based platform, every scale-up step needs to be carefully verified—in molecular farming, each plant is a bioreactor. The more plants are grown, the more product is made; scale-up does not change the upstream production processes[82,85]. Other positive attributes of the molecular farming platform are the low manufacturing costs, the inability of human pathogens to replicate in plant cells (hence safety), and relatively non-sophisticated infrastructure that could be implemented worldwide also in low-resource countries. While the Bill and Melinda Gates Foundation is funding new factories for potential coronavirus vaccines[86], efforts should also be made to prepare for large-scale manufacture of plant molecular farming solutions. Many entities have already announced COVID-19 responses, including for example, Medicago, iBio and Kentucky BioProcessing, all of who set out to develop subunit vaccines[87] (https://www.medicago.com/en/newsroom/; https://ir.ibioinc.com/press-releases) as well as Plantform and South Africa-based CapeBiopharms, who set out to produce antibodies and test reagents. Adding to that, further developments and innovations are sprouting from academic labs; including a team at the Spanish Research Council (CSIC) at the Centre for Research in Agricultural Genomics and our laboratories at the University of California, San Diego[88,89].

The practical vaccine delivery, distribution and administration

Challenges of vaccine administration for a global pandemic must inform the selection of vaccine platforms. An ideal vaccine platform would have facile integration into devices designed to be supplied far and wide, manufactured at low cost and administered with minimal supervision. (Table 3 and Fig. 4). Several vaccine formulations require constant refrigeration. The need for a cold chain makes their global distribution and application logistically difficult and for under-developed and developing nations with tropical climates, nearly impossible. In fact, one of the largest challenges has been the reliance on refrigerated transport of solution-based vaccines. The WHO also reported that 2.8 million vaccines were lost in five countries due to cold chain failures, and less than 10% of countries met WHO recommendations for effective vaccine management practices. While some lyophilized vaccines are available that may be stored at room temperature, such solutions are difficult to produce and present challenges for the healthcare professionals who must reconstitute them on site[90].

Table 3 Comparison of stability and global reach for cold chain versus non-cold chain delivery options
Full size table

Fig. 4: Application of a slow-release implant versus degradable microneedle patch.

Vaccines are encapsulated in polymeric components in either an implant or microneedle patch. Over time the polymer will hydrolyse in the aqueous environment of the body and release the active vaccine. The degradation rate of the device and subsequent release rate of the vaccine can be tuned based on the material in which the vaccine is embedded. The primary difference between the two devices is the means of administration. Implants are administered subcutaneously by a qualified healthcare provider, while microneedle patches can be painlessly self-applied.

Full size image

A highly suitable nanotechnology platform is derived from plant viruses and bacteriophages that evolved as stable nanocontainers protecting their genome cargo under various environmental conditions. Cowpea mosaic virus, for example, is stable at temperatures above 60°C in buffered solution for at least one hour and pH values from 3.5–9.0 indefinitely at room temperature[91]. Furthermore, plant virus nanoparticles are stable under gastrointestinal conditions[92] and orally bioavailable[93], therefore opening the door for global distribution and oral vaccination. Vaccines could be produced in edible leaf tissue to enable vaccination of the human population but also livestock, since SARS-CoV-2 is a zoonotic virus that can infect humans and animals. This would be a step forward to meet the goals of the One Health Initiative to unite human and veterinary medicine, which will likely be important to prevent future outbreaks.

Effective vaccination campaigns also require access to health care professionals (HCP), which is challenging in resource-poor or densely populated developing countries under normal circumstances but presents a greater challenge during a global pandemic where the health care system is already strained or breaking. Recently, modern alternatives to such distribution and access challenges have come to light, such as single-dose slow-release implants, film-based vaccines[94], and microneedle-based patches that could reduce reliance on the cold chain and ensure vaccination even in situations where qualified HCP are rare or in high demand. Microneedle-based patches could even be self-administered, which would dramatically hasten roll-out and dissemination of such vaccines as well as reduce the burden on the healthcare system. Such modern vaccine delivery devices can be made by solution methods or fabricated via traditional polymer melt-processing (for example, injection moulding). The advantage of melt-processed devices lies in their potential for rapid manufacturing at large scale and their long-term stability independent of the cold chain[95,96,97,98]. The potential to break the cold chain and ease the burden on the medical system by offering a safe and effective self-administered prophylactic vaccine has been capitalized on by a number

of companies such as Veleritas Inc., Zosano, Corium International and Debiotech, and has led to the filing of over 10,000 patents worldwide[99].

Concluding remarks

Advances in bio/nanotechnology and advanced nano/manufacturing coupled with open reporting and data sharing lay the foundation for rapid development of innovative vaccine technologies to make an impact during the COVID-19 pandemic. Within 40 days of initial structural and genomic reports of SARS-CoV-2, the first vaccine candidate entered into the clinical development pipeline and as of 1 June 2020, there are already 16 vaccine candidates in clinical trials, many in Phase II and even one in Phase III. While any vaccine is still months-to-years away from clinical reality, the parallel and rapid efforts from academic laboratories and industry provide hope for success. A plethora of nanotechnology platforms are being pivoted against SARS-CoV-2; while highly promising, many of these may be several years away from deployment and therefore may not have an impact on the SARS-CoV-2 pandemic. Nevertheless, as devastating as COVID-19 is, it may serve as an impetus for the scientific community, funding bodies, and stakeholders to commit more focused efforts toward development of platform technologies that bolster the preparedness for future pandemics. Several nanomaterials afford platform technologies that are amenable to scalability, stability, portability, distribution and device incorporation for self-administration. Moreover, several platform technologies described herein may serve as plug-and-play technologies that can be tailored to seasonal or new strains of coronaviruses. Indeed, COVID-19 harbours the potential to become a seasonal disease; underscoring the need for continued investment in coronavirus vaccines. SARS and MERS vaccine candidates did not make it to market due to lack of financial incentive given the low infection numbers, and because the risk of a global pandemic from a newly emerged virus were largely ignored. Yet, because there is some conservation between the coronaviruses, continued research and product development is critical to tackle any new version of coronavirus that emerges in the future.

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See also:

PCR Inventor: "It doesn't tell you that you are sick"

The MSM have been going all out trying to pretend this never happened, turns out it did

By David James | *OffGuardian* | October 5, 2020

There has been a great deal of controversy over claims that Kary Mullis, the creator of the PCR technology that is being widely used to test for so-called 'cases' of COVID-19, did not believe the technology was suitable for detecting a meaningful presence of a virus.

Those making these assertions were attacked and 'fact checked' (deemed inappropriate by propagandists) by news outlets claiming that Mullis' comments had been taken out of context.

So when a video surfaces with Mullis talking about the efficacy of the technology it is worth paying close attention to what he is saying. He died last year, so it is the best 'fact check' available. In the video, Mullis is discussing AIDS. He first deals with a criticism from the audience that the PCR technology is being misused [timestamp – 48:40].

"I don't think you can misuse PCR. [It is] the results; the interpretation of it. If they can find this virus in you at all – and with PCR, if you do it well, you can find almost anything in anybody."

Mullis does not explicitly say that the PCR technology is unsuitable for detecting a meaningful presence of COVID-19. How could he, given that he died before it came to light? But such a conclusion can safely be inferred:

"It starts making you believe in the sort of Buddhist notion that everything is contained in everything else. If you can amplify one single molecule up to something you can really measure, which PCR can do, then there is just very few molecules that you don't have at least one single one of in your body."

Mullis then addresses the question of what should be considered meaningful, which is the central issue with the use of the PCR tests. Do the 'case' numbers being used around the world by governments to impose police states and egregious lockdowns of the population, especially in my home state of Victoria, actually mean anything? The answer seems to be 'no':

"That could be thought of as a misuse: to claim that it [a PCR test] is meaningful. It tells you something about nature and what is there. To test for that one thing and say it has a special meaning is, I think, the problem. The measurement for it is not exact; it is not as good as the measurement for apples. The tests are based on things that are invisible and the results are inferred in a sense. It allows you to take a miniscule amount of anything and make it measureable and then talk about it."

Mullis also addresses, by implication, another question about the incidence of 'cases'. If you test positive – and Australia's Therapeutic Goods Administration has admitted that they do not know if this means you are infected or not – are you actually sick? In the past that is what the word 'cases' has meant: someone unwell from a disease. Mullis' position is clear [emphasis added – timecode 51:49]:

"PCR is just a process that allows you to make a whole lot of something out of something. **It doesn't tell you that you are sick, or that the thing that you ended up with was going to hurt you or anything like that."**

Mullis' comments are unsurprising for anyone who has been paying attention to the behaviour of the authorities during the COVID-19 catastrophe. The technology relies on amplifying results many times over. If they are amplified less than about 35 times, no-one will test positive. If they are amplified 60 times, everyone will test positive. The flawed thinking is obvious enough.

Why is there such a concerted effort to quell anyone exposing problems with the use of the technology? There is no doubt that these attacks are designed to deceive (including predictable use of that shoddy *ad hominem* phrase 'conspiracy theory', a rhetorical trick to insult people rather than address their arguments).

Look closely at the 'fact checking'. The *Reuters* article uses a mixture of a straw man argument and a red herring. It asserts it was wrong to claim that Mullis said that: *"PCR tests cannot detect free infectious viruses at all"*.

This is obviously a deliberate misrepresentation intended to wrongly characterise the opponents' argument and then 'expose' it as false.

Then we get the red herring. The *Reuters* article claims that: *"The quote is actually from an article written by John Lauritsen in December 1996 about HIV and AIDS, not COVID-19 (here)."* Neat trick. Assert that your opponents got their sources wrong, and then dismiss them because of their poor research.

It is transparently untruthful, but why are these news outlets pushing such propaganda?

In one way, it could be said to be just business as usual. For those of us who have worked in newsrooms, especially in the finance and business sections, being subjected to propaganda is as routine as the daily cups of coffee.

The techniques are endless: outright lying, misleading but true facts, half truths, quarter truths, lack of context, lack of corporate memory, deceptive jargon, false statistics, lobbying by astro-turf organisations, threats of legal action, threats to complain to the editor or proprietor, threats of removal of access to important sources, promises of getting first access to important stories, subtle requests from former colleagues for assistance, and, of course, my favourites – free lunches at expensive restaurants and travel junkets.

The situation, always bad, has worsened with the destruction of the media's business model by Facebook and Google, who have taken half the world's advertising revenue. It has forced the hollowed out newsrooms to rely more on outside news feeds. And, as Matt Taibbi has noted, mainstream media organisations are, for commercial reasons, no longer interested in *"selling a vision of reality they perceive to be acceptable to a broad mean"*.

Instead, they deliberately sow division and only appeal to niches. Forget facts; inciting prejudice comes first.

But none of that explains why there is such intense propaganda about COVID-19.

The endless spin inflicted on media organisations is transparently related to satisfying greed or enhancing power, but what is the motive here? True, the US health system is one of the biggest profiteering exercises in the world, corrupting health everywhere. Health accounts for 16 per cent of US GDP, which is about twice the level of, say, Australia or the UK (countries that have universal care).

That extra eight per cent equates with $1.6 trillion in profiteering, or about two per cent of the global economy – an eye-watering scam conducted by pharmaceutical companies, hospital conglomerates, insurance companies, lawyers, consultants and so on. Those vultures will be trying to control the media to profit from a vaccine and who knows what else.

But they will only be one group of players and probably not the main ones. The most important question is who is funding the 'fake news' that COVID-19 is an existential threat and what is their agenda? Most countries have been greatly harmed. It has resulted in a medical dictatorship that has shut down Victoria; health bureaucrats may, absurdly, be given police powers.

There is a very sinister international agenda here, but the outline of it is, so far, only blurry.

1 Comment »

1. God bless Kary Mullis…..if he were still alive, this entire scam of Covid-19 would not be able to be happening! Faiuci wouldnt have a leg to stand on. Mullis also stated many facts against Fauci's claims of HIV…..as a virus period, and also using PCR testing for HIV, which Mullis stated was inaccurate and told Fauci not to use it…….Fauci did anway – just as he is doing today with PCR, rapid tests, and pushing his Covid agenda for socialstic government control. Fauci, Gallo, and their cohorts pushing this false agenda all belong in prison!

   Comment by Elizabeth Harkins | November 14, 2020 | Reply

https://www.globalresearch.ca/moderna-covid-vaccine-trials/5713705

Robert F. Kennedy, Jr.: Moderna's "Clinical Trial Results for Its Groundbreaking COVID Vaccine Could Not Be Much Worse"

By Robert F. Kennedy Jr and Peter Koenig
Global Research, May 22, 2020
Robert F Kennedy Jr Instagram

The Warp Speed Timeline – is what Dr. Fauci, NIAID / NIH and Bill Gates called the Covid-19 vaccination program that should have started in a few weeks ('should have' – hopefully now it won't).

The world should know about the type of fraud that is planned to being administered to Mother Earth's 7 billion people.

If the trials' side disastrous effects are any indication – the vaccination would cause considerable harm or injury – and possibly death – to people of Planet Earth

This is what **Robert F. Kennedy Jr.** – JFK's nephew – who is intimately involved in Children's Protection from vaccines – had to say about it.

Peter Koenig, May 22, 2020

***

Moderna's "Clinical Trial Results for Its Groundbreaking COVID Vaccine Could Not Be Much Worse"

by Robert F. Kennedy Jr.

"Despite Moderna's (pharmaceutical company created by the Bill Gates Foundation) cheery press release this morning (20 May 2020), the clinical trial results for its groundbreaking COVID vaccine could not be much worse.

*The vaccine, developed and championed by **Anthony Fauci** and financed by Bill Gates, used an experimental mRNA technology that the two men hoped would allow rapid deployment to meet President Trump's ambitions "warp speed" timeline.*

Dr. Fauci was so confident of his shot's safety that he waved ferret and primate studies (Moderna suspiciously reported no health data from its mouse studies).

That appears to have been a mistake. Three of the 15 human guinea pigs in the high dose cohort (250 mcg) suffered a "serious

adverse event" within 43 days of receiving Moderna's jab.

Moderna did not release its clinical trial study or raw data, but its press release, which was freighted with inconsistencies, acknowledged that three volunteers developed Grade 3 systemic events defined by the FDA as "Preventing daily activity and requiring medical intervention".

Moderna allowed only exceptionally healthy volunteers to participate in the study.

A vaccine with those reaction rates could cause grave injuries in 1.5 billion humans if administered to "every person on earth".

That is the threshold that Gates has established for ending the global lockdown.

Moderna did not explain why it reported positive antibody tests for only eight participants.

These outcomes are particularly disappointing because the most hazardous hurdle for the inoculation is still ahead; challenging participants with wild COVID infection.

Past attempts at developing COVID vaccines have always faltered at this stage as both humans and animals achieved robust antibody response then sickened and died when exposed to the wild virus.

Moderna's press announcement heralded "Positive Interim Phase 1 findings".

I have forwarded that claim to my colleagues in securities law; FTC rules restrict the amount of lipstick public companies may slather on bad donkeys."

***

Note to readers: please click the share buttons above or below. Forward this article to your email lists. Crosspost on your blog site,

internet forums. etc.

Peter Koenig *is an economist and geopolitical analyst. He is also a water resources and environmental specialist. He worked for over 30 years with the World Bank and the World Health Organization around the world in the fields of environment and water. He lectures at universities in the US, Europe and South America. He writes regularly for Global Research; ICH; New Eastern Outlook (NEO); RT; Countercurrents, Sputnik; PressTV; The 21st Century; Greanville Post; Defend Democracy Press; The Saker Blog, the and other internet sites. He is the author of Implosion – An Economic Thriller about War, Environmental Destruction and Corporate Greed – fiction based on facts and on 30 years of World Bank experience around the globe. He is also a co-author of The World Order and Revolution! – Essays from the Resistance. He is a Research Associate of the Centre for Research on Globalization.*

DEFENSE INTELLIGENCE AGENCY

BIOLOGICAL EFFECTS OF ELECTROMAGNETIC RADIATION (RADIOWAVES AND MICROWAVES) EURASIAN COMMUNIST COUNTRIES (U)

PREPARED BY U.S. ARMY
MEDICAL INTELLIGENCE AND
INFORMATION AGENCY
OFFICE OF THE SURGEON GENERAL

Releasable Report

BIOLOGICAL EFFECTS OF ELECTROMAGNETIC RADIATION (RADIOWAVES AND MICROWAVES) - EURASIAN COMMUNIST COUNTRIES (U)

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PREFACE

The purpose of this review is to provide information necessary to assess human vulnerability, protection materials, and methods applicable to military operations. The study provides an insight on the current research capabilities of these countries. Information on trends is presented when feasible and supportable.

The study discusses the biological effects of electromagnetic radiation in the radio- and microwave ranges (up through 300,000 megahertz). It is not within the realm of this study to provide detailed descriptions of every laboratory experiment. Such data have been purposely omitted in favor of an analytical approach. An attempt has been made to identify the principal areas of research and to discuss the significance of experimental results.

The information reported in this study has been drawn from scientific, medical, and military journals, intelligence reports, magazines, news items, books, and other publications. The information cut-off date for this study was 1 October 1975.

(U) Constructive criticism, comments or suggested changes are encouraged, and should be forwarded to the Defense Intelligence Agency (ATTN: DT-1A), Washington, DC 20301.

DST-1810S-074-76
March 1976

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(Reverse Blank)

SUMMARY

(U) The thermal effects of electromagnetic radiation have been reasonably well established through experimental investigation. The nonthermal effects, however, remain a controversial issue between scientists in the West and in the Eurasian Communist countries. The difficulties encountered in conclusively demonstrating the nonthermal effects of electromagnetic exposure are likely responsible for differences in exposure standards; some standards are based largely on the demonstrable thermal effects, while others allow for possible nonthermal effects at subthermal intensities.

(U) The Eurasian Communist countries are actively involved in evaluation of the biological significance of radiowaves and microwaves. Most of the research being conducted involves animals or in vitro evaluations, but active programs of a retrospective nature designed to elucidate the effects on humans are also being conducted. The major systems, system components, or processes currently under study include the blood, the cardiovascular system, cells, the central nervous system, the digestive system, the glandular system, metabolic effects, and the reproductive and the visual systems. Other aspects of exposure are also being studied, but the limited number of reports uncovered makes assessment of the importance placed upon this research impossible. These lesser reported research areas include nonthermal effects, immunological studies, and use of radiowaves for functional control of organ systems.

No unusual devices or measures for protection from radiowave exposure were noted, but a continued stress upon personnel protection in occupational situations was apparent. Here, protective goggles and clothing are recommended when working in regions of microwave radiation. Although some differences in standards remain between the various Communist countries and between military and civilian standards, the Communist standards remain much more stringent than those of the West. An exception to this may be Poland where a recent relaxation of their standards has occurred. This is the first significant shift of an East European country away from the standard first set by the USSR in 1958.

If the more advanced nations of the West are strict in the enforcement of stringent exposure standards, there could be unfavorable effects on industrial output and military functions. The Eurasian Communist countries could, on the other hand, give lip service to strict standards, but allow their military to operate without restriction and thereby gain the advantage in electronic warfare techniques and the development of antipersonnel applications.

The potential for the development of a number of antipersonnel applications is suggested by the research published in the USSR, East Europe, and the West. Sounds and possibly even words which appear to be originating intracranially can be induced by signal modulation at very low average-power densities.

Combinations of frequencies and other signal characteristics to produce other neurological effects may be feasible in several years. The possibility of inducing metabolic diseases is also suggested. Animal experiments reported in the open literature have demonstrated the use of low-level microwave signals to produce death by heart seizure or by neurological pathologies resulting from breaching of the blood-brain barrier.

(U) As may be expected, the bulk of the research being done in this area is in the USSR. However, a notable volume is also being produced by Poland, Czechoslovakia, Bulgaria, Rumania, and Hungary.

Western scientists who have followed the Soviet research efforts on the biological effects of microwaves have expressed a variety of reactions ranging from disbelief to passive acceptance. The overall impact of current Soviet work is not overly significant, at least on their civilian sector. One possible exception may be their studies of the central nervous system where some interesting work is being done. Elsewhere, most of their work tends to be outdated, some of their experiments cannot be duplicated, and others are of doubtful credibility. No real new developments or fresh approaches have been identified. Nevertheless, a large volume of material continues to be published on the effects of radiowaves and microwaves on biological systems, indicating a fairly high degree of interest and a genuine desire to pursue these investigations. No significant research and development has been identified that could be related to work in this field in the People's Republic of China, North Korea, and North Vietnam.

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SECTION I

INTRODUCTION

(U) The effects of radiowaves and microwaves on biological systems have traditionally been separated into two basic classifications, (1) thermal effects, and (2) nonthermal effects. The thermal effects are widely recognized and the mechanism of action reasonably well understood. Nonthermal effects, however, are controversial since the mechanisms involved are not clearly understood. Soviet and East European scientists believe that biological side-effects occur at power densities that are too low to produce obvious thermal effects. Such effects have been questioned in the West because experimental evidence, obtained largely in US laboratories, does not corroborate occurrence of nonthermal side-effects.

(U) Divergences in opinion between Bloc and Western researchers concerning the effects of microwave radiation are the result of nonstandardized research protocols and materials. In addition, mechanisms underlying observed biological effects are at present poorly understood by any of the world's scientists engaged in microwave research. The exchange of scientific information on microwave hazards has increased greatly since the active participation of Soviet, Czechoslovak, and Polish scientists in the International Symposium on Biological Effects and Health Hazards of Microwave Radiation in Warsaw in October 1973.

(U) It is now generally agreed that biological systems irradiated with electromagnetic waves in the radiowave and microwave frequency ranges (one kilohertz to more that 10^5 megahertz) absorb varying amounts of energy depending on the irradiation frequencies and the physical properties of the system. Typically, however, 40-50 percent of the incident energy is absorbed by the biological system and the remainder reflected. In reality, only the shorter wavelengths represent any appreciable hazard as a result of thermal heating. Radiation fields in the microwave range vary in wavelength from about one meter to very short wavelengths on the order of a millimeter. The depth of penetration of the waves is also variable and again depends on the frequency, wave polarization, and the physical properties of the system (i.e., dielectric and geometric), but typical penetrations are on the order of 1/10 of the wavelength. Therefore, very short waves are absorbed primarily by the skin, while long wavelengths penetrate to much greater depths.

(U) The degree of heating appears to be a function of the water content of the tissue and probably results from oscillations of water molecules or dipoles. Another possibility is a resonance absorption of energy by protein molecules of the cell. As might be expected, the actual damages resulting from a given exposure are functions of the thermal regulatory

and active adaptation processes of the organ or animal. Less vascularized tissues are more susceptible to thermal damage because of a poorer ability to dissipate the heat, therefore, crystalline lens damage or cataract formation may be observed.

(U) Many techniques and indices have been employed to study the effects of irradiation on biological systems. These include:

Body weight.
Biochemical studies.
Cardiovascular studies.
CNS effects (including conditioned and unconditioned reflexes).
Electrophysiological measurements.
Fertility and mutation studies.
Histology and pathology studies.
Metabolic studies.
Temperature.

While these and other experimental studies have been conducted on animal and cellular models, knowledge regarding human exposure has been almost exclusively obtained retrospectively. Accordingly, information regarding the amount and/or portion of the body exposed, field intensities, and duration of exposure are usually ill defined.

(U) As can be seen from the above, quantitation of the biological responses to electromagnetic exposure is a very complex problem because of the wide frequency spectrum, the large number of physical and biological variables, and the interrelationships of those variables. Factors requiring consideration include the frequency, intensity, waveform, (pulsed, CW, or modulated) configuration of the body, its orientation with respect to the source, portion of the body irradiated, exposure time-intensity factors, environmental conditions (temperature, humidity, and air currents), and shielding. Other complicating factors include the subject's state of health and previous or concomitant medication. In addition to the above factors, the animal species used and its comparative relation to man is important. Accordingly, experimental results from animals cannot easily be extrapolated and assumed to apply to human exposure because of size differences relative to exposure wavelength which can markedly influence the system or organ being damaged.

(U) With these complicating factors in mind, the evaluation contained in this report was undertaken. The data presented were obtained from the sources outlined in the preface and sometimes contained insufficient information to make absolute decisions regarding their significance. The sources were, however, indicative of the types of effects being reported and suggested those areas of research being emphasized, thereby permitting assessment of recent Eurasian Communist attempts to define the biological effects of radiowaves and microwaves.

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SECTION II

BIOLOGICAL SIGNIFICANCE OF RADIOWAVES AND MICROWAVES

PART 1 - BLOOD

(U) Effects of electromagnetic irradiation on the blood include biochemical variations, effects on erythrocytes, changes in coagulation, and alterations in the blood forming system. As would be expected, most communist country reports originate from in vitro or in vivo animal experiments rather than from human data.

(U) Long-term ultrahigh frequency (UHF) exposure in rats reportedly reduced the iron and copper content in both the blood and muscle with a concomitant increase in iron content in the liver. Similar exposure in chicks caused an increase in total proteins and globulins, but decreased the albumin in the plasma. Rats exposed to 0.04 W/cm^2 for 25 days demonstrated similar shifts. In some studies with dogs, irradiation with microwaves significantly decreased the lifetime of erythrocytes, while other studies indicated no changes in the granulocytic system after exposure. In the lymphocytic system, however, mitotic disturbances and changes of nuclear structure occurred. Rabbits exposed to "an electromagnetic field" showed significant increases in the number of monocytes, basophils, and lymphocytes/mm. Although undesirable, these shifts are not significant enough to impair the functional performance of humans. However, they are significant enough to warrant further experimentation. Soviet researchers will emphasize more experiments with animals and they will continue to try and relate these experiments to data on human exposure to microwave environments. They will most likely work toward relating such changes in different species of animals to particular intensities or exposures.

(U) One study involved the observation of several thousand persons working in microwave-irradiated workshops, as well as animal experiments. In the human subjects, three kinds of damage were found:

(1) Lymphocytosis and monocytosis.
(2) Granulocytopenia, monocytosis, and eosinophilia frequently accompanied by absolute lymphocytosis.
(3) Moderate neutrophilia.

The degree of changes in the blood could be correlated with exposure and/or duration of working period. This determination was based on the relative changes as a function of period of employment, which was felt to indicate a cumulative effect of microwaves in the human body. The type and intensity of the exposure was not documented.

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(U) Blood coagulation indices of dogs subjected to high intensity super-high frequency fields were studied at intervals of ten minutes to thirty days after irradiation. Initially the coagulation time was prolonged, but two hours after irradiation it was accelerated as a result of protective compensatory changes in neurohumoral factors. The protective reaction was, however, of short duration; the irradiation-induced prolongation of coagulation time reappeared and the animals' clotting times did not return to normal until at least fifteen days after exposure. Another study showed that long-term exposure to microwaves at a power density of 10mW/cm^2 decreased the overall activity of butyrylcholinesterase in the blood serum of rats. Under conditions of whole-body exposure, the microwaves did not exert a consistent effect on the enzyme molecule. The decrease in the overall activity of butyrylcholinesterase was correlated with a decrease in its concentration in the blood of the irradiated animals.

(U) The action of microwaves on human erythrocyte permeability to potassium and sodium ions was also investigated. The mechanism of action appears to be an inhibition of active transport and an altered diffusion through the pores in the membrane. The latter may be caused by the influence of UHF energy on the membrane itself or on the hydrated sodium cation and potassium cation. The microwaves either change the membrane structure thereby increasing the passive sodium cation and potassium cation diffusion and reducing the concentration gradient, or somehow block the mechanism of active ion transport.

(U) The question of stability of microwave-induced changes in blood components was addressed in chronic and acute tests using dogs and rabbits. The irradiation was at a frequency of 2375 MHz with a field strength of thirty microwatts per square centimeter. The rabbits were subjected to between one and ten irradiations of sixty minutes duration each, and the dogs were subjected to repeated irradiations over a period of more than a year. The changes in the blood and marrow of rabbits were found to be unstable and to pass after a period of five to ten days. Changes observed in the chronically exposed dogs were more stable, but became normalized over a period of twenty-five days. Investigation of chronic microwave irradiation on the blood-forming system of guinea pigs and rabbits was also reviewed. Both continuous wave (CW) and pulsed microwaves were utilized at an intensity of 3.5 mW/cm^2 and a wavelength of 10 cm. Increases in absolute lymphocyte counts in peripheral blood, abnormalities in nuclear structure, and mitosis in the erythroblastic cell series in the bone marrow and in lymphoid cells in lymph nodes and spleen were observed. The changes appeared to be a cumulative result of repeated irradiations and were attributed to nonthermal effects. There is limited evidence to support the belief that these cumulative effects are reversible upon cessation of exposure. It is still not quite clear if similar results could be observed in humans since wide species-variations have been observed by Soviet researchers working with animals.

(U) The primary concern of the present study was with electromagnetic field effects, but numerous reports regarding the effects of constant magnetic fields on the blood system were noted during the review. As with electromagnetic effects, effects on coagulation, biochemical properties, and formed elements were observed.

(U) To summarize the effects of electromagnetic radiation exposure on the blood, the following general changes emerge although conflicting reports are also present:

(1) General decrease in hemoglobin content.
(2) Generally reduced coagulation times.
(3) Decrease in leucocyte count.

These findings are based largely on animal experimentation. While detrimental in themselves, the extent of these changes would not be expected to be great enough to materially affect an individual's performance or general health, especially under stress conditions, where other factors such as physiological protective responses would be far more important.

PART 2 - CARDIOVASCULAR SYSTEM

(U) Heavy emphasis has been placed on investigations involving electromagnetic radiation on the cardiovascular system. Effects on hemodynamics include blood pressure variations and cardiac arrhythmias. Also included are reports of a slowdown of intraventricular and intra-atrial conduction, diffuse cardiac muscular changes, and ventricular extrasystole. As with other effects, animal studies are frequently reported and human reports are typically retrospective in nature. Many of the variations noted on the cardiovascular system result from central nervous system effects.

(U) Several reports concerning human cardiovascular effects from super-high frequency exposure were reviewed. Functional changes were noted, including a slight increase in the asynchronous contraction phase, a tension period, as well as other data indicative of moderate dystrophic changes of the myocardium accompanied by a disruption of its contractive capacity.

(U) Comparison of a group of engineers and administrative officials who were exposed to microwaves for a period of years and an unexposed control group revealed a significantly higher incidence of coronary disease, hypertension, and disturbances of lipid metabolism among the exposed individuals. Hereditary predisposition to heart disease was approximately the same in both groups, but overt disorders developed much more frequently in the previously exposed group. It was concluded that microwaves may act as a nonspecific factor which, under certain conditions, interferes with adaptation to unfavorable influences. Exposure may, therefore, promote an earlier onset of cardiovascular disease in susceptible individuals.

(U) Hemodynamic indices for thirty men in the 25-40 year age range who had been exposed to UHF exposures for from two to ten years were studied. These men showed a tendency to bradycardia, moderate decrease in the stroke and minute volumes, and a slowing of the rate of blood ejection from the left ventricle. Arterial pressure was essentially normal, but a compensatory constriction of the precapillary bed was noted in response to the decrease in cardiac ejection. There was also an increase in the tone of the large arteries. EKG changes indicated an intensification of vagotonic influences on the heart; possible fluctuations in the potassium-sodium balance were also postulated. In a similar study, it was concluded that hemodynamic changes resulted from disturbances occurring in the structural and functional state of the regulating system.

(U) Morphological changes in experimental mice exposed to short and ultrashort wavelengths were observed. Two series of experiments were conducted using 14.9 MHz and 69.7 MHz waves. In the first series, twelve animals were subjected to single lethal doses of the electromagnetic radiation. Very pronounced vascular dystrophic changes were found throughout the organism. In the second series, 37 mice were given daily 60-minute exposures to nonthermal intensities for five months. Morphological studies of these animals showed slight vascular disorders and compensatory proliferative processes in the internal organs as well as dystrophic changes in brain cells.

(U) In a group of patients suffering from "radio wave disease," cerebral hemodynamic changes were observed. These included reduced intensity of the pulse blood volume and an increase in tonicity of the intra- and extracranial vessels. The changes did not, however, appear to be functional in nature.

Personnel exposed to microwave radiation below thermal levels experience more neurological, cardiovascular, and hemodynamic disturbances than do their unexposed counterparts. Some of the cardiac and circulatory effects attributed to exposure include bradycardia, hypotension, and changes in EKG indices (sinus arrhythmia, extrasystole changes in intraventricular and intra-atrial conduction, diminished amplitude of EKG deflections, etc.).

(U) The cardiovascular effects have always been of primary interest, therefore, it is likely that research in this area will continue. It is not apparent if cardiovascular effects were first observed in animals or in patients suffering from the so-called "radiowave disease." It is probable that further research will more accurately establish hemodynamic variations in both animals and humans. Greater emphasis will be placed on animal studies which will allow for more precise dose-response quantitations.

PART 3 - CELLS

(U) Histological techniques have been used extensively for evaluating the effects of electromagnetic radiation on cellular systems. Such studies have included in vivo investigations of the cellular effects resulting from whole body irradiation and in vitro studies employing cell cultures.

(U) The most popular cells for study appear to be those of rat or mouse liver. Nonthermal effects on subcellular structures include the formation of binuclear cells and irregular thickening of the nuclear membrane. Invagination of cytoplasm into the nucleus has also been observed, frequently accompanied by breaks in the nuclear membrane. Marked changes in the endoplasmic reticulum and the mitochondria have also been noted. The available data, although still insufficient and inconclusive, seem to indicate that the magnitude of these effects is frequency dependent.

(U) The liver cells of rats exposed for three hours to a 1.625 MHz field showed damage to the protein synthesizing structures. Distinct changes were seen in the nucleoli or ribosome synthesizing apparatus. The ultrastructure of mouse liver cells was investigated after exposure to the same frequency. The mitochondria became swollen and underwent lysis. Some giant mitochondria also appeared. The cellular reactions observed were largely the same as those observed after the action of many other environmental factors.

(U) Phagocytic function has reportedly been increased by exposure to an electromagnetic radiation field and induction of colicin synthesis has been observed in E. coli irradiated with a nonthermal intensity.

(U) In many cases, electromagnetic radiation effects occur at the cellular level, therefore tissue culture techniques provide a well controlled and accurate method for study of those effects. Ultrahigh frequency exposure of cultures of rat fibroblasts, monkey kidney cells, and human embryo fibroblasts led to degeneration of the culture in four to six days. The earliest degeneration occurred in primary cell cultures. Studies are now under way on cell permeability, cell interfaces, cell stimulation, and the electrical characteristics of nerve cells. Other Bloc research will include study of microwave effects on mitosis, cell differentiation, and subcellular deoxidation potentials. The data obtained from these studies of cellular and subcellular responses to electromagnetic stimulation will be highly significant, since they may lead to the eventual understanding of basic mechanisms underlying biological changes which occur during and after microwave radiation.

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PART 4 - CENTRAL NERVOUS SYSTEM

(U) Research on the effects of radiowaves and microwaves on the central nervous system of humans was relatively widespread. A number of reports are discussed in this section, as well as research results regarding central nervous system effects on animal models and isolated nerves.

(U) Subjects exposed to microwave radiation exhibited a variety of neurasthenic disorders against a background of angiodystonia (abnormal changes in tonicity of the blood vessels). The most common subjective complaints were headache, fatigue, perspiring, dizziness, menstrual disorders, irritability, agitation, tension, drowsiness, sleeplessness, depression, anxiety, forgetfulness, and lack of concentration.

(U) Various neurological disorders were investigated by studying the vestibular and visual analyzer functions in persons exposed to radio waves of varying types for various periods. Elevation of the threshold of excitability was also accompanied by a lengthening of the time required for dark adaptation. The magnitude and intensity of the changes tended to increase with length of exposure. Similar studies showed increases in the threshold of olfactory sensitivity. EEG automatic frequency analysis was performed on 80 persons exposed to one meter wavelength radiation and 80 healthy controls. No differences were found between the exposed group and the controls regardless of length of the exposure, intensity of the field, or frequency. Presumably, all of these exposures were of a nonthermal nature. Conversely, thirty-seven persons occupationally exposed to a superhigh frequency microwave field (10 $\mu W/cm^2$) over periods of two to eight years, were studied; symptoms of asthenic and autonomic vascular disturbances, endocrine shifts, and abnormal EEG's were observed in half of the patients. Their reflexes in response to light and sound were weak, distorted, or nonexistent and their skin galvanic reaction to flashing light was abnormally intense and prolonged. Additional data will be required in order to assess the significance of these human studies.

(U) Long-term experiments conducted on rabbits demonstrated that irradiation with intermittent or continuous low intensity microwave fields elicits qualitatively and quantitatively different changes in the EEG. Intermittent radiation had a more pronounced effect on the recovery time. It has also been observed that long-term exposure of humans to microwave radiation results in extremely flattened EEG patterns.

Exposure of rabbits to low levels of microwave radiation resulted in alteration of brain electrical activity, but caused no detectable macroscopic or microscopic histological changes. Examination of the brains of rabbits sacrificed immediately after exposure to 10 centimeter microwaves at power densities of 20 to 30 mW/cm^2 revealed hyperemia of the meninges, distension of superficial vessels, and small extravasations of blood in deeper brain areas. Some, or all of the observed changes, could have been thermal rather than nonthermal effects, since the power density employed in the experiment was powerful enough to have caused a fairly great temperature rise. The effects noted immediately after exposure were apparently reversible, since no changes in the condition of the brain tissue were found in animals sacrificed on the day following exposure.

(U) Study of the rabbit visual cortex after a one minute exposure of the head to 40 $\mu W/cm^2$ at a wavelength of 12.5 cm revealed changes in the frequency of the background activity of 52 percent of visual cortical neurons. Chronic irradiation (two weeks) of rabbits caused the development of a prevalence of slow, irregular biological currents; this was interpreted as evidence of progressive establishment of an inhibitory state in the cortex of the cerebral hemispheres. Normalization of the electrical shifts required up to two months in some cases. Similar studies with rats indicated apparent decrease in cholinesterase activity in the central nervous system.

(U) Histological examination of the cerebral cortex cells from rats exposed to UHF at 5 to 15 $\mu W/cm^2$ revealed the onset of sclerosis and the formation of vacuoles in some of the cells.

(U) Some excellent studies using biopotential recordings were performed to determine the effect of microwaves on the kinetics of nerve impulse conduction. Frog sciatic nerves were irradiated with 12.5 cm wavelength microwaves for one minute and parallel temperature measurements were made. Calculations showed that the absorption of one calorie of microwave energy per gram of material per minute gave a temperature rise of 1.1 degrees C in the experiment. The effects of microwaves and of direct contact heating (from three to nine degrees) on nerve impulse parameters (the rate of excitation conduction (EC) and the biopotential amplitude (BA)) were measured and compared. For thermal effects alone, one degree increased the values of EC and BA about five percent. Changes in EC were characterized by rapid increases as absorption of microwave energy increased, followed by a fairly sharp drop upon switching off the microwave irradiation and normalization within three minutes. These increases in EC values (higher than values obtained by thermal effects alone) were especially pronounced in a study where the samples were heated three and six degrees. In a series where $\Delta t = 9.1$ degrees, EC was lower, although the temperature did not exceed physiological normal limits. Changes in BA

during microwave irradiation were also characterized by a much faster increase, followed by a sharp drop to below the original level after irradiation and essential recovery in three minutes. In a series where the temperature increased to 31°C, the microwave effect at first was the same as the thermal effect; after thirty seconds the BA value was even lower than for the thermal effect alone, possibly due to overlap of ionic currents at such high temperature. This was followed by a substantial drop after irradiation, and very little recovery in three minutes. The differences in results in this series were attributed to different initial conditions of the preparations.

(U) These experiments indicate that microwaves may have a specific effect of a nonthermal nature on EC and BA, causing sharp and reversible changes in these functional parameters of nerve impulse. Further experimentation will be needed before extrapolations of similar functional changes to in vivo conditions, or to humans, are attempted. It is expected that Soviet research on these and other CNS responses will continue during the next five years.

PART 5 - DIGESTIVE SYSTEM

(U) A number of alterations in the function of the gastrointestinal system were observed. Reportedly, exposures of subjects working for long periods of time in the presence of low intensity centimeter and decimeter waves resulted in numerous disorders. These included dyspeptic disorders, edema of the gums, bleeding gums, alteration of the gastric acidity, and a reduction of the tonus and evacuator functions of the stomach.

(U) Numerous animal studies have been conducted on the motor function of the gastrointestinal tract and the secretory function of the stomach. Non-thermal intensities were reportedly used. In general, suppression of the stomach's evacuatory function, with signs of adaptation upon repeated exposure, was found. After partial denervation of the stomach, the opposite occurred. It was concluded that the waves have a dual effect - a mediated action through changes in the function of the CNS and a direct effect on the organ or its local innervation. In general, gastric juices increased and little change in acidity was noted. This work tends to support observations of functional changes in humans and indicates that they may actually result from a CNS interaction. Other animal results are discussed below, but do not relate to the human observations.

(U) The effects of high frequency radiowaves on the content of nucleic acids in the digestive organs of rabbits were studied. The total nucleic acid content and the individual levels of DNA and RNA were assayed in the liver, pancreas, stomach, small intestines, and blood. It was found that the content of nucleic acids in the organs was a function of the power and duration of exposure. Low doses were found to considerably stimulate the nucleic acids, while higher doses reduced their content. Significant shifts in DNA content required very high level exposures. In a similar study on frogs exposed to microwaves (2307 MHz), the highest nucleic acid content was found in the pancreas and the lowest in the stomach. Again, low doses increased the total nucleic acid content while higher doses induced insignificant increases or reductions in their content.

(U) The effects of microwaves (2307 MHz) on radiophosphorus resorption in the stomach, duodenum, ileum, and colon were studied in rabbits. Simultaneously, absorbed radiophosphorus distribution in the liver, lungs, kidney, and spleen was investigated. It was found that rates of radioactive phosphorus resorption by sections of the alimentary canal differ. Under microwave exposure, resorptive activity of the stomach is somewhat decreased, while in the small and large intestines, it is increased. Lower intensity exposure accelerated the intestine resorptive function to a greater extent than large doses of lower frequency waves. Radiophosphorus deposition in the viscera is also a function of the dosage.

PART 6 - GLANDS

(U) Investigations of the effects of radiowaves and microwaves on the glandular system have been concentrated mainly on the adrenal, pituitary, and the thyroid. The glandular effects, however, do not appear to be a high priority area when compared to other systems currently under investigation.

(U) The functional status of the adrenal cortex in shipboard specialists subjected to the effects of a UHF field was reviewed. Thirty-eight men were exposed to the field for periods of 24 to 1800 hours and ketosteroids and oxycorticosteroids (which reflect androgenic function) were monitored. The results indicated that androgenic, glucocorticoid, and mineral corticoid functions of the adrenal gland cortex do not deviate from the normal. Microwave exposure also increased thyroid function in these subjects. The increase was attributed to secondary effects of the radiation and was felt to result from disturbances of the sympathetic nervous system in the hypothalmic region. In guinea pigs, the weight of the adrenal glands increased after continuous exposure at low levels for fourteen days, but decreased in animals exposed to interrupted exposures. Modification of lipid metabolism appears to be the mechanism of action. Similar exposure

using chicks resulted in increased ascorbic acid content in the cytoplasm of the adrenal cortex, but other work has produced conflicting results regarding the effects on the adrenal cortex.

(U) A quantitative assay of the gonadotropic hormones and growth hormones in the pituitary body of rats exposed to microwave radiation indicated that for a certain time after exposure, blocking or inactivation of gonadotropin-releasing agents occurs in the hypothalamus. Both neural-hormonal and pituitary gonadotropic hypofunctional effects resulted from whole-body microwave irradiation.

(U) The general conclusion that can be drawn from various (both animal and human) studies of the anterior pituitary and adrenal cortex is that exposure to radiowaves and microwaves of thermal intensities results in suppression of the hormone producing functions but exposure to nonthermal intensities tends to enhance production.

(U) An increase of the thyroid function indices was found in animals undergoing microwave irradiation for four months at a power density of 5 mW/cm^2. In histological sections of the cylindric epithelium covering the thyroid, follicles were seen and electron microscopy revealed reticulum.

PART 7 - METABOLISM

(U) Electromagnetic radiation exposure has been found to produce disturbances in carbohydrate energy and nitrogen metabolism in the brain, liver, and muscles. It appears that under electromagnetic exposure, macroergic compounds become deficient due to disjunction of the oxidative phosphorylation processes and deranged metabolism of carbohydrates. With respect to nitrogen metabolism, radiation causes an intensification of the ammonia formation processes in the absence of correspondingly more vigorous processes for its elimination.

(U) Exposure of rats to various intensities of electromagnetic fields with a frequency of 48 KHz produced an increase of lactic and pyruvic acids and a decrease in glycogen content in brain tissue. The changes depended on the field intensity and exposure duration and one month after cessation of the exposure the titer of lactic acid in the rat brain had not returned to normal.

(U) The role of metabolic disturbances of the heart in development of functional and structural changes under the influence of low frequency impulse electromagnetic fields was studied. Test animals were rats and it was found that exposure decreased ATP and creatinphosphate by

causing disturbances of the oxidative changes of carbohydrates and divergence of conjugation of oxidation and phosphorylation processes. It was concluded that changes in carbohydrate energy and nitrogen metabolism preceded the inception of structural changes in the myocardium.

(U) While these animal studies indicated an upset of some metabolic pathways, the degree of functional impairment was relatively small and probably not a significant factor. No human metabolic variations were noted and meaningful extension of these animal studies to the human is not possible. Research in this area is likely to remain low key and will be conducted mostly on animals.

PART 8 - REPRODUCTION

(U) The effects of electromagnetic radiation on reproductive systems have been the subject of numerous animal studies. Experiments with female white mice revealed changes in the estrus cycle. During the five-month study, the mice were irradiated twice daily for one hour, using a 10 cm wavelength of low intensity (10 mW/cm^2). Although the average number of normal cycles was unchanged, normal cycle duration increased. Prolonged diestrus and metestrus, along with a shortened estrus period, resulted in a decrease in the reproductive function of the ovaries. A weight loss was found to occur starting at about two weeks, reaching a maximum loss after four months.

(U) The fertility of female white mice was also investigated. The animals, irradiated as above, were mated during proestrus or early estrus with nonirradiated males. Conception in fifty-eight control animals was 94 percent, but only 75 percent in irradiated animals. Long-term non-thermal microwave irradiation of male mice evoked diffuse changes in the testes. Subsequent mating of the animals resulted in reduction in the size of litters.

(U) Microwave radiation at 10 and 50 mW/cm^2 intensity was administered for twenty and fifteen minutes respectively at various stages of the twenty day gestation periods. The progeny showed reduced viability, poor development, and anomalies. Changes in rate of postnatal development and disturbances of higher nervous system activity were also observed.

(U) Female white mice were irradiated twice daily for one hour with 10 cm waves of low intensity (10 mW/cm^2) up to the eighteenth day of pregnancy. There were stillbirths, a significant number of weak newborn, and a general retardation of body weight gain and growth. Other researchers found similar effects in litters from females which had been exposed twice daily for one hour to a 10 cm wavelength at an intensity of 10 mW/cm^2 for five months prior to mating.

(U) Genetic effects of electromagnetic radiation were observed in other studies. Male rats, irradiated with microwaves at 50-55 mW/cm^2, were mated with nonirradiated females. Litters displayed reduced viability and abnormal development, reduced rate of development and nervous disorders.

(U) Although researchers noted a certain degree of specificity in the pathological changes induced by microwave irradiation of mice, they concluded that the pathological processes occurring in male or female animals resulted from different mechanisms of action.

(U) Both sexes of the fruit fly, Drosophila melanogaster, were exposed to microwaves to study the effects of radiation-induced mutation. Group A, exposed for five seconds to 38 MHz, showed an increased frequency of mutation when bred five to nine days after irradiation. The results were not statistically conclusive, however. Group B, exposed for ten minutes to 2375 MHz, showed no effect on frequency of mutations.

(U) A strain of Staphylococcus aureus, known to be resistant to penicillin, was exposed to an electromagnetic field. A mutant was found to be sensitive to penicillin, probably due to a change in lipid content.

(U) In summary, a large amount of research has been done on the reproductive effects of EMR. However, effects on human reproduction, especially on male fertility, have not been demonstrated.

PART 9 - VISUAL SYSTEMS

(U) The role of microwaves in cataract formation and visual damage has been studied extensively in the past and is reasonably well understood. Primary attention in many studies has been directed at the biological effects of superhigh frequency electromagnetic radiation on the crystalline lens of the eye. Biomicroscopic techniques have been used to study cataract development in persons regularly exposed to microwave fields. A four-year study involving 600 workers and 300 controls revealed no significant difference between the two groups. Cataracts were discovered in only one percent of those persons exposed to such radiation; most of these cases resulted from safety violations. Cataracts which occurred were characterized in their early stages by turbidity of the lens and changes in form and color.

(U) In another study, thirty-five workers regularly exposed to microwave fields and having pronounced congenital lenticular cataracts were examined over a one to three year period; the results of their examinations were compared to those of twelve persons with similar cataracts who had no history of exposure to radiation. No progression was noted in any of the exposed individuals; changes were slow and probably attributable solely to natural aging of the lens.

(U) Combined wavelengths over the range of the millimetric spectrum were used in an animal study involving nine rabbits exposed for 35-70 minutes. Although the radiation used was of considerable intensity (120-495 mW/cm^2), no damage occurred in the deeper media of the eye, in particular the lens, during the 2 to 2½ months observation period. However, erosion of the epithelium of the cornea did occur along with damage to the conjunctiva and its vessels. Multiple tiny hemorrhages in the mucosa and submucous tissue were also evident.

(U) The Soviets have reported the occurence of "acute attacks" (sic) of glaucoma (1304 cases) which were correlated with geomagnetic disturbances. Moreover, recurring "acute attacks" came primarily on days when the mean value of the horizontal component of the geomagnetic field varied significantly. The significance of this report is questionable, but it indicates that the Soviets are examining all aspects of magnetic and electromagnetic radiation which might cause changes in vision.

(U) Although a growing body of evidence suggests that the microwave power density required to produce cataracts is incompatible with life, the Soviets will continue to investigate the visual effects of EMR but their effort will be reduced from its previous level.

PART 10 - INTERNAL SOUND PERCEPTION

(U) Perception of modulated microwave signals which seem to be originating intracranially as characteristic sounds is a phenomenon which was first reported in the US open literature more than thirteen years ago. To produce sounds, peak power densities of up to 80 mW/cm^2 may be required, but the average power density usually is 5 $\mu W/cm^2$. The Soviets have studied this phenomenon in order to determine the underlying physiological mechanism(s) and to define the optimum irradiation parameters needed to evoke the response. They found that when the fundamental frequency of the electromagnetic stimulus was raised from 2050 to 2500 MHz, the reaction threshold rose significantly, but at a frequency of 3000 MHz there was no reaction in the auditory centers. The average intensity of electromagnetic radiation required to evoke the response was less than 10 mW/cm^2; it was concluded that the fundamental signal frequency rather than the amount of energy constituted the primary stimulus and that the observed phenomenon was sensory in nature.

(U) The Soviets will continue to investigate the nature of internal sound perception. Their research will include studies on perceptual distortion and other psychophysiological effects. The results of these investigations could have military applications if the Soviets develop methods for disrupting or disturbing human behavior.

SECTION III

MISCELLANEOUS OBSERVATIONS

(U) Most of the reported biological effects from radiowaves and microwaves result from exposure to the higher frequency ranges. Many of the observed physiological changes probably occur as a result of thermal effects arising from the vibration of ions and dipoles of water molecules in tissues; the vibrations are set into motion more efficiently by the shorter wavelength (high frequency) waves. For example, a radiowave of ten centimeters wavelength converts about fifty percent of its energy into heat in this manner, whereas a three-centimeter wave converts nearly ninety-eight percent of its energy into heat. A study of the biological activity of low frequency (seven KHz) impulse electromagnetic radiation of different intensities and durations was done on rats. It was found that the pathological changes were a function of dose; susceptibility to radiation was governed by metabolic processes and morphology and the organs and systems could be classified as to sensitivity in the following order: testicles, liver, kidneys, heart, and central nervous system. Another study indicated that relatively low frequency electromagnetic fields generated sonic and ultrasonic oscillations in living organisms which in turn produced elastic deformations. If the frequency of the source field corresponded to the oscillation frequency of the cells (the resonance frequency most likely), the cells deteriorated as a result of the mechanical resonance.

(U) Clinical studies were done on thirty subjects, aged 25 to 40 years, exposed to industrial ultrahigh frequency centimeter waves at power densities of 10 to 500 mW/cm^2 for periods of time ranging from 4 to 13 years. Subjective complaints included generalized weakness, afternoon and evening apathy, fatigue, headache, sleep disorders, and nonradiating precordial pain suggestive of asthenia or neurasthenia with autonomic dystonia. Electroencephalography revealed periods of absence of alpha wave activity alternating with low R waves, increased frequency of potentials, dysrhythmia, periodic low peak potentials, and reactions to afferent stimuli. Peripheral blood studies revealed lymphocytosis or monocytosis in eight subjects; increased alpha and gamma globulins were found in 18 subjects. Erythrocyte potassium was within the lower limits of normal, while urine potassium was within the upper limits of normal. Adrenal cortex function was evaluated by urine levels of 17-ketosteroids, which were elevated to 22 to 40 mg in 11 subjects; average levels were 20.5 mg. Urine levels of epinephrine and norepinephrine were elevated in some subjects. Thyroid function was evaluated by rate of radioiodine uptake. Average uptake within two hours was 11.3 percent, and in four hours 16.9 percent. The 24 hour uptake did not differ from normal values. Electrocardiography revealed changes in the heart conduction system in six subjects; the $T_{v1}>_{v6}$ syndrome was found in ten

subjects and a U wave was registered in lead V_3 in eight subjects. Hemodynamic and myocardial function parameters were studied by tachooscillography and polysphygmography. Arterial pressure was usually within normal limits, although it was of a labile nature. Bradycardia was present in 14 subjects and decreased minute volume was observed in eight; increased peripheral resistance was found "in a significant number" of subjects. Autonomic-vascular changes and emotional lability and reactivity were attributed to CNS changes and increased pituitary-adrenal gland function. It was also noted that such shifts in neuroendocrine function could lead to circulatory disorders manifested by changes in the hemodynamic indices and electrical activity of the heart.

(U) A second study was done on two groups of workers occupationally exposed in the radio industry. The first group consisted of 100 subjects who had worked for several years under conditions of periodic exposure to microwaves of considerable intensity (up to several mW/cm^2). The second group consisted of 115 subjects who had begun work after the introduction of protective measures and had been exposed to microwave intensity levels approximately the same as those to which the first group was exposed. A control group of 100 subjects not exposed to the action of microwaves was also continuously examined. The study showed adverse effects, primarily on the nervous and cardiovascular systems, in both exposed groups. These effects were more pronounced in the first group. They were manifested by more frequent complaints of asthenic syndrome and vegetative vascular dysfunction.

(U) A lack of standards for measuring power levels represents a problem which probably accounts for conflicting reports regarding the effects of a given frequency and intensity. Other problems with dosimetry and experimental technique also exist. Such differences make comparison of results from one investigator to another, as well as from one country to another, extremely difficult.

(U) Only a few studies involving electromagnetic interaction with the immunological system have been reported. In one, rabbits were employed to study the body immunological reactivity under long-term irradiation. The rabbits were immunized with typhoid antigen and divided into two groups. One group was exposed to waves of 50 and 10 mW/cm^2 intensity for four hours a day over a four-month period. Analysis of the data obtained indicated that chronic exposure to the effects of low intensity high frequency radiowaves can influence the immunoreactive state of the body as evidenced by differences in phagocytic activity of neutrophils, blood serum complement level, and specific antibody titers.

(U) Soviet investigators have conducted studies on the effects of microwave frequencies in combination with ionizing radiation, magnetic fields, drugs, and nonionizing electromagnetic radiation of other wavelengths. Generally, synergistic effects have been observed. Continued work in this area is expected, and possibly new safety standards for these combined effects will be developed.

(U) In summary, this section shows the rather broad front on which Soviet researchers are investigating the biological effects of EMR. It is apparent that their interest covers all body systems which could reasonably be expected to display responses to such radiation. As with Western researchers, they have concentrated their efforts on the higher frequency spectrum which would be expected to produce more thermal responses. However, they also continue to be interested in nonthermal effects, which, by Western standards, they have yet to conclusively demonstrate.

SECTION IV

DISCUSSION OF RESEARCH METHODOLOGIES

The Soviet interest in the nonthermal effects of microwave radiation is evident both from the standards established and the many low intensity irradiation experiments conducted by their researchers.

The results of the research have encouraged the Soviets to investigate methods for exploiting microwaves and radiowaves to produce controllable psychophysiological effects. Laboratory facilities for investigating the combined effects of several microwave frequencies have been established at various institutes. Other research involves examining the pathological effects of UHF radiation from 300 to 3,000 MHz on man. This work supports the view, contested by some non-Soviet authors, that there are nonthermal modes of action. While no specific research results are reported, it appears that on the basis of results obtained the Soviets will not alter their standards. Part of this effort apparently involves development of prophylactic procedures against nonthermal UHF radiation as well as development of therapeutic techniques for those exposed. Beneficial effects of exercise and nutrition in increasing body resistance to radiation have been postulated. Physiotherapy, vitamins, and stimulants are recommended for the treatment of this type of radiation sickness.

Recently, US and other Western scientists have been quite concerned with the vast difference between the two standards. So far, there has been no serious attempt to reconcile or explain these dissimilarities. However, two interesting possibilities presented below may partially explain the lack of agreement:

a. Soviet researchers are using batch exposure techniques. They expose a number of animals in compartmented cages to the same radiation dose. Western experience with batch exposure has shown that such a practice tends to exaggerate or perturb the field. This exaggeration is due to reflected energy and the phenomenon of standing waves. What the exaggeration means in terms of comparison to the exposure of a single animal is that one is likely to be dealing with higher power levels than he realizes. This may, to some extent, explain the different findings at supposedly identical dosage levels.

b. Much of the difference between US and Soviet thermal and nonthermal positions may exist because of a definition problem. The Soviet definition of "thermal" means a measurable increase in body temperature measured rectally.

"Nonthermal" means that no increase in rectal temperature is measurable. Therefore, it appears that if a change or an effect is noted without an increase in rectal temperature it is a nonthermal effect explainable as an energy coupling. This definition does not take into account localized temperature increases which may not be reflected in rectal temperatures.

It has been reported that some European Communist countries have established two standards - one for military and one for the civilian sector. Although the civilian standards are lower, some researchers feel that they are not low enough. Reports also indicate that a number of female workers in industry may have aborted as a result of exposure to microwave radiation ostensibly within the safety standards.

The extent to which microwaves and other nonionizing radiation causes chromosome aberrations is somewhat of a controversial subject as is the question of the reversibility of any possible injury. It has been suggested that studies on the surface properties and perméability of cell membranes could supply some answers to these questions.

SECTION V

SAFETY PRECAUTIONS AND STANDARDS

(U) Safety precautions and standards have been established in both the US and USSR to protect not only persons who are occupationally exposed but also to protect the health of persons living or working near powerful generating or transmitting facilities. Significant differences in these standards exist and appear to be primarily due to different viewpoints on nonthermal effects in the two countries. Both nations' standards take into account the potentially lethal thermal effects resulting from high-intensity exposure, but the biological effects of nonthermal irradiation are not well defined or documented. In addition, some research has indicated the possibility of a cumulative effect on humans, but this is also very poorly defined.

Soviet research has produced guidelines which were used to establish a value of 10 $\mu W/cm^2$ per working day as the maximum admissible value for microwave irradiation. Higher exposures, at values of 0.01 to 0.1 mW/cm^2, are permissible for up to two hours per day or 1 mW/cm^2 for 15 to 20 minutes per day. Protective glasses are required in the latter case. The Czechoslovakian standards for frequencies above 300 MHz allow a maximum of 0.025 mW/cm^2 in the continuous wave mode for eight hour exposures. The standard for pulsed operation for the same exposure period is 0.01 mW/cm^2. In June 1973, Poland revised its exposure safety standards for nonionizing radiation in the frequency range of 0.3 to 300 GHz. The new standard permits unlimited exposure of humans to field intensities of 0.01 mW/cm^2. Eight hours per day exposure is permitted for intensities up to 0.2 mW/cm^2 for fixed fields and 1.0 mW/cm^2 for rotating fields. Exposures of up to 10 mW/cm^2 are permitted for limited periods of time without safety equipment. Exposures greater than 10 mW/cm^2 are prohibited without approved safety equipment. Prior to June 1973, the maximum radiation exposure level for all nonionizing radiation was 0.01 mW/cm^2 for up to eight hours per day, which is the same as the safety standard for the USSR. The 0.1 mW/cm^2 limit remains in effect for 0.1 MHz to 300 MHz, but revised standards for this frequency range are under consideration. The East German maximum permissible exposure to microwaves is 10 mW/cm^2, but neither the exact frequency range or duration for this exposure is specified. By comparison, the United States Standards Institute recommends 10 mW/cm^2 as averaged over any 1/10 hour period. The US Army and Air Force use the following equation to determine permissible exposure time (T_p).

$$T_p = \frac{6000}{W2}$$

where T_p = permissible exposure time in minutes during any one hour period and
W = the power density in the area in mW/cm^2.

Potential problem areas for exposure to excessive electromagnetic radiation which were found in the Communist literature included a wood processing plant, coastal radiotransmitting centers, radio equipment on ships, and flight communications equipment in the crew cabins of aircraft. Open feeder lines were identified as major sources of exposure.

(U) Protective devices described for use in working near unacceptable intensity fields include protective (metal-coated) eye glasses and clothing and shielding of the source with special absorbers or sheet metal or wire mask shields. A small semiconductor indicator instrument used to warn workers of dangerous conditions from electromagnetic fields has been developed. It rings an alarm when the field intensity exceeds the allowable level. An indicator paper for visual determination of the intensity of an electromagnetic field has also been developed. The indicator is prepared by impregnating a filter paper with a thermosensitive chemical compound.

(U) In an animal study, it was reported that oral administration of caffeine in doses of 20 mg per kg lowered the duration of resistance against hyperthermia caused by microwave irradiation. Caffeine did not influence the temperature at which the animals died, but it shortened the time to death. The reason for the lowered resistance of rats to microwaves was attributed to caffeine's exciting effect on the CNS which caused increased metabolic activity and consumption of oxygen. Although caffeine might exert similar effects on the human CNS, any lowering of resistance to hyperthermia would be insignificant; trained personnel working with properly operating, adequately serviced microwave equipment would probably almost never be exposed, even accidentally, to the tremendous radiation intensity required to induce heating of the human body. Nevertheless, monitoring of Soviet research on the action of drugs in combination with microwave radiation should continue, since such studies may eventually result in the detection of nonthermal safety hazards resulting from the mutually potentiating effects of radiation fields and pharmacological compounds.

Should subsequent research result in adoption of the Soviet standard by other countries, industries whose practices are based on less stringent safety regulations could be required to make costly modifications in order to protect workers. Recognition of the .01 mW/cm^2 standard could also limit the applications of new electronic technology by making the commercial exploitation of some products unattractive because of increased costs imposed by the need for additional safeguards.

SECTION VI

TRENDS, CONCLUSIONS, AND FORECAST

(U) A significant amount of research continues to be performed in the Eurasian Communist countries to establish the effects of radiowaves and microwaves on biological systems. It is often difficult to evaluate the reported results, however, because details of the exposure in terms of frequency, duration, and intensity are quite variable, and sometimes poorly reported. This, coupled with problems of measurement encountered in such studies, creates a rather confusing body of data from which to draw objective and absolute conclusions regarding the significance of the research. The Eurasian Communist investigators tend to place greater importance on the potential nonthermal effects than do their counterparts in the West, but information regarding the precise nature of the exposure under consideration is often difficult to establish. A move toward improved statistical analysis of data and standardization of dosimetry can be expected as Eastern Bloc researchers react to criticism of their work by Western scientists.

(U) The types of responses reportedly exhibited by the various biological organs, processes, or functions are in line with what has been reported by Western investigators. Again, most of the responses which are reported can be linked with the thermal action of the radiation. Studies which report on nonthermal effects deal largely with subjective responses, relying on reports of headache, sleepiness, loss of appetite, etc. The presence of nonthermal effects, in addition to thermal effects at higher intensities, has also been postulated by Eurasian Communist investigators, but no detailed investigative support for this possibility was noted. Accordingly, it is difficult to establish whether or not a trend toward this type of research will begin. It is safe to say that research on nonthermal effects at thermal intensities will be exceedingly difficult since another dimension to an already formidable problem will have been added.

No Eurasian Communist research activity has been identified which can be clearly or directly related to any military offensive weapons program. However, Soviet scientists are fully aware of the biological effects of low-level microwave radiation which might have offensive weapons application. Their internal sound perception research has great potential for development into a system for disorienting or disrupting the behavior patterns of military or diplomatic personnel; it could be used equally well as an interrogation tool. The Soviets have also studied the psychophysiological and metabolic changes and the alterations of brain function resulting from exposure to mixed frequencies of electromagnetic radiation. One physiological effect which has been demonstrated is heart seizure. This has been accomplished experimentally in frogs by synchronizing a pulsed ultrahigh

frequency microwave signal of low average-power density with the depolarization of the myocardium and beaming the signal at the thoracic area. A frequency probably could be found which would provide sufficient penetration of the chest wall of humans to accomplish the same effect. Another possibility is alteration of the permeability of the blood-brain barrier. This could allow neurotoxins in the blood to cross. As a result, an individual could develop severe neuropathological symptoms and either die or become seriously impaired neurologically.

The above study is recommended reading material for those consumers who have an interest in the application of microwave energy to weapons. A discussion of weapons is not within the scope of this study.

SECTION VII

INFORMATION GAPS

(U) Little information regarding the effects of relatively low frequency radiowaves was available. These frequencies produce few thermal effects, but although Eurasian Communist research frequently investigates nonthermal effects, few reports of studies at these low frequencies could be found.

(U) A limited amount of information regarding the effects of environmental conditions on susceptibility to damage from radiowave exposure was reviewed. In fact, the few articles available on these factors present conflicting results. In addition, a few reports on the effects of the very complex fields encountered in the near field situation (i.e., very close to the source) were found.

(U) The effects of relatively low level exposure to radiowaves (such as might be encountered by persons living in the vicinity of high powered radio stations) are not well documented. One report suggests a statistical evaluation of the health of persons living in such areas as compared to persons living in areas with a more normal electromagnetic level. This would be a very difficult study to undertake if statistically significant data were to be obtained.

(U) No official safety standards have been identified for Albania, Bulgaria, Hungary, Yugoslavia, and the Asian Communist countries.

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

(U) This study was undertaken to provide a review and evaluation of the current Eurasian Communist country state-of-the-art in the area of the effects of radiowaves and microwaves. It generally covers the 1968-1975 period. The major topics include discussions of the effects on humans and animals. The study provides information on the general trends of research with special attention to possible military applications. Where appropriate, information on safety standards and research personalities and facilities is provided.

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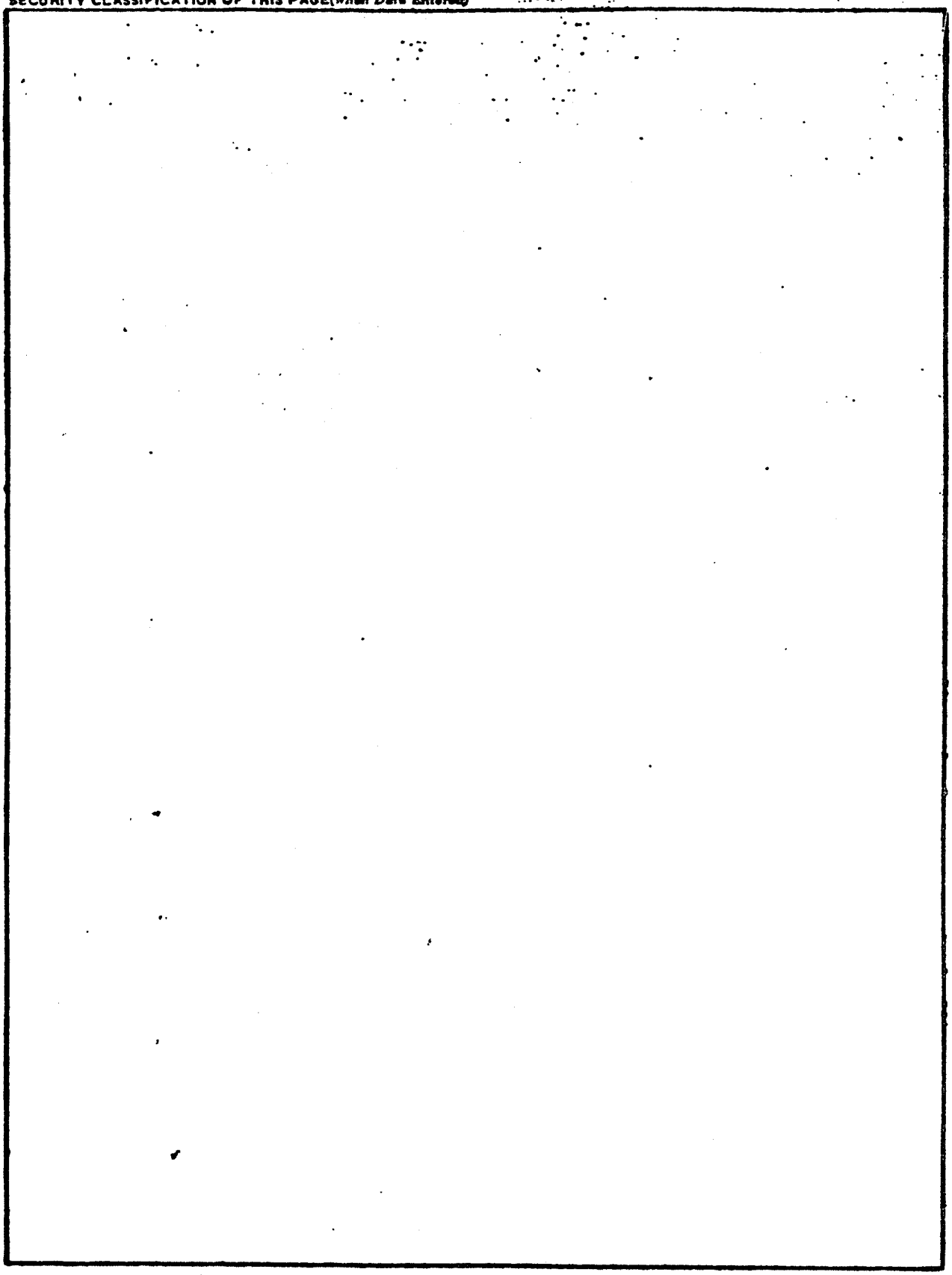

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ORIGINAL RESEARCH

Effects of electromagnetic radiation exposure on bone mineral density, thyroid, and oxidative stress index in electrical workers

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Background: In the literature, some articles report that the incidence of numerous diseases increases among the individuals who live around high-voltage electric transmission lines (HVETL) or are exposed vocationally. However, it was not investigated whether HVETL affect bone metabolism, oxidative stress, and the prevalence of thyroid nodule.

Methods: Dual-energy X-ray absorptiometry (DEXA) bone density measurements, serum free triiodothyronine (FT3), free thyroxine (FT4), RANK, RANKL, osteoprotegerin (OPG), alkaline phosphatase (ALP), phosphor, total antioxidant status (TAS), total oxidant status (TOS), and oxidative stress index (OSI) levels were analyzed to investigate this effect.

Results: Bone mineral density levels of L1–L4 vertebrae and femur were observed significantly lower in the electrical workers. ALP, phosphor, RANK, RANKL, TOS, OSI, and anteroposterior diameter of the left thyroid lobe levels were significantly higher, and OPG, TAS, and FT4 levels were detected significantly lower in the study group when compared with the control group.

Conclusion: Consequently, it was observed that the balance between construction and destruction in the bone metabolism of the electrical workers who were employed in HVETL replaced toward destruction and led to a decrease in OPG levels and an increase in RANK and RANKL levels. In line with the previous studies, long-term exposure to an electromagnetic field causes disorders in many organs and systems. Thus, it is considered that long-term exposure to an electromagnetic field affects bone and thyroid metabolism and also increases OSI by increasing the TOS and decreasing the antioxidant status.

Keywords: bone mineral density, electromagnetic radiation, electrical workers, thyroid, RANK, RANKL

Introduction

Electromagnetic field (EMF) is a space of mobile and electric-loaded particles affected by power and appears as a result of spinning of the electrons inside atoms around the atomic core and themselves.[1] Human body acts like an electromagnetic machine where each cell has a specific electric circuit.[2] Therefore, human being has a magnetic field. The magnetic field in the human body appears by the movements of bioelectrical loads, and the magnetic field signals of the substances creating human to intercommunicate are consistent with each other. Alongside the internal and external magnetic field existing in the nature, human beings are exposed to some magnetic fields such as cell phones, computers, electrical household appliances, and high-voltage transmission lines. The electromagnetic balance of the human body is disrupted by these magnetic fields.[2]

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EMFs reach into the tissues, causing cellular dysfunctions.[3] They lead to disorders such as insomnia, headache, and stress. These fields negatively affect blood biochemistry, digestive and circulatory systems, and increase the risk for cancer.[4–8] High-voltage transmission lines were detected as a cause for leukemia and brain cancer in children; and a close relation between childhood cancers, especially leukemia and living in close proximity to high-voltage electric transmission lines were observed.[8,9] Studies conducted in the USA and Finland determined that Alzheimer's disease is observed four times more in men and three to four times more in women among the workers (radio operators, industrial equipment workers, data processing device mechanics, phone-line workers, those working in electric plants, and substations) who are frequently exposed to EMFs.[2]

Since a magnetic field is not visible, not directly sensed, and the effects are observed cumulatively after a long period, it is not regarded enough. Although, it is still problematic whether a poor magnetic field is harmful for human health, studies carried out on animal cells revealed that poor magnetic field causes many biological effects such as changing hormone and enzyme levels, preventing motion of tissue chemicals.[10–15] In the literature, some articles report that the incidence of numerous diseases increases among the individuals who live around high-voltage electric transmission lines (HVETL) or are exposed vocationally.[16–18] However, it was not investigated that whether HVETL affect the bone metabolism, prevalence of the thyroid nodule, and oxidative stress levels in electrical workers. Furthermore, since biological effects of EMF are observed after a long period, the electrical workers are an appropriate group to search this effect. In the present study, we examined the effects of exposure to an EMF on bone mineral density (BMD), thyroid nodule formation, serum free triiodothyronine (FT3), free thyroxine (FT4), RANK, RANKL, osteoprotegerin (OPG), alkaline phosphatase (ALP), phosphor (P) levels, total antioxidant status (TAS), total oxidant status (TOS), and oxidative stress index (OSI) of electrical workers.

Patients and methods

The study group included 47 electrical workers employed in Electricity Generation Company (EGC) Transmission-Operation Facility 6, Kütahya and their ages varied between 29 and 52 years (mean 38.4 years). Mean working period of the study group was determined as 15.9±6.72 years. The control group was created from 47 healthy individuals with a similar socio-economical status with an age range between 28 and 52 years (mean 39.1 years) who were not exposed to ionizing and non-ionizing radiation for diagnostic and therapeutic purposes and who complied with the study group in terms of smoking and exercise habits. Consent of Clinical Researches Ethics Committee of Afyonkarahisar with a consent number of 2012/15-123 was obtained on July 6, 2012. This study was supported by Afyon Kocatepe University Scientific Research Projects Unit (Project no: 12.TIP.11).

The participants of the study were informed and their written consent was obtained. Individuals who work as electrical workers at least for 10 years were enrolled for this study. Individuals working for less than 10 years were excluded. Individuals without diseases that may affect the bone metabolism (thyroid/parathyroid disorders, kidney failure, autoimmune or tumoral diseases) and those who do not have the aforesaid conditions in their medical history were enrolled for this study. The participants were investigated for osteoporosis factors such as body mass index, smoking, alcohol use, nutritional status, familial medical history, and exercise and exposure to EMF including use of cell phones, computer, and hair dryer. The participants did not expose to any radiation such as magnetic resonance imaging (MRI) for diagnosis and treatment purposes. Furthermore, all the participants were informed about the study and told the minimal risk of radiation absorption related to the dual-energy X-ray absorptiometry (DEXA) scans and, included in the study after their consent was received. The data about the familial and personal medical history, dietary habits, exercise and physical activity status, and the conditions such as fatigue, anxiety, and headache after work were obtained through a face-to-face survey including 34 questions. Furthermore, the measurements of EMF and body temperatures of the electrical workers were performed in their units. Blood analyses, ultrasound scan (USS) of the thyroid gland, and bone DEXA scan of the participants were used as a tool for data collection.

USS of the thyroid gland

USS of the thyroid gland was performed in the control and the study group. The scan was performed with a LOGIQ 7 (General Electric Medical System, Milwaukee, WI, USA) ultrasonography device through a 7.5–10 MHz linear probe. The procedure was applied after positioning the patient's neck to extension by placing a lifter under the patient's shoulder. During the scan, images on the coronal, horizontal, and sagittal planes were obtained and thyroid gland size, homogeneity of the thyroid parenchyma echo, the presence of the nodule (present–absent), and vascularity through Doppler ultrasonography were assessed.

DEXA measurements

BMD of the lumbar area and hip of the individuals in both groups were measured by using the DEXA method (DXA.

Hologic QDR 4500) and the lowest t-score value was used for statistical evaluation. Baltas et al mentioned that the DEXA method was approved by WHO (World Health Organization), NOF (National Osteoporosis Foundation), and IOF (International Osteoporosis Foundation) for diagnosis and follow-up of osteoporosis,[19] and it is an essential tool to measure the BMD. The measures of the lumbar vertebra and femur are accepted as general measurement areas for the diagnosis of osteopenia and osteoporosis. It is a routine method for BMD. In the present study, the DEXA method was utilized to measure BMD and measures of the lumbar vertebrae and femur were performed.

T-score shows the difference of BMD scores between the patient and young adults who have the same sex and ethnicity with the patient. T-score values of the groups were used in the study.

(Hip) BMD measurement: While the patient was lying on supine position on the table, her/his feet were positioned on internal rotation by 25° with a 30 cm gap between the feet and fixed in a foot positioner. Hip joint, femur head, and femur neck were included into the screening.

(L1–L4) BMD measurement: The patient was positioned on supine position and full contact of the waist was provided by placing a support under the knees. Vertebrae between L1 and L4 were taken into the shot.

Biochemical analyses

Analyses of bone metabolism parameters (OPG, RANK, RANKL)

Blood analyses were performed by collecting venous blood samples of the patients with an empty stomach; and serum levels of three different parameters including OPG (e-Bioscience, Vienna, Austria), RANK (Cusabio, Wuhan, Hubei, People's Republic of China), and RANKL (BioVendor, Shenzhen, People's Republic of China) were analyzed by an ELISA device (Biotek ELx800) in accordance with human-specific kit protocols. During the ELISA analysis, the standards procured with the kits were thawed, then diluted. Eight standards were prepared to create the calibration curve required for calculating the concentrations in ELISA device automatically by using the absorbance of the samples. Standards and samples were analyzed twice, and the mean value of each standard and sample was used for statistical calculations.

The kits used include OPG (e-Bioscience), Ref no: BM2021INST, Lot no: 74889021; RANK (Cusabio) Catalog no: CSB-E13539h, Lot no: F15069918; RANKL (BioVendor) Ref no: RD193004200R, Lot no: E12-054.

Analysis of thyroid functions

All tests were analyzed in the same laboratory. Serum concentrations of thyroid-stimulating hormone (TSH), FT3, and FT4 were analyzed with the original kits of Abbott Architect 1600 Chemiluminescence method.

Analysis of TAS and TOS

Methods such as TAS to measure the antioxidant status in a medium are generally calibrated by using a standard antioxidant solution called Trolox Equivalent which is analogous of vitamin E; the TAS levels measured were read as mmol Trolox Equiv/L. TAS measurements were performed by kinetic reading in the spectrophotometer 5 minutes after the sample and reagent were mixed. TOS measurements were done by reading at end-point 560 nm in the spectrophotometer 3–4 minutes after mixing the samples and reagents, and the results were expressed in hydrogen peroxide liter (μmol H_2O_2 equiv/L).

Calculation of OSI

After TAS and TOS measurements, the OSI levels, which allow us to make an exact comment on the oxidant and antioxidant balance, were calculated according to the following formula specified in the catalog of the kit (rel assay diagnostics). OSI = (TOS μmol/L)/(TAS [mmol Trolox Equiv/L] ×100).

Statistical analysis

The data of the individuals who were exposed to the magnetic field and consisted of healthy individuals as the control group were analyzed by SPSS for Windows 15.0 package program of statistics. Compliance of the data to normal distribution was investigated by the Kolmogorov–Smirnov test. The analysis of the data compliant to the normal distribution was performed by independent sample *t*-test and one-way analysis of variance (ANOVA) for comparisons between the groups. The Least Significant Difference (LSD) test was used to determine the source of the statistically significant difference as a result of ANOVA test. Paired comparisons between the groups for the data that are not compliant with normal distribution were performed through Mann–Whitney *U*-test. The chi-square test was used for the comparison of the qualitative data. As a result of the analysis, *P*-values smaller than 0.05 were accepted as statistically significant.

Results

Age average and mean working period of the electrical workers were determined as 38.4 years and 15.9 years, respectively; age average and mean working period of the control group were 39.1 years and 17.2 years, respectively.

Table 1 The characteristics of the groups

Patient features and EMA exposure	Control Group (n=47)	Study Group (n=47)
Age (years)		
Average age*	39.05±5.85	38.37±7.53
Minimum/maximum age	28–52	29–52
Work experience (years)*	17.21±6.64	15.89±6.72
Smoking	11/47	18/47
Body Mass Index (kg/m^2)*	26.65±4.16	26.21±4.67
Body temperature measurements (°C)*	36.73±5.14	36.92±5.61
Fatigue, anxiety and headaches	16/47	34/47
The average measurement of HVETL exposure (μT)*	N/A	0.53±0.25
Mobile phone usage time* (minutes/month)	537.46±8.47	504.55±7.69
Hair dryer (times/week)*	1.6±0.61	1.1±0.77
Computer use (hours/week)*	23.33±5.61	21.82±4.22

Note: *The data is given as mean ± standard deviation.
Abbreviations: EMA, electromagnetic area; HVETL, high-voltage electric transmission lines; N/A, not applicable.

Age average and mean working period of the study and control group were consistent with each other. Smoking, exhaustion, anxiety, and headache were found lower, whereas the use of cell phone, computer, and hair dryer was found higher in the control group. Body mass indexes were comparable between both groups (Table 1).

No significant difference was observed between the groups in terms of the dietary habits and physical activity ($P>0.05$). In the evaluation of the nutritional habits in the participants, weekly consumption of protein, milk, yogurt, and vegetables were found to be similar. In addition, alcohol addiction, salt habits, and activity levels were found to be quite low, moderate, and low, respectively (Table 2).

Table 2 Nutrition and habits of the participants

Feature	Experimental group	Control group
Smoking	15/47	11/47
Alcohol consumption	5/47	5/47
Salt consumption		
Salt-free	0	0
Low salty	6	3
Moderate salty	43	37
High salty	0	0
Coffee consumption (cups/day) (n)		
None	0	4
1	44	39
2 and over	3	4
Milk consumption (glasses/week) (n)		
1–4	43	42
5–8	4	5
Type of Nutrition	Mixed	Mixed
Exercise and sports activity within the last 5 years;		
Sport such as walking and weight lifting at least 3 times per week on a regular basis.	3	5

In bone DEXA scans, mean BMD of L1–L4 was found −1.13 g/cm^2 in the study group and −0.16 g/cm^2 in the control group. Similarly, BMD of femur was found −63 g/cm^2 and 0.31 g/cm^2 in the study and control group, respectively. A significant difference was observed between BMD measurements of lumbar vertebrae L1–L4 and femur ($P<0.05$). Additionally, a significant difference was found between ALP and P levels ($P<0.05$). Mean ALP values in the control group and the study group were found as 76.00 versus 88.04 U/L, respectively. Blood phosphorus levels were in the control group, and the study group detected as 2.80 versus 3.43 mg/dL, respectively. RANK, RANKL, and OPG levels seem to support a possible increase for tendency to a severe osteoporosis in the individuals working around HVETL ($P<0.001$, $P<0.001$, and $P=0.004$, respectively) (Table 3, Figures 1–3).

Although thyroid function tests (FT3 and TSH) were lower in the study group, they were not statistically significant. The FT4 level was detected significantly lower in the study group than the control group. Furthermore, anteroposterior diameter measures of the thyroid gland of the study group increased when compared with the control group according to the morphometric measurement by USS; however, the result was not statistically significant. Left anteroposterior diameter measure of the thyroid gland was found significantly higher in the study group ($P<0.05$). There was not any significant difference between the groups in terms of nodule and parenchyma (Table 4).

Mean BMD values of L1–L4 and femur according to the age were detected lowest in 20–29 years of age and highest in 30–39 years of age in bone DEXA measurements. No significant difference was observed between BMD measurements of L1–L4 of the lumbar vertebrae and femur (Table 5).

Table 3 Comparison of bone mineral density and blood chemistry parameters between the study and control group

Measured parameters	Control group	Study group	*P*-value
RANK (pg/mL)	82.24 (4.63–263.27)	102.21 (48.63–294.84)	$P<0.001$*
RANKL (pmol/L)	322 (112–1,272)	408.06 (191–1,262)	$P<0.001$*
OPG (pg/mL)	51.98 (29.54–107.22)	45.06 (25.35–83.85)	$P=0.004$*
BMD (L1–L4)	−0.16±0.93	−1.13±0.99	$P<0.05$
BMD (FEMUR)	0.31±1.00	−0.63±0.84	$P<0.05$
ALP (U/L)	76.00±19.71	88.04±22.25	$P<0.05$
P (mg/dL)	2.80±0.41	3.43±0.37	$P<0.05$

Notes: *Mann–Whitney *U*-test was used for binary comparisons between groups in these data, and the values were given as median (minimum–maximum). *t*-test (independent samples *t*-test) for independent samples was applied in other data and values were given as mean ± standard deviation.
Abbreviations: OPG, osteoprotegerin; BMD, bone mineral density; ALP, alkaline phosphatase; P, phosphor.

Depending on the work experience, BMD values of L1–L4 and femur of the electrical workers with work experience of 20 years and over were found higher than those working for 10–19 years in both measurements. There was not any significant difference observed between BMD measurement levels of L1–L4 lumbar vertebrae, whereas a significant difference was observed between BMD levels of femur ($P<0.05$; Table 6).

Due to the work experience, Ca, ALP, RANK, and RANKL values of L1–L4 and femur of the electrical workers with work experience of 20 years and over were found higher than those working for 10–19 years. No significant difference was observed between values of Ca, RANK, and RANKL and a significant difference was detected between serum ALP values ($P<0.05$) (Table 7).

A significant elevation in the OSI and a significant reduction of total oxidative stress were found in the study group. These findings suggest that EMF increases the TOS, decreases the antioxidant status, and causes oxidative stress damage in the electrical workers ($P<0.05$) (Table 8).

Discussion

Electromagnetic waves (EMWs) damage tissues of the body through heating and changing chemical reactions.[20] High EMWs cause damage by heat; hazardous effects appear on the tissues by long-term exposure to low EMWs because of chemical changes. Some energy spreaded by EMW due to the heat effect is absorbed by the human body, and heat accumulation occurs inside the body. Such heat may cause undesired outcomes. The second effect is disruption of the molecules and atoms which are bonded to each other in a living organism.[20]

The limit of professional exposure is 500 μT for a magnetic field.[21] The highest exposure was found on electrical workers by a mean value of 0.161 μT in the studies conducted on different occupational groups.[22] Despite the fact that no measurements could be performed in the substation areas because of security measures and risk of accident, mean daily exposure was found 0.53 μT in the EMF measurements carried out on the workplaces and walking areas. Exposure to an EMF increases sodium, calcium, and magnesium levels in the plasma[23] and the oxidative stress.[15] Studies carried out with a Guinea pig showed that exposure to an EMF causes a significant increase in oxidant products and a decrease in antioxidant enzyme activity.[13] The studies assessing the exposure level generally detected that the exposure at 0.4 μT and above increases the risk of leukemia during childhood.[24,25] Similar studies revealed a relationship between electrical workers exposed to EMF and increased risk for leukemia.[26] In the blood analyses of the electrical workers

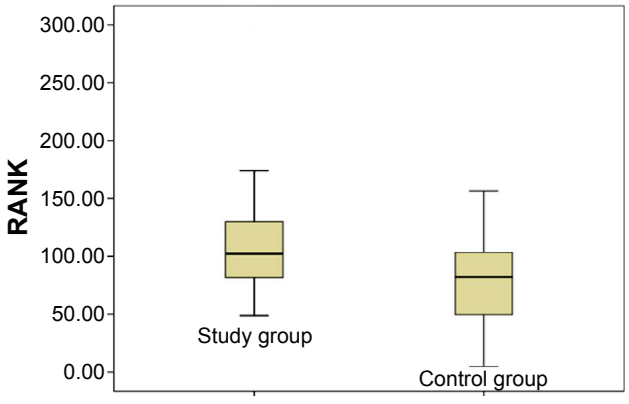

Figure 1 Distribution of RANK values in the study and control groups.

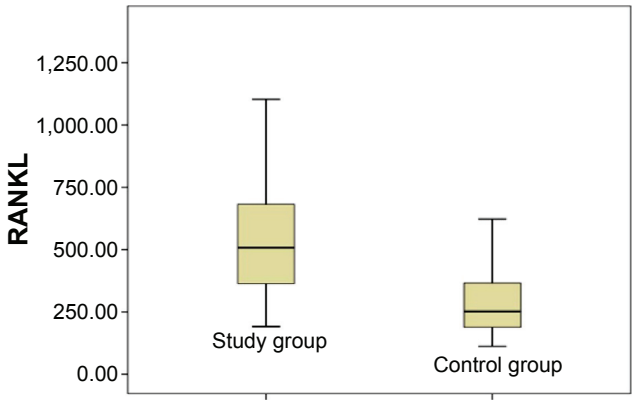

Figure 2 Distribution of RANKL values in the study and control groups.

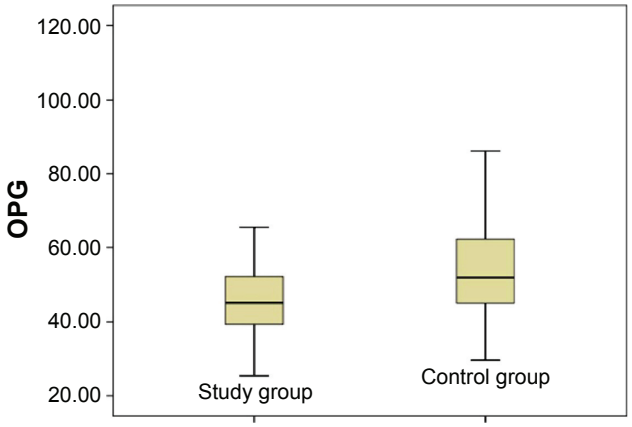

Figure 3 Distribution of OPG values in the study and control groups.
Abbreviation: OPG, osteoprotegerin.

in the present study, an increase in Ca, P, and oxidative stress levels and a decrease in antioxidant enzyme activities were detected. We believe that such effects which were observed on electrical workers who are exposed to high EMF even in breaks might have been caused by spending a significant part of their shift in substations and high-voltage transmission lines.

Important health problems of the present day include osteoporosis, fractures, and stress fractures. In bone DEXA scans, mean BMD measures of L1–L4 lumbar vertebrae and femur as well as ALP and P levels were observed significantly higher in the study group than the control group. Moreover, levels of RANK, RANKL, and OPG support the idea that a strong predisposition for osteoporosis may increase for those working around HVETL. In comparison between the experimental and control groups, bone loss was found to be resulted from the EMF exposure and not from age. These results indicate that bone damage may increase due to the EMF exposure.

Experiments on mice indicated that bone density and volume decrease, osteoporosis progressing with fractures and deformities appear in the absence of OPG,[27,28] and osteoporosis is reversed by intravenous OPG injection.[29] Osteopetrosis characterized with osteoclastogenesis was observed on the mice of which genetic structure of OPG was modified.[30] These data show that OPG is necessary to preserve the bone mass physiologically. RANKL, which is an agent stimulating the dendritic cells, acts as a life factor for mature T cells and regulates proliferations.[31,32] Such activities were observed to be dependent to the activation of RANKL by binding to membrane receptor RANK.[33] Similar approaches with OPG were tried to understand the role of RANKL in the bone metabolism. Despite OPG, severe osteoporosis was observed on the mice with genetically modified RANKL;[8] complete disappearance of osteoclasts and development of osteoporosis were observed in the mice without RANKL.[34,35] According to these data, OPG is a strong bone protective agent, whereas RANKL is a preresorptive factor. In vitro trials also seem to support the in vivo data.[34–37] Although there are studies indicating that low-frequency EMF provides an increase on recovery of bone fractures and BMD in the literature,[38–41] therapeutic doses of EMWs for osteoporosis were only observed when they were applied in pulses with low doses of 15–72 Hz.[42] Long-term occupational exposure to EMWs in higher doses has

Table 4 Comparison of thyroid function tests and thyroid's diameter measurements between groups

Measured parameters	Control group	Study group	*P*-value
FT3, mean ± SD	3.34±0.32	3.22±0.51	0.302*
FT4, mean ± SD	1.21 (0.92–2.67)	1 (0–3.19)	**<0.001****
TSH	1.66 (0.48–4.34)	1.41 (0.01–7.72)	0.180**
RapD	16.15 (12.5–24)	18 (8–37)	0.056**
LapD	15.6 (12.1–24.3)	17 (10–30)	**0.037****
Istmus D	3.35 (2.20–5.9)	3.3 (1–13)	0.647**

Notes: *Independent *t*-test and **Mann–Whitney *U*-test was applied. The data were presented as median (minimum–maximum) unless stated otherwise. Bold *P*-value shows the difference was statistically significant ($P<0.05$).
Abbreviations: RapD, right anteroposterior diameter; LapD, left anteroposterior diameter; Istmus D, tiroid istmus diameter; TSH, thyroid-stimulating hormone; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid-stimulating hormone; SD, standard deviation.

Table 5 Comparison L1–L4 and femoral BMD values with the DEXA results as per study group's ages

Bone type	Age (years)	N	T-score	*P*-value
L1–L4	20–29	4	−1.35±0.65	
	30–39	24	−0.97±0.53	0.504
	40–49	15	−1.28±0.57	0.904
	50 and older	4	−1.28±0.62	0.918
Femur	20–29	4	−1.02±0.51	
	30–39	24	−0.39±0.48	0.167
	40–49	15	−0.88±0.58	0.770
	50 and older	4	−0.78±0.34	0.674

Note: Independent *t*-test was applied. The data were given as mean ± standard deviation.
Abbreviations: BMD, bone mineral density; DEXA, dual-energy X-ray absorptiometry; *t*-test, independent samples *t*-test.

Table 6 Comparison L1–L4 and femoral BMD values with the DEXA results according to work experience

Bone type	Work experience (years)	N	T-score	*P*-value
L1–L4	10–19	32	−1.02±0.55	0.255*
	20 and older	15	−1.36±0.76	
Femur	10–19	32	−0.44±0.28	**0.021***
	20 and older	15	−0.94±0.51	

Notes: *Independent *t*-test was applied. Bold *P*-value defines the significant difference ($P<0.05$). The data were given as mean ± standard deviation.
Abbreviations: BMD, bone mineral density; DEXA, dual-energy X-ray absorptiometry.

Table 7 Comparison of the bone biochemistry parameters according to work experience

Biochemistry parameters	Work experience (years)	N	Mean	*P*-value
Ca	10–19	32	9.27±0.27	0.872*
	20 and older	15	9.29±0.50	
P (mg/dL)	10–19	32	2.85±0.44	0.281*
	20 and older	15	2.71±0.31	
ALP (U/L)	10–19	32	84.93±13.63	**0.044***
	20 and older	15	94.67±23.63	
Creatine (mg/dL)	10–19	32	0.90±0.11	0.69*
	20 and older	15	0.89±0.08	
RANK (pg/mL)	10–19	32	96.89±41.96	0.182*
	20 and older	15	113.56±82.20	
RANKL (pmol/L)	10–19	32	391.33±109.84	0.166*
	20 and older	15	443.78±168.88	

Notes: *Independent *t*-test was applied. Bold *P*-value defines the significant difference ($P<0.05$). The data were given as mean ± standard deviation.
Abbreviations: ALP, alkaline phosphatase; P, phosphor.

a reverse effect. Atay et al[42] detected a significant decrease in BMD levels in the iliac wing area where mobile phones with 900–1,800 MHz are carried when compared with the other side in their study. Similarly, Cidem et al reported a decrease in bone density of the forearm which are used by the mobile phone owners while holding the phone.[43] Kunt and Dayıoğlu and Kunt et al found in their study conducted on the radiology employee that the lowest densitometry level was in MRI employee.[44,45]

In the clinical trials reporting the preventive effect for osteoporosis and increase of BMD, treatment protocols applied to the study groups are dependent on the principle of application of a certain EMW dose for a certain period. In other words, a doze of exposure is certain and may be limited. However, a decrease in femoral and lumbar BMD levels of the electrical workers was met. This is contrary to the protective effect of low-frequency EMWs on bone metabolism. Possible factors include dose of the magnetic field exposed and duration of exposure. Although the effect of low-frequency EMWs to prevent osteoporosis was brought into the forefront in the literature, long-term exposure to the magnetic field around HVETL may cause a hazardous effect in the bone metabolism rather than a protective effect and creates an effect which is similar to those by devices creating high-frequency EMF such as cell phones. From this point of view, we believe that low-dose EMFs may have a therapeutic effect, whereas long-term and high-dose EMWs have a destructive effect on the BMD.

Effects of low-frequency EMWs of which electrical workers who are exposed to electromagnetic radiation most is not like the effects of a high-frequency EMWs. No temperature increase was detected in the temperature measurements performed on the electrical workers. Therefore, heat-dependent effects such as MRI devices creating high-EMWs are not observed in electrical workers. However, the exposure of these individuals to low-frequency EMWs intermittently for a long period, in other words, the effects of chronic exposure may appear after years. The reason for that is the inability of the organism to repair the damage until next exposure and accumulation of the damages for exposures to repetitive EM radiation, even in low frequencies.

Besides studies reporting that EMF activates the formation and growth of the bones, inhibits osteoblastic activity, provides contribution to the healing of the bone fractures, and affects the granulation of formation of fibrous tissues in the wound healing;[46,47] some studies demonstrated that biological effects of the low-frequency at the cellular level include creating change at the levels of proliferation and differentiation,[48,49] changes at the levels of messenger ions such as Ca^{2+},[50,51] and creating changes in the shape and format of the cells.[52,53] Studies conducted about the effects of EMFs on the bone formation and fracture healing report different mechanism of action. In these studies, the mechanisms of action have been explained as the osteogenesis-stimulating mechanism,[54–58] and physiological and physical effects on the bone metabolism and cellular processes. Furthermore, it has been reported that EMF has effects on the calcium channels, intracellular ionized calcium changes, receptor behavior and genes, and that EMF increases the synthesis and transcription of deoxyribonucleic acid (DNA), intercellular calcium and the synthesis of messenger ribonucleic acid of type-I collagen, stimulating the production of extracellular

Table 8 Comparison of serum oxidative stress index between groups

Oxidative stress parameters	Control group	Study group	*P*-value
TAS (mmol Trolox Equiv/L)	1.93 (0.40–3.73) 0.84	1.62 (0.16–3.96)	**0.017****
TOS (μmol H_2O_2 equiv/L)	7.63±3.10	9.39±3.68	**0.013***
OSI (AU)	487.82±462.29	957.32±1,201.97	**0.013***

Notes: *Independent *t*-test, **Mann–Whitney *U*-test. Data are median (minimum–maximum) unless otherwise indicated. Bold *P*-value defines the significant difference ($P<0.05$).
Abbreviations: TAS, total antioxidant status; TOS, total oxidant status; OSI, oxidative stress index.

matrix.[56,58] According to all of these results, further radiologic, biochemical, and histopathologic studies are needed to demonstrate the effects of the low- and high-frequency EMFs on the bone tissues and fracture healing as well as to clarify EMFs' mechanisms of action.

Many studies were carried out for the effect of EMF to thyroid hormone synthesis and different results were reported. In a large-scale study, Bergamaschi et al detected no significant difference on the workers exposed to EMF because of cell phone use in terms of the TSH level;[59] Selmaoui et al found that low-dose EMF exposure for every other night or continuously did not affect serum total-free thyroxin (T4) and triiodothyronine (T3) as well as TSH levels.[60] No significant effect of low-dose EMF exposure for a long period was found on TSH in human studies carried out in a similar manner with less participation,[61,62] whereas no difference was detected on individuals exposed to low-density EMF for a long period in terms of the frequency of thyroid cancer.[63] Koyu et al found a significant decrease in T3, T4, and TSH levels in the rats who were exposed to a low-dose EMF for 4 weeks when compared with the control group.[64] Another study carried out with rats detected a significant decrease in serum thyroid hormone levels as a result of low-dose EMF exposure for a long period in comparison with the control group.[65,66] De seze et al detected on volunteer males that cell phone use for 2 hours a day for one month reduced TSH levels by 21%.[67]

A positive correlation was shown between the effect of radiation on different endocrine organs and radiation dose and exposure duration.[68] Low TSH levels were shown more frequent in those with longer duration of exposure to EMF and duration of talking with cell phone,[46] whereas some studies showed an increase in thyroid hormone and TSH levels as a result of long-term exposure to EMF of rats.[69,70] In the present study, we found FT4 levels significantly lower in the workers who are exposed to EMF for a long period, and no significant difference in FT3 and TSH levels were detected. Although a low dose causes a decrease in T4, it may depend on long-term exposure to EMF. Moreover, more nodules were observed in the study group in percentage when compared to the normal population, but no statistically significant difference was detected. In the comparison for gland sizes, a significant increase was detected in the dimensions of the left lobe particularly in the study group than the control group. Rajkovic et al detected an increase in the volume density of thyroid follicles histologically on the rats exposed to a low-dose EMF for 3 months.[65] Exposure to ionizing radiation increases the risk of benign or malign nodule. Palpable thyroid nodules are detected in 20%–30% of the population affected by radiation.[71] However, there is not any study which investigates the effect of electromagnetic radiation on the thyroid gland in the literature. In the present study, occupational higher electromagnetic radiation is not confronted as a significant risk factor statistically in terms of thyroid nodule frequency and parenchyma echogenicity. Nevertheless, the increase in the gland sizes is statistically significant.

Conclusion

One of the occupational groups who are exposed to electromagnetic radiation most is electrical workers. The electrical workers who are exposed to EMF radiation caused by high-voltage transmission lines and transformers for a long period were observed to complain about general indisposition, exhaustion, apathy, anxiety, and headache. Furthermore, a decrease in BMD, serum ALP, Ca, P, RANK, RANKL, and antioxidant enzyme levels as well as an increase in oxidative stresses and OPGs were observed. Consequently, it was observed that the balance between construction and destruction in the bone metabolism of the electrical workers who are employed in HVETL replaced toward destruction and led to a decrease in OPG levels and an increase in RANK and RANKL levels. In line with the previous studies reporting that long-term exposure to an EMF causes disorders in many organs and systems, it is considered that long-term exposure to an EMF affects bone and thyroid metabolism and also increases OSI by increasing the TOS and decreasing the antioxidant status.

Periodical investigations, EMF measurements around the workplaces, and raising awareness of the electrical workers about these exposures should be done to detect possible negative impacts on the electrical workers who are exposed to electromagnetic radiation.

The present study has some limitations. The first limitation is that the majority of the employees had not any thyroid USS before and were not aware of the nodule during the study. The second limitation is the requirement of new studies including more electrical workers to obtain more reliable data.

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Disclosure

The authors report no conflicts of interest in this work.

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Deborah Tavares Interview with Barrie Trower

Barrie Trower's background and personal warning in his own words: *"In the very early 1960's I trained with the government microwave warfare establishment. I looked at all aspects of microwave warfare and when I finished my time in the military, because I had a lot of expertise in the microwave field, I was asked if I would carry on with this research. We are in a new Cold War and this is why countries are developing this. And this is why all the microwave transmitters are going up everywhere because somebody, if they wanted to, could use them for other effects. The system is up and running. Years ago our government said to our scientists when it comes to microwaves you will only talk about things to do with heat, and that is it. So they won't even discuss anything else. They will deny anything that doesn't have anything to do with heat. They even deny all their 40 years of research leading up to this, although they've said that this can cause cancer and all the damage, they say no it can't. We're only looking at heat and heat is all that matters. So for the last 40 years the English government has been lying to the people. And the American, the Canadian, the Australian, they have been lying. They have been lying to protect industry, to protect their profits, to protect themselves from lawsuits. So they are really just liars and it is provable, sanctioned by the World Health Organization, without a shadow of a doubt. It is the same people that sit on the ICNAP certificate, sit on our government health protection agencies, sit on the World Health Organization . . . . it is the same people. There are probably no more than 20 of them. But, yes, they are going to, in my opinion, commit the worst genocide this planet has ever known, not just people, but animals and plants. They are probably going to cause more destruction than a global war, and in several hundred years time, people will look back, whoever survives, and look at what we tried to do to stop them."*

Deborah Tavares: Hello. This is Deborah Tavares with **StoptheCrime.net** and I'm here with Barrie Trower from the UK and we're going to be and we're going to be talking about specifically this document today which was found on the White House website and it is entitled *Realizing the Full Potential of Government Held Spectrum to Spur Economic Growth*. And it says President's Council of Advisors on Science Technology, dated July 20, 2012.

Now we're quite honored to have an opportunity to discuss this document with Barrie today. And a little bit about Barrie, he is, of course, visiting the United States right now from the UK and in the very early 60's he was trained in microwave warfare by the microwave warfare establishment and he looked at aspects of microwave warfare and when he finished the time that he spent in the military he had a lot of expertise in the microwave field and he was asked to carry on with this research. And it was a new cold war that he discovered with microwaves. Would there be anything else you would like to add to that?

Barrie Trower: Only that microwaves from the 50's were used as a stealth weapon as they still are today, only they're obviously much, much more sophisticated. The 50's was really a trial time where different countries were just using people who had no choice, prisoners, psychiatric patients, dissidents, and it was really beam people with this and see how long it takes this pulse frequency to have any effect and, if it does, we try a different type of group. There were 25 different categories of people including children and pregnant women. Twenty-five different categories, and so from the 50's, 60's, 70's, 80's we've been developing microwave weapons right up to today and they are *incredibly* sophisticated today. So if any government says that microwaves have no effect on you, the question is then why have you been spending billions upon billions of dollars with the military for the last sixty years improving them?

Deborah Tavares: That would be true and in this document, Barrie, it has listed a number of experts that are involved in this particular technology and in this particular document and I'll just name a few of those experts now. They're called the Key Members and Spectrum Experts. And they would include, and not limited to, Stanford University, because, of course, many universities are involved in this technology that are funded by the military. But the White House Spectrum Management team is Google, Microsoft, Stanford and Harvard Universities. And I want to draw the attention to Harvard University as being one of the universities involved in the origination of Silent Weapons, Quiet Wars technical manual that is on StoptheCrime.net, but also Virginia Tech, UC Berkeley, the National Communications and Telecommunications Association, the FCC and NSA, and many others that are involved in this as well.

So as we go through this, Barrie, I would like for you to explain some of what you see in this document, if you would, because it's going through thirteen pages, and they're talking about what the purpose of the spectrum is and if we could just flip slowly each portion represents one page that is on our website.

Barrie Trower: One of the things you said, the universities, for instance, they may not be guilty. And I can give you an example. The government holds massive amounts of funds for research and the universities apply for research grants. Now to give you one example in the United States, the government asked one university if it could devise a method whereby if you beamed microwaves into somebody's ears the vibrational frequencies in the cochlea, they would actually produce sound in the person head so nobody else around could hear, just the one person being beamed could hear the sound. And the University was told this would aid the deaf enormously because people could talk into a device and they would just hear it straight through. It was also picked up by the super store manufacturers who said we could also use this for good because if we have shoplifters, we can beam the pulse frequencies to the shoplifters to say, "You're being watched. Put this down." We'll prevent crime, and that was used for good. It didn't take people very long, especially the military and other super stores to

think, 'well, hang on, we can use this for our own devices'. So the military can now put voices into people's heads to do whatever deed they wish it to achieve, and the super stores have also realized that rather than say 'put that down, you're going to steal it' , if you're indecisive and you're shopping, they can say 'you really do want to buy this', and after nine months, and I got the figure from one of your calls, somebody took one of your super stores to court for beaming them. And they made a phenomenal profit in just nine months, *phenomenal profit*. But because your Federal Communications Committee says that microwaves were safe, the case fell.

So all I'm saying is that when you're reading out the universities, they may be acting totally innocently and it may be that the recipients, after the research is done, say now we will turn this to our advantage.

Deborah Tavares: And that's because so much is compartmentalized and that's how they keep this monster escalating to the degree that they are.

Barrie Trower: Yes. It's perception.

Deborah Tavares: Absolutely. What I find so true in the Silent Weapons document is that they talk about "the real and the stated goals" and we're saying what the real goals are but what they tell us is what the stated goals are. So we're buying a lot of these advancements in technology based on what sounds good as a stated goal, but then there's the real goal. And I think as a global population when you look at the Silent Weapons protocol, that 44-page document that we spoke about just a bit ago, we can see that this is a well planned program overall by a few, and so certainly while many are unaware, a few are; the most wealthy, knowledgeable, the ones in the technologies, to carry this out without our knowledge or consent.

Barrie Trower: This is from a program in 1976. I can tell you by its title that it was a program in 1976 because in 1976 your government produced a list of all of the illnesses that you can develop from continuous low-level microwave radiation, everything, physiological, neurological illnesses. But in the same document that was released under the Freedom of Information Act, and I referenced it in my latest paper that I'm reading from tonight. If you get a copy of that paper, it's referenced in that. But what your government also did that was rather naughty; they asked all the other governments in the world, the influential governments in the world, basically to deceive the public. And they were to deceive the public really for two reasons. The first is to avoid law suits, and the second was to protect industrial profit.

Deborah Tavares: So the bottom line is massive corporate profit.

Barrie Trower: And your government printed it and I've written it down. They say that, basically, the public must be deceived to protect industrial profit and this is here, it's in the title, *Economic Growth*.

Deborah Tavares: That's exactly right and also in the Silent Weapons document, which you're well aware of, they also talk about the key to global control is through energy. And we see that happening now with the frequencies and the microwaves. It's all energy. We're energy. And they want to control it all, even us.

Barrie Trower: There is a counter argument. I deliberately do not take sides. I look at arguments from both sides and I decide myself who I think is right and wrong. But a counter argument that I *do not accept* from the English or the American governments, is that enemy countries are also developing this technology. I know forty countries that are developing this. And their argument is that if other countries are developing this technology, we have to develop it in order to defeat it. Okay so far, but I don't go along with the argument that you must use your own people for experiments. So they are using Americans for experiments.

There are forty some countries developing this technology and the governments argue that for combat, if the waves were used on the United States, the United States would know exactly what to look for, they would know the frequencies, they can jam them. And I can go along with that. We pay governments to protect us. What I cannot go along with is the fact that 25 categories of persons without their choice and in many cases without their knowledge, are being experimented upon with these particular frequencies to cause all of this. That is wrong.

Deborah Tavares: Now would, say at this point, at the increased level of technology, that we're roughly unaware that they have an advanced technology base 50 years beyond our even being aware of what they have available?

Barrie Trower: Are you asking . . . I'm not sure I fully understand the question, sorry.

Deborah Tavares: What we understand is that minimally there is a 50-year advancement of technologies that are out there ahead of time that we're not even aware exist right now.

Barrie Trower: No. No. You can't have technology 50 years hence. You can have ideas 50 years hence. You cannot have technology 50 years hence because the world can't keep that many secrets. I go to countries all over the world. I go to countries that despise the United States and I go to countries that love the United States. I go to countries that are at war with countries I've just left. And I really don't take a stand for or against anybody. But the scientific community that I talk with at these conferences, they often say to me, 'if you go to this country, please warn them about this'. Scientists, in the whole, do not want mass genocide. They do not want total government control because they have families and children and grandchildren

and great grandchildren. And a lot of the help that I get are from talking virtually all night to international scientists who say 'well, we've done this' and they will also say 'well we've done that' and if you put these two together it agrees with what 'he' says. Scientists talk and 50 years hence, it wouldn't be kept secret. The ideas can be there, but the knowledge which I have today of where we are at the moment cannot be exceeded because we do not have the people that clever to exceed it.

Deborah Tavares: Would you say that as far as the microwave targeting of mass populations now, which is what this is showing (holds White House document up), is the intention where we were talking about more specific targeted people hundreds of thousands globally?

Barrie Trower: Yes.

Deborah Tavares: Now we're looking at a map that really does show a mass targeting particularly of the United States?

Barrie Trower: Oh yes. Absolutely. Really this is one of the ideas behind the Smart Meter where they put them on everybody's homes. What they can do now. They can watch every single person in that house. They can watch you go to bed. They can watch what you're doing in bed. They can watch you on the toilet and in the bath. They can hear every single word you're saying. They have a machine which will measure your hormone levels. They have a machine, provided they're within a 150 feet, they can measure your brain activity and they can even tell what frame of mind you're in. Now, if they can do this to an entire population, most people would not like it done to them but would be unaffected, and from the government point of view is, we're really not interested in 98% of the population anyway, but we want the 2% that could be dangerous to the American citizens. But that doesn't' apply. They then do on to say, "Well hang on, there's a group there that are obstructing us doing this, demonstrators. We'll watch those." And then you get to people of specific religions, and people with long hair, and people who smoke cannabis, and the level comes down and down and down to the point where they're actually monitoring about 75% of the population and they have the computer technology to do this.

Deborah Tavares: Well, that is what we're understanding is the intention of this (holding up the White House document). And what this is of course depicting is psychotronic weapons for mass mind control and about quantum computers and mind control, mind theft, and invasion of the human brain with artificial intelligence. Could you explain to people what that means.

Barrie Trower: The first thing, with this (referring to the White House document) when you blanket a whole area, there are different reasons for monitoring populations, and right now in the United States there could be to my knowledge between 40 to 45 countries blanketing people with microwaves, and all you need is a few vehicles, blanketing people with microwaves

for specific purposes. Now I grew up in the Cold War era with spies, and forget James Bond or anything silly like that, the main weapon of a spy, any spy from any country, the main weapon is blackmail. That is the main weapon. Because, for instance, if I'm from a country and I want to get a spy into the United States they're going to need documentation. To get a passport or a birth certificate or some form of documentation you need a professional person or two, like a lawyer, to sign an affidavit or something to say I have known this person since they were zero years old, they are now 22. I can identify them . . . everything. They are a person. To get a professional person like a lawyer, if you blanket an area with microwaves, you know every conversation they're having, you know where they go, what they're doing. For instance, if you have a person who is a pedophile, a person who has a mistress or two, a person who is a secret alcoholic or gambler and they would lose their job if it became known, all they have to do is go up to that person and say is this is what we have on you, and you're from another country obviously, this is what we have on you and we will give you a choice and you make your decision now. And this is what they do. You make your decision *now*. Either this goes in your local press in the Sunday newspaper or you will lose your job, your children come out of university with disgrace, your wife will leave you and run away and hide, you will lose your house, everything, and you will never work again. You will be a beggar on the streets, if you're lucky. Or you can sign this piece of paper to say you know this individual. They're an upstanding person. They deserve the passport. They deserve a job reference because they should get this job. You'll highly recommend that. You will sign it and we will go away. You will never see us again. Most people, given ten seconds thought, will sign and walk away and breathe a sigh of relief. That is why I suspect this, the blanketing the whole area (points to the White House document). It may not be the United States. It could be up to 40 countries. And I can assure you there are at least 40 countries who would like to get spies in the United States. And when they're in, they're in. Then it goes on from there.

I don't like the word 'mind control' because you don't really control the mind. You can change it to act in a different behavior, but you do not permanently control it. You can make people do things, and that's very easy. I could do it. I could do it to you in less than three days.

Deborah Tavares: Such as assassins?

Barrie Trower: I could turn you into an assassin in less than three days. That's easy. So there are lots, and lots and lots of different reasons for blanketing an area and watching people. And 98% of the population probably would not be affected, but it is the fact that you have no choice. And if you upset somebody in the government, they can abuse their authority and target you.

Deborah Tavares: In this document that is actually next to the map that is in the document itself (showing the White House document) it says that they will use extended white space system already in operation as a starting system.

Barrie Trower: There is a contradiction in terms there because white zones, white area, white space is usually an area totally free from radiation or it can mean an area which is blanketed like a white blanket across an area, so different countries use different terms. So it could mean a totally free area, a zone free area, or it could mean an area which is already totally blanketed so that no other country can put their frequency into this area because it would be jammed and only the United States will control this area.

Deborah Tavares: Okay, so in respect to this document, this could be a white space then in place that would protect the United States.

Barrie Trower: This document is so bland that when you read anything it could mean three or four different things. It really is so bland and deliberately so.

Deborah Tavares: Yes, exactly. Well, they also talk about modifying the rules to allow general authorized access devices to operate in two bands. Are you familiar with what this may mean?

Barrie Trower: Again, there are around 300,000 million bands they could use so whichever ones they're talking about I don't know. Again, it isn't specific enough. It sounds interesting to the person and profitable and technology is going to roll, but what they are going to do with it is anybody's guess. This was written in case it fell into enemy hands so people wouldn't understand what they were doing or clever people wouldn't understand what they were doing.

Deborah Tavares: Well, we do know one thing just by the title which I know you've discussed in Ireland when you brought this document up, where it said realizing the full potential of government held spectrum to spur economic growth. And the economic growth is not for the country's citizens.

Barrie Trower: It's for the industry.

Deborah Tavares: It's for the corporations and the industry, that's correct. And then, again, we have a variety of participants here, major industry participants, Google, and we know the World Bank is involved, we know that much of the corporate banking structure globally is involved and interested in this.

Barrie Trower: Again, I'm not taking their side, but I do talk to these people, and some of these people, if government advisors and chief scientists approach somebody in industry, and the person in industry has generally done a degree in law, civil law or something, or some other economic degree, they do not have degrees in nuclear and atomic physics, they do not have

qualifications in microwave warfare, they do not have other qualifications. So and in England it might be a knighted person, if somebody who is highly respected by the government with a government chief advisor goes along and sits down and says, "We can make you a lot of money if you do this and we're also going to benefit the population", they will believe them. Again, if you have the industries there, it is probably not true that they know or realize the harm they are going to do because they have families and grandchildren and great-grandchildren and I suspect a lot of them wouldn't go ahead with this if they fully understand the situation.

Deborah Tavares: There are many scientists who realize what their scientific experiments have now caused. They're not being used for the benefit of mankind and they now see how those are being used against their children, their families, and the world at large and they're coming out and they're letting this be known. And they're not being targeted microwaves and the inventions that they've created are now being used against many of these whistleblowers, would you say?

Barrie Trower: Yes. And I can give you a specific example from a chief scientific officer in England. But, if you're going to become a whistleblower you must realize first of all you're going to receive death threats and these are very serious death threats. You are going to lose your job. Your children are not going to get a job or go to university. It is a family sacrifice, as well as yours. I can give you an example. I've received many cryptic and strange messages from senior persons. I received a message from a very, very senior scientist in the top secret experimental place in England. He said, "I need to talk to you, Barrie." I said okay and we met. He said I am going to give the perspective from where I am sitting. We have received a contract from the government to do research. I'm researching the effect of microwaves on the brain and the heart. I am one of the country's leading research scientists. What they have asked me to do is study the brain and the heart being exposed to various microwaves, a specific pulse frequency known to affect the brain and the heart. I know and you know, because a part of my degree was experimental physics, that if we're going to do a study on the heart and the brain we're looking at about 15 years. It would take about ten years to do the study and another five years to tie up the loose ends, write it, have it peer reviewed, go to publication. You and I know, because if I said to you how long would it take to do these experiments, you would say ten to fifteen years, which is what the drug companies do when they're testing a new drug. It's always a minimum of ten years, maybe longer. They don't always get it right, but at least they have a go. And he said to me there's a lot of money involved here. Do you know how long they've given me to do the experiments on the brain and the heart? One of them, ten minutes and the other one is 20 or 25 minutes. I can do them both in an hour and have time for a cup of coffee. He said now I know that when I do these, the results are going to show SAFE, SAFE, SAFE, SAFE, SAFE. And I know that they are going to use this with the stamp of my laboratory to say 'this is safe—sell it'. And this particular system has now been sold to 150 countries as

safe. And he said to me, now I've done nothing wrong. I did the experiments. I produced the results, which are safe, but I know this is going to be abused. I know that people are going to die because this is going to be published. Women are going to get breast cancers, miscarriages; all sorts of things are going to happen. But they're going to do that—not me. He said now I am in a top government scientist job. I have a top salary. I have two children at university, one at college. I have a mortgage on a big beautiful house. If I spill the beans, I will lose everything today and I will never work again. My children will come out of university and my life will be a mess. What do I do? I said you only have two choices: you give up your family and your children's university educations and everything, or you keep quiet. And those were the only two choices, and he decided to keep quiet.

Deborah Tavares: Well, of course, we know in many of these decisions the dangers beyond the family, and the fact that the family is going to be assaulted and confronted by increased frequencies anyway, as well as all of his friends and the rest of the world.

Barrie Trower: So this is the dilemma that some of the scientists are put in. so even when you read up laboratories, it may be that the scientists did nothing wrong, he did nothing wrong. He did what he was asked to do. He gave the results he was asked to give. It was the other people who are doing something wrong. But again, I'm very, very wary of reading out lists of corporations and laboratories because the people responsible may not be responsible.

Deborah Tavares: I can see that where they're compartmentalized and they're really unaware. I had a few other questions too. I know that you were a part of the government back in your early days government microwave warfare establishment and you were carrying on research. Are you involved with the government at this point anymore, or are you completely separated from the functions that you were previously working with.

Barrie Trower: Oh, no, completely separate now. I mean then I had top security clearance. I'm completely away from them now. Absolutely away, I have nothing to do with them.

Deborah Tavares: With all of the people you speak with, are their counter measures that you're aware of coming online to help mitigate some of the damages from the effects of the targeting on some of the people that are being severely electronically harassed?

Barrie Trower: Yes and no. I'm very, very cautious about devices, medicines, or anything to do with countermeasures. I often receive letters from people saying would you endorse this? And I always say no. Unless somebody can prove through rigorous scientific experiment that something works . . . . I may work, I don't know. But there are all sorts of charlatans who will make a device to sell to people who are vulnerable to make money.

Deborah Tavares: Another way of corporate profiteering.

Barrie Trower: So the devices may work. I don't know. I honestly don't know. I haven't tested any of them, but if somebody produced something . . . if the body is suffering, there are obviously chemicals and medicines that will help, and they will help. For instance, boosting the antioxidants or boosting the nighttime melatonin. That certainly works. But you have to be very, very careful about buying devices that will protect you. They may, but they may actually be even more dangerous especially if they're jamming signals because they're also sending other microwaves into your body. You have to be incredibly careful.

Deborah Tavares: Since this is now a new Cold War that we're finding ourselves in . . .

Barrie Trower: Yes, it's a Cold War now between, I would say, certainly between 15 to 45 countries.

Deborah Tavares: So everyone's targeting everyone.

Barrie Trower: Oh, without a doubt. And I can be even more specific. And when I speak to schools, you see, the problem is microwaves are so easy to produce and from the lists I got from when I was talking to spies, and things like this, the lists are available now. All you need to do is make a microwave transmitter, which is incredibly easy and at the pulse frequency which is even easier, you can make these weapons. So what I say to schools, to the students in schools, I say please be incredibly careful. Every time you touch keyboards, or an I-pad or an I-pod, every time you put a finger on any microwave device that transmits, up to 45 countries can be storing that. So if you are a young couple in love, and you've got the people in separate houses and they're in their bedrooms and one is saying 'can we do this' and the reply 'I'd love to' and send me a picture of your chest, and they carry on. Now I say to the schools to assume that 45 countries are actually recording this and they have the capability. And when you are a graduate and you are a professional, they're going to come back and they're going to sit in front of you one day, if they wish, and they are going to say, do you remember writing that? You should have a criminal record. Your job doesn't allow people with criminal records. How about just doing a little favor for us and we'll tear this up. And if you think of what teenagers, and the average American student sends 3,000 texts a month, if you imagine some of these texts going back and forth and up to 45 countries could be storing this, and you're all clever and you're all going to university and you're going to be exactly where they want you. And if they want to, and they want you, they're going to come back and you're going to regret this.

Deborah Tavares: Speaking of universities here in the United States as well as internationally, in the United States specifically we have a new curriculum that's been introduced called Common Core Curriculum. And it is a curriculum, essentially, of dumbing down both math and science. They will not be teaching cursive writing any longer which helps to fire off the right and left brain. The children will not be learning how to read a calendar and math and science,

as I say, is going to be dumbed down. In the Silent Weapons Quiet Wars document they say that it will become enslavement by lack of knowledge. So in conjunction with the microwaves that we're all being faced with, that are certainly causing confusion, inability to sleep and levels of anger and all types of emotional and mental and physical ailments along with the dumbing down of the global population, whether everyone is targeted or not, they are being targeted through the entire process of the system even beyond the frequencies. Would you say that's your experience with what you're seeing in other countries as well?

Barrie Trower: Funnily enough, we touched on this at lunchtime with the Congress lady today. You've touched an area that leaves an incredible bitter taste in my mouth. The problem as I see it, we have virtually the entire United States being microwaved and there are a small group of people in the United States who are untouchable, namely your Federal Communications Committee. Because if you have a complaint, or lawyers have a complaint, or anybody else has a complaint, it will go to Congress people, Senators or government officials but no matter where these complaints and questions go out to, they all funnel back to one person. Even the judiciary cannot get involved in this. They've been whitewashed out. So everything goes back. What we're seeing in the United States is that you have one person, maybe two, certainly not any more than three, who is dominant in committee. And this person is the only person in the United States who can be asked these questions; the only person and nobody else is allowed to answer them, nobody. Everything is funneled through to this one person. So you have this one person who is all powerful, is above the judiciary, is above Congress, above everybody because Congress cannot change his safety levels. So you have this one person and this is where I have trouble with this because with the current states, and this is well established research because it is your government research, in 60 years time, if nothing changes, three generations of 20 years, you are going to be down to one-eighth of your children's population, one-eighth. Now how many people walking the streets today are going to be working and paying taxes in 60 years time? Not many. So, the United States, if nothing is done, is going to become unfunctionable on the world stage. You're not going to be able to run your industries. You're not going to be able pay your taxes. You're not going to be able to fund your military. So the United States on the world stage is going to disappear.

Deborah Tavares: They say in many of the documents, the source documents that we have read, that of course the pre-eminence of the United States is being dismantled.

Barrie Trower: Within 60 years, the United States won't exist as you know it today. You will be in the position that England was in at the end of the war when we just didn't have the people, our soldiers had been shot, we didn't have the people coming back to run the buses, the factories, the trains. There was very little money to pay taxes. We couldn't afford anything. And a worldwide appeal went out for any nation to send as many people as they could to run

our buses. Now this is where you're going to be in 60 years. But the one thing that really, really puzzles me is why is this all powerful American doing this to his own country?

Deborah Tavares: Well, some of the source documents that we have referred to address that. This is for a One World System.

Barrie Trower: One person, no more than two, are dominant on this committee . . . why would this one person, because he has to know more than me, because of the virtue of his position and his expertise with microwaves, he has to know more than I do, and if I know this, he has to know it. So, he has to, in my brain only, her has to be intentionally bringing the United States to its knees and the question I want to know is why? I can't get around that because he's made himself untouchable and why should one person decide Congress will not interfere with my levels (of frequencies allowed). The judiciary will not interfere with my levels. I am going to control this. And he must know he is bringing the United States down and you only have 60 years and that is it. You'll be finished.

Deborah Tavares: Well, certainly many of the source documents that we have on our website **StoptheCrime.net** . . . .

Barrie Trower: He ignores them. That's the thing.

Deborah Tavares: Well, many of them are written by them too and we're looking at transhumanism as the coming agenda where they're going to be bringing online a replacement for humans. And we see much of that research occurring now in most of the major universities. Certainly here in the United States, but this document here this NASA plan talks about robot cyborgs and humans and we're really starting to see the replacement of humans by machinery.

Barrie Trower: Well, again, and I'm not being deliberately obstructive, but I'm going to rush to the defense of the industry. And I do know because I've spoken to the scientists. The government approaches an industry and it says if we could implant something, and it can be nanotubes, and a chemical can be triggered, or an electrical signal will be triggered with a microwave pulse going to the brain. Or you have the creatures that live in the oceans that photosynthesize from the sun, and when you photosynthesize like euglena or coqolithapores, they produce miniscule electric currents. Now they can be guided to certain areas of the brain by viruses and the industry is working on these and the paralyzed get electrical systems going through the body to get them to move and think. And by beaming them with microwaves you can actually get paralyzed people moving again. Or brain damaged people; you can get the electrical current moving back into that part of the brain. So they are doing an immense amount of good, but again, as I said earlier, the harm comes when the military come along and they say if we put this into these people and we stimulate this part of the brain, for instance, a balance between the frontal cortex and the amygdale which will induce severe violence. So you

can use things for good and they're developed for good, and the other people can use them for bad. So I can say that because the corporations are there it doesn't mean they're bad. It means that they have actually done some incredible Nobel prize winning research that somebody has then said 'thank you very much, we paid for this, we have the rights to this, now we're going to put our scientists to work'. There is a see-saw effect here and you have to be incredibly careful reading out names of universities and organizations because they may be doing it for good and they do absolutely brilliant work.

Deborah Tavares: That's absolutely true and I know that much of what they have done has been hijacked.

Barrie Trower: Oh, it's all been hijacked.

Deborah Tavares: That's why we're here today, because we're sitting in a very precarious hijacked reality.

Barrie Trower: If it's been hijacked, somebody authorized it. And if somebody authorized it, they would have had permission. Now where is this leading back to? That is where we should be going . . . the Source. And it's even kept from presidents. The people involved here, and it's the same with the English government, you have just a small band, no more than a hand full of people who are all powerful and they know what is really going on. And Presidents and Prime Ministers and Ministers and Senates they come and go every few years and they are absolutely immaterial to this. They are told what they need to be told, that is it.

Deborah Tavares: It's just like a script for a Hollywood movie.

Barrie Trower: Yep. And the people at the top, they lie for a living and I've met them. They lie for a living. The truth is so obscure to them, they wouldn't know the truth if they tried to tell it. Lying is just norm. And so you have this small band of people and they are controlling virtually everybody else. So if they say to the President 'I am the country's top scientist, this is safe' the President believes them because he's only going to be there another two years anyways and then a new one comes in and they tell them what they will say and what they will do.

Deborah Tavares: This, of course, is why we have Bohemian Grove and the Bilderbergs. They set global policies. They meet and they organize and they orchestrate the corporations. And we've heard much about the Bilderbergs there in Europe and their offices are, of course, in Switzerland and they meet annually just as the Bohemian Grove does here in Northern California, meet once a year and at times in between to create policies.

Barrie Trower: Personally I've never met them and I've never attended a meeting, so I honestly can't comment on that.

Deborah Tavares: I also have a question. Have you heard anything about the activation of catalytic genetically spliced virus and bacteria? I know you were just mentioning some of this. Via bacteria hybrid by the use of advanced targeted psychosyntronics and there have been rumors from insiders for years that psychosyntronic can also be deployed to reduce a person's natural immunity allowing the opportunist virus and bacteria the ability to gain control when they would normally be suppressed. Could this be true?

Barrie Trower: You've covered about 50 years of complicated research there. I mean just any three of those words could spark about an hour worth of conversation. Is it being done? Yes. Can I go into that? No. I can answer it. We would need to sit here for a week and not even scratch the surface. Yes, it can be done. Are they doing it? I don't know because they haven't told me. Is it possible? Yes. But I don't know that they're doing it because if they are doing it, it is in secret, and I don't have access to their secrets. I've never been told by anyone that they're doing it. Theoretically it can be done. Whether it's being done practically, I don't know.

Deborah Tavares: There are people concerned too about the electronic warfare and how we can use it against terrorists, but it seems as though since we have 45 countries all engaged in inflicting electromagnetic on other countries, it seems like we're all battling one another, so do you see an opportunity to control this?

Barrie Trower: It's uncontrollable. I mean, what we have now started is a runaway train. It is absolutely uncontrollable because if the United States stops research, there are 45 other countries, some of whom probably do not like the United States that will say 'that's good, we will now be the world leaders'. It is uncontrollable. People now have to progress. Where it is all going to end up I don't know but it is absolutely uncontrollable now. There are too many different laboratories over the world studying too many different things. There are too many different organizations looking into microwave weapons. It is absolutely uncontrollable and as you've said we have now gone into a new Cold War. I don't know where it is going to end.

Deborah Tavares: Well, this certainly is a Silent Weapons system for Quiet wars.

Barrie Trower: It's been that for 60 years, no problem with that.

Deborah Tavares: Somebody asked and was wondering, of course, about WIFI in restaurants, etc., and in the coffee shops that are globally situated now with WIFI opportunities. What would you say to the general population about WIFI and what other kinds of repressive stances can they make against this attack of artificial frequencies.

Barrie Trower: WIFI uses a known weapons frequency. That's known. And it is going to cause harm. There is no doubt there. And again, the owners of cafes and bars that have WIFI, they would have been told something that wasn't true. So the only thing you can do is advise them

to fit a fiber optic cable, high-speed fiber optic cable, if they can be told the truth. Again, it is not their fault, and people come in with their computers and their Smart thingies and they sit at the tables and they press away. So the café owners, they're just giving people what they want. They're making money from it. It's good for business. They're employing people, which is good. But, if they were to run just a few cables, they would make just as much money and they wouldn't be doing harm. But you can't tell them they're doing harm because of the control over the press and the television companies and the radio companies. Because if you even begin to mention it, the industry will come down like a ton of bricks and say 'we are pulling out our advertising, now how would you like that'.

Deborah Tavares: So what we are really saying is for the protection of people, they either have to be hard wired, and/or stay away from locations that have WIFI. They need to stay as far removed from the cell phone towers, the antennas, the Smart Meters, the electro smog that our cities are experiencing. Is that the only thing?

Barrie Trower: The system can be made a lot more safe. But, of course, they don't know it needs to be made a lot more safe. Maybe our conversation from the Congress lady this morning, if we develop some way there we can get something broadcast nationally. But at the moment, the system can be made a lot safer all over the country to the point where the minimum of persons will be harmed.

Deborah Tavares: How long would that take in order to implement?

Barrie Trower: If you started now and provided you had . . . I mean, once this bubble bursts there is going to be an *enormous* business for somebody. *Enormous profits* in fiber optics and things to do with even cell phones . . . I've read from Dr. Andrew Goldsworthy who is an incredibly clever scientist from Imperial College London. Imperial College is sort of the Oxford and Cambridge of London and you don't get to teach there if you're stupid. He has described how microwaves can be made safe. I don't understand at the moment the full technology behind it. But, he has described how they can be made safe and they will work. (Put) fiber optic cables everywhere you can. Technology is there . . . everyone can still have their toys and they can still use them, and they will probably work better, and it will be a lot more safe. The problem is it needs to get to everybody. The technology is there today, and in terms of how long it would take depending on manufacturing outputs, depending on how quickly you can convert a few factories—but whoever comes up with this first there is going to be billions upon billions to be made with this.

Deborah Tavares: The concern of course would be that we have a corporate structure that is engaged in massive profits over people that are becoming quite ill.

Barrie Trower: Yes, but the profits will only last until people like me who touches the right person, who touches the right person who says: Why does that man have so much power? Why doesn't he answer to Congress? Why doesn't he answer to the Judiciary? Why doesn't he answer to the President? And when the people in authority say well hang on, he has too much power, let's ask him a few questions and see how right he is' and when you can show that this person is actually wrong, and I know he's wrong and I would challenge him here to face me live on television and I would stand my ground and I would prove he's wrong in less than five minutes. When these people can be brought down, and it's not going to take long because these have immense power but there is one thing they cannot do . . . they cannot stop people dying. They don't have that power. God has that power and they have no more power than God. Too many people are going to die. Too many schools are going to get leukemia clusters. And when that happens the swell is going to change. And I suspect, and I'm going to choose my words very carefully here, some industries are going to crash overnight. The shareholders are going to think 'hang on, half my life is buried in this industry'. Zonk! I'm going to go into this (other) industry and you're going to have some industries crashing. And this is going to be money orientated, not orientated by morality. It's going to be pure greed. And one industry is going to crash and the other industry is going to go zonk (points straight up) with billions and we will have a safe system. How many people have to die? I don't know.

Deborah Tavares: For us to get to that point.

Barrie Trower: I don't know but I can tell you it will be between here and 60 years, which is not long.

Deborah Tavares: If we can survive 60 years under the current bombardment of frequencies because people are becoming so ill already.

Barrie Trower: Exactly. And the problem is, it was calculated several years ago, and I have the paper, the cost of your sick from electromagnetic radiation, and it was the tens of billions and it is going up enormously. So there is going to be a point when the cost of treating people is just prohibitive for the country and people are going to die and the bubble is going to burst. And when it bursts, I fear a lot of influential people will be standing in the dock. And I really wouldn't like to be in their position standing in a dock. In my mind, and this is a personal opinion, a personal opinion, and whatever libel or slander, I'm not doing that, but I would think with the death rates, an equivalence in my mind, and you can tell me if I'm wrong, would be if Adolf Hitler stood in the dock for all of the deaths in the second world war. I think it will be on that scale.

Deborah Tavares: So for the time being, right now, for those that are becoming aware of this enormous threat to humanity, what would you say would be the most important things for people to do right now?

Barrie Trower: Leave it to me and I'll tell you why. The moment an individual puts their head above the water the industry is so skilled with the government at putting people down. You won't stand a chance. You will lose your job. You will lose your family. You will lose your house. That is unnecessary. I don't need that. Leave it to people like me. Our work is slow, but we are getting there. I have now spoken to around 40 royals, leaders of countries, leaders of peoples, the message is getting through. Nothing is ever fast, but we are getting there. But my advice to the ordinary is to leave it to us. We know what we're doing. We have the expertise. We've had all the death threats. We will get there. As we go along, academics suddenly jump in and they say 'I am an expert in this; I believe what you're doing and please let me help'. And we are getting there. It's not going to be quick. I mean, trying to stop World War II wasn't quick. So if a person is going to take risks, I say don't do it. Leave it to me and people like me. Let us do our job.

Deborah Tavares: So then what the average person could do is to stay hard wired with every device they have, keep it hard wired. Spread this information everywhere they can. Refer people to the youtubes that you have so that we create a wider understanding through education of what we are facing.

Barrie Trower: Exactly. If everybody started to go with cable, the WIFI industry would collapse anyway.

Deborah Tavares: Now what about the schools because we're noticing now that in many of the major universities, the elementary schools, the high schools, because the economy being what it is, and the telecom industry paying monthly rent to anyone that will allow a cell phone site on police stations, on fire stations here in the United States. We're seeing these cell phone towers crop up everywhere. They're disguised as trees. They're in church steeples. They're in flag poles. Some are not disguised, but many are and we're seeing that they are lining all of our major highways nationwide now and they are in communities everywhere. We are just staying a place here in Portland in downtown Portland and collectively from the AntennaSearch.com search that we did, between the cell phone towers and the antennas within a four-mile radius we have a combination of 660 cell phone towers and antennas.

Barrie Trower: Again, the school governors and principals would have been told from our one person that this is safe. And they would have been told that there is nothing to worry about, research is inconclusive. It shows that it is safe and you're on a good thing. Whether or not there is a legal argument here, and there is in the United Kingdom, in the United Kingdom a

teacher, and I was a teacher, a teacher is under law in what they call en loco parentis. In other words, when the parents take a child to school and hands that child over to the teacher, the teacher is obliged by law to look after that child as the parent would. You cannot do anything to that child that the parent would forbid. It's against the law. That's the easy bit. And they are trying this in the UK now. So if a parent says to the teacher, "I do not allow you to microwave my child", and the teacher does, the teacher is breaking the law. That's en loco parentis. It has nothing to do with the other laws. The teacher is breaking the law and the teacher can be taken to court. That's the easy bit. In the UK for somebody to take someone to court for microwaving, it has been estimated, you need 31 million pounds.

Deborah Tavares: Well, that's putting an enormous burden then on any of us to try to bring litigation against them.

Barrie Trower: They've said time and time again in England 'take us to court, our part of the trial is three years for all of the witnesses we want to call, a thousand witnesses, it will take about three years for our part of the trial'. Court costs, 100,000 pounds a day, no legal aid, and then of course, your part takes three years and if you lose, we'll have your house, your car and everything else.

Deborah Tavares: Well, that brings me to an interesting situation that we discovered here in California that all of the cities, and in fact it is actually nationwide by Executive Order, in their planning departments have to initiate what is called a Climate Action Plan or an Energy Action Plan, one of the two is the title for this plan. In California where we have looked at a number of these Climate Action Plans, it's requiring, even though California has an opt-out now for Smart Meters with utility companies by paying $75 initially to opt-out and $10/month. Many people feel, of course, that's an extortion fee. But what we have found out now is with these Climate Action Plans it is ***required*** that cities have Smart Meters and that all of the appliances that are not EnergyStar rated, that are considered inefficient appliances, must be retrofitted now to the EnergyStar appliances which is a backdoor hookup of the initial intention to begin with. So many people are discovering that the opt-out was an appeasement plan, a momentary sense of victory to reduce the fight against the Smart Meters. And while still they are being deployed, which is what industry calls this, a deployment, which is a military word, instead of installation, and this is now occurring nationwide here through the backdoor in all of our cities.

Barry Trower: It will do, because the Smart Meters can be used for their WIFI enabled. They can be used with WIFI, with all other things, and again, we're back to the man at the top. And it's not until enough people have died that these will be stopped and turned off or made safe. But, sadly, people are going to die. They are going to make an enormous amount of money on the back of this, but it's not until people such as myself can raise the issue with the people who need to be told and enough people have died that we can make this bubble burst, but it's not

going to be quick. It's like the start of the second world war and people are going to suffer, they're going to die, and there is nothing we can do to stop that. Nothing. The people are too powerful. It's like the Storm Troopers, the SS. They are too powerful. They answer to nobody and the only question is will the bubble burst before the United States can recover? That is the only question. And it depends on who I can talk to and when.

Deborah Tavares: In the United States?

Barrie Trower: In the United States. I need to talk to Congress. If I can talk to Congress, we may have a chance.

Deborah Tavares: Is there anyone or two people in Congress that you've identified as . . .

Barrie Trower: I won't give you their names, but to date there are two people who may be trying to get me to talk to Congress.

Deborah Tavares: And so then in the meantime for the safety of all of us, we reduce our frequencies, we hardwire and we do everything we can to get the word out on our level so that more and more people become aware so that then in our local cities, in our city councils, in our county board of supervisors, we're getting this information to them who may also possibly be carriers to higher levels of government with the information that we provide them. So all of this is going to help your efforts and other scientists who are very much aware of this cataclysmic situation we're all finding ourselves in.

Barrie Trower: Well, It is and there is no easy way out of this. Too few people have too much power. And as I've already said, we have people who do not answer to the judiciary and the President and Congress, and they are causing this. And until somebody actually takes their power away and questions them, this is going to go on, and it's only a matter of how many people have to die until it can be stopped.

Deborah Tavares: Well, Barrie, I want to thank you for speaking with us today and sincerely express our appreciation for what you're doing.

Barrie Trower: But there is some good news, and I won't name them on camera in case the industry suddenly turns against them, but to my knowledge now, and I've had no input into some of them and I've had some input into of them, so I'm not saying this is my work. There are lots of other people doing what I do. But there are now ten countries who realize this is happening and they are making changes to protect their children and their population, so the world is turning. Ten countries isn't a lot but it's a start. And, if we go back a few years, we didn't have any. Now we've got ten.

Deborah Tavares: Now with the level of remote targeting and now with the use of satellites as well, how are those ten countries, even though they're becoming aware of this type of new weaponry, how will they protect themselves? What kind of shielding is available to them in the industry?

Barrie Trower: Well, their scientists are working on this now and shielding is actually quite easy. So that really isn't a problem. I've spoken to some of the scientists. You can virtually make the shielding from half a dozen old bed springs. That's not complicated.

Deborah Tavares: So that would be more of an individual, house to house, shielding?

Barrie Trower: Yep, yep. But the ten countries are now actively going against the industry. They're still using all the equipment, but they're making it a lot safer and they're protecting their children.

Deborah Tavares: Are there instructions somewhere for people to create this shielding if they find they are being targeted?

Barrie Trower: No and if there were you would need quite a lot of expertise and you wouldn't be allowed to do it because it means transmitting certain waves and you wouldn't be allowed to do that.

Deborah Tavares: So it would be basically sending waves out against the incoming.

Barrie Trower: Right.

Deborah Taveras: Ok. That was actually one of the questions that I had so as far as the general population having that information that's not available.

Barrie Trower: As hard as it sounds, for the general population, and I hate to be bitterly truthful here, but I haven't come all this way to lie, the only thing that you can do is protect yourself, protect your family, and wait out the war. And that's it.

Deborah Taveras: So there was a question specifically to that. What specific microwave signals and frequencies are deployed in this new Cold War weaponry and what, in your opinion, is the core reason for them being deployed against the United States? And the second question is: Do you have any experience chopper frequencies being deployed as countermeasure?

Barrie Trower: I call it the Silly Boy Syndrome. You have these young graduate boys or girls. They graduate in Computer Science at university. They then go to firm or to industry and they think I'm going to make something that does *this.* And they turn out this little black box and it does all of this but they haven't taken into consideration the frequencies, the pulse frequencies, the modulations, how it's going to affect, children, adults, pregnant women. They

have no knowledge. Nobody says to them go and talk to people who were alive in the Cold War or study the frequencies that are used by industries and see if they're dangerous. Nobody says that to them. They make their little black boxes. They want to earn a million dollars. They put them on the market and to all intents and purposes they're considered safe. They don't do the background checks and this is the problem. So if you're saying what frequencies are there? I'm saying, well, how many apps are produced each week? How many black boxes that you plug into are produced each week? How many different websites are there? It grows; it evolves over time so you would never keep up with it anyway.

Deborah Tavares: And then, one final question, if I may? For a number of people that I know that are stocked, and followed by organized stalking, and are targeted by neighbors next door, by people that live up above them in an apartment setting, or below them, or where they're walking on the street and they're suddenly targeted, they're going to have to wait out this war?

Barrie Trower: If you're being stalked, they're studying you for your fear electronically. If you're being stalked, and it's usually have a dozen big ugly men doing it, I would go up to them and say, well, I've finished in this store, I'm going over there (pointing), and then I'm going over there (pointing) and then I'll be stopping for coffee, follow me, come on and lead them around. They won't be violent to you in a public place. There's no good going to the police. It's no good complaining to your representative because they'll say you're mad, which is what they want you to do anyway. I would just go up to them and say, I'm here and I'm going to buy the most gorgeous pair of shoes in two hours but I would value your opinion and come out with a shoe and ask what do you think about these and these? Turn it into a game. It's what you can do. Turn it into a game and let them know you're not scared.

Deborah Tavares: So what we understand with the documents, the *Silent Weapons Quiet Wars* document, the *NASA document*, is just what Barrie Trower has just said, that they're winning by creating massive fear and terror, massive disinformation and media propaganda, and creating a division between all of us so that we don't band together. So I guess it would be fair to close this discussion right now with the understanding that we are in a war. They're going to be immeasurable amounts of casualties. We're going to have to overcome our fear because we know that part of the corporate structure benefits on that mass chaos. They make mass amounts of money on creating mass chaos, fear and misinformation. So in order to create our safer realities, besides getting all our technologies hardwired or to stay away from them, and to certainly not partake in establishments that have WIFI and perhaps going in and letting them know why you cannot go into their establishment and passing out fliers and just covering with information because we now are the media. And until it becomes trendy enough for other portions of the population to weigh in on this significant, irrefutable massive death campaign that is being waged on us through fear, again, and media propraganda, we will be able to help

you (Barrie Trower) do your work as we're able to get this information out and live outside of fear. And understand that this is a massive media propaganda campaign and they're keeping us divided and it's all through lack of knowledge.

Barrie Trower: There is just one last quite interesting conversation I had with one of the people doing this and he was an incredibly highly paid lawyer and going back then it was something like $2,000 an hour, and he was involved in finding loopholes to support industry. And I was involved in a legal case, and I tend to lose, I was involved in a legal case and during the lunchtime session I went over the row and I sat in a pub for a sandwich and he came in and sat down next to me. I'm saying this because it may be a question that somebody listening to this can ask somebody who is immensely powerful. And this man was immensely powerful. And he sat down next to me and he said, "You know you're going to lose this, Barrie, don't you?" And he said, "I've got this, I've got this, and I've got this. You don't stand a chance." And he was right. I didn't stand a chance. The people wanted representing, I was representing them, but legally he had got every single loophole tied up and legally he was going to win and he did win. He sat there and he went on about how sort of insignificant I was and the protestors and everything else and how powerful he was and why didn't we give up because we didn't stand a chance *ever*. And I said, "Would answer me just one question? "What are you going to say when you stand before God?" And that was it.

Deborah Tavares: This is a powerful way to wrap up our talk. I just want to thank you so much for saying what you've said today and we will be sure to get this out far and wide and support your work with getting your youtubes out and doing all that we can.

Barrie Trower: I actually worry about these people because when they go into the afterlife and they have to live the sorrow that they have caused to every single person and every single family, and they are going to feel it, and there is no time limit, they have no idea what they are going to face. And I think if they did, they may think twice. But I stopped this man in his tracks. He had no answer. Nobody in the afterlife is impressed by a yacht, a Rolls Royce, a big house, fancy clothes when you stand there naked and there is no lying, you can't lie, and they have no answer. That is what I would ask them and if I saw the head of your Federal Communications Committee that is one of the two questions I would ask him. What are you going to say to God?

Deborah Tavares: Thank you. I think this really ends it on a powerful note, Barrie. Thank you, thank you so much.

DEFENSE INTELLIGENCE AGENCY

BIOLOGICAL EFFECTS OF ELECTROMAGNETIC RADIATION (RADIOWAVES AND MICROWAVES) EURASIAN COMMUNIST COUNTRIES (U)

PREPARED BY U.S. ARMY
MEDICAL INTELLIGENCE AND
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OFFICE OF THE SURGEON GENERAL

Releasable Report

BIOLOGICAL EFFECTS OF ELECTROMAGNETIC RADIATION (RADIOWAVES AND MICROWAVES) - EURASIAN COMMUNIST COUNTRIES (U)

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PREFACE

The purpose of this review is to provide information necessary to assess human vulnerability, protection materials, and methods applicable to military operations. The study provides an insight on the current research capabilities of these countries. Information on trends is presented when feasible and supportable.

The study discusses the biological effects of electromagnetic radiation in the radio- and microwave ranges (up through 300,000 megahertz). It is not within the realm of this study to provide detailed descriptions of every laboratory experiment. Such data have been purposely omitted in favor of an analytical approach. An attempt has been made to identify the principal areas of research and to discuss the significance of experimental results.

The information reported in this study has been drawn from scientific, medical, and military journals, intelligence reports, magazines, news items, books, and other publications. The information cut-off date for this study was 1 October 1975.

(U) Constructive criticism, comments or suggested changes are encouraged, and should be forwarded to the Defense Intelligence Agency (ATTN: DT-1A), Washington, DC 20301.

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SUMMARY

(U) The thermal effects of electromagnetic radiation have been reasonably well established through experimental investigation. The nonthermal effects, however, remain a controversial issue between scientists in the West and in the Eurasian Communist countries. The difficulties encountered in conclusively demonstrating the nonthermal effects of electromagnetic exposure are likely responsible for differences in exposure standards; some standards are based largely on the demonstrable thermal effects, while others allow for possible nonthermal effects at subthermal intensities.

(U) The Eurasian Communist countries are actively involved in evaluation of the biological significance of radiowaves and microwaves. Most of the research being conducted involves animals or in vitro evaluations, but active programs of a retrospective nature designed to elucidate the effects on humans are also being conducted. The major systems, system components, or processes currently under study include the blood, the cardiovascular system, cells, the central nervous system, the digestive system, the glandular system, metabolic effects, and the reproductive and the visual systems. Other aspects of exposure are also being studied, but the limited number of reports uncovered makes assessment of the importance placed upon this research impossible. These lesser reported research areas include nonthermal effects, immunological studies, and use of radiowaves for functional control of organ systems.

No unusual devices or measures for protection from radiowave exposure were noted, but a continued stress upon personnel protection in occupational situations was apparent. Here, protective goggles and clothing are recommended when working in regions of microwave radiation. Although some differences in standards remain between the various Communist countries and between military and civilian standards, the Communist standards remain much more stringent than those of the West. An exception to this may be Poland where a recent relaxation of their standards has occurred. This is the first significant shift of an East European country away from the standard first set by the USSR in 1958.

If the more advanced nations of the West are strict in the enforcement of stringent exposure standards, there could be unfavorable effects on industrial output and military functions. The Eurasian Communist countries could, on the other hand, give lip service to strict standards, but allow their military to operate without restriction and thereby gain the advantage in electronic warfare techniques and the development of antipersonnel applications.

The potential for the development of a number of antipersonnel applications is suggested by the research published in the USSR, East Europe, and the West. Sounds and possibly even words which appear to be originating intracranially can be induced by signal modulation at very low average-power densities.

Combinations of frequencies and other signal characteristics to produce other neurological effects may be feasible in several years. The possibility of inducing metabolic diseases is also suggested. Animal experiments reported in the open literature have demonstrated the use of low-level microwave signals to produce death by heart seizure or by neurological pathologies resulting from breaching of the blood-brain barrier.

(U) As may be expected, the bulk of the research being done in this area is in the USSR. However, a notable volume is also being produced by Poland, Czechoslovakia, Bulgaria, Rumania, and Hungary.

Western scientists who have followed the Soviet research efforts on the biological effects of microwaves have expressed a variety of reactions ranging from disbelief to passive acceptance. The overall impact of current Soviet work is not overly significant, at least on their civilian sector. One possible exception may be their studies of the central nervous system where some interesting work is being done. Elsewhere, most of their work tends to be outdated, some of their experiments cannot be duplicated, and others are of doubtful credibility. No real new developments or fresh approaches have been identified. Nevertheless, a large volume of material continues to be published on the effects of radiowaves and microwaves on biological systems, indicating a fairly high degree of interest and a genuine desire to pursue these investigations. No significant research and development has been identified that could be related to work in this field in the People's Republic of China, North Korea, and North Vietnam.

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SECTION I

INTRODUCTION

(U) The effects of radiowaves and microwaves on biological systems have traditionally been separated into two basic classifications, (1) thermal effects, and (2) nonthermal effects. The thermal effects are widely recognized and the mechanism of action reasonably well understood. Nonthermal effects, however, are controversial since the mechanisms involved are not clearly understood. Soviet and East European scientists believe that biological side-effects occur at power densities that are too low to produce obvious thermal effects. Such effects have been questioned in the West because experimental evidence, obtained largely in US laboratories, does not corroborate occurrence of nonthermal side-effects.

(U) Divergences in opinion between Bloc and Western researchers concerning the effects of microwave radiation are the result of nonstandardized research protocols and materials. In addition, mechanisms underlying observed biological effects are at present poorly understood by any of the world's scientists engaged in microwave research. The exchange of scientific information on microwave hazards has increased greatly since the active participation of Soviet, Czechoslovak, and Polish scientists in the International Symposium on Biological Effects and Health Hazards of Microwave Radiation in Warsaw in October 1973.

(U) It is now generally agreed that biological systems irradiated with electromagnetic waves in the radiowave and microwave frequency ranges (one kilohertz to more that 10^5 megahertz) absorb varying amounts of energy depending on the irradiation frequencies and the physical properties of the system. Typically, however, 40-50 percent of the incident energy is absorbed by the biological system and the remainder reflected. In reality, only the shorter wavelengths represent any appreciable hazard as a result of thermal heating. Radiation fields in the microwave range vary in wavelength from about one meter to very short wavelengths on the order of a millimeter. The depth of penetration of the waves is also variable and again depends on the frequency, wave polarization, and the physical properties of the system (i.e., dielectric and geometric), but typical penetrations are on the order of 1/10 of the wavelength. Therefore, very short waves are absorbed primarily by the skin, while long wavelengths penetrate to much greater depths.

(U) The degree of heating appears to be a function of the water content of the tissue and probably results from oscillations of water molecules or dipoles. Another possibility is a resonance absorption of energy by protein molecules of the cell. As might be expected, the actual damages resulting from a given exposure are functions of the thermal regulatory

and active adaptation processes of the organ or animal. Less vascularized tissues are more susceptible to thermal damage because of a poorer ability to dissipate the heat, therefore, crystalline lens damage or cataract formation may be observed.

(U) Many techniques and indices have been employed to study the effects of irradiation on biological systems. These include:

Body weight.
Biochemical studies.
Cardiovascular studies.
CNS effects (including conditioned and unconditioned reflexes).
Electrophysiological measurements.
Fertility and mutation studies.
Histology and pathology studies.
Metabolic studies.
Temperature.

While these and other experimental studies have been conducted on animal and cellular models, knowledge regarding human exposure has been almost exclusively obtained retrospectively. Accordingly, information regarding the amount and/or portion of the body exposed, field intensities, and duration of exposure are usually ill defined.

(U) As can be seen from the above, quantitation of the biological responses to electromagnetic exposure is a very complex problem because of the wide frequency spectrum, the large number of physical and biological variables, and the interrelationships of those variables. Factors requiring consideration include the frequency, intensity, waveform, (pulsed, CW, or modulated) configuration of the body, its orientation with respect to the source, portion of the body irradiated, exposure time-intensity factors, environmental conditions (temperature, humidity, and air currents), and shielding. Other complicating factors include the subject's state of health and previous or concomitant medication. In addition to the above factors, the animal species used and its comparative relation to man is important. Accordingly, experimental results from animals cannot easily be extrapolated and assumed to apply to human exposure because of size differences relative to exposure wavelength which can markedly influence the system or organ being damaged.

(U) With these complicating factors in mind, the evaluation contained in this report was undertaken. The data presented were obtained from the sources outlined in the preface and sometimes contained insufficient information to make absolute decisions regarding their significance. The sources were, however, indicative of the types of effects being reported and suggested those areas of research being emphasized, thereby permitting assessment of recent Eurasian Communist attempts to define the biological effects of radiowaves and microwaves.

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SECTION II

BIOLOGICAL SIGNIFICANCE OF RADIOWAVES AND MICROWAVES

PART 1 - BLOOD

(U) Effects of electromagnetic irradiation on the blood include biochemical variations, effects on erythrocytes, changes in coagulation, and alterations in the blood forming system. As would be expected, most communist country reports originate from in vitro or in vivo animal experiments rather than from human data.

(U) Long-term ultrahigh frequency (UHF) exposure in rats reportedly reduced the iron and copper content in both the blood and muscle with a concomitant increase in iron content in the liver. Similar exposure in chicks caused an increase in total proteins and globulins, but decreased the albumin in the plasma. Rats exposed to 0.04 W/cm^2 for 25 days demonstrated similar shifts. In some studies with dogs, irradiation with microwaves significantly decreased the lifetime of erythrocytes, while other studies indicated no changes in the granulocytic system after exposure. In the lymphocytic system, however, mitotic disturbances and changes of nuclear structure occurred. Rabbits exposed to "an electromagnetic field" showed significant increases in the number of monocytes, basophils, and lymphocytes/mm. Although undesirable, these shifts are not significant enough to impair the functional performance of humans. However, they are significant enough to warrant further experimentation. Soviet researchers will emphasize more experiments with animals and they will continue to try and relate these experiments to data on human exposure to microwave environments. They will most likely work toward relating such changes in different species of animals to particular intensities or exposures.

(U) One study involved the observation of several thousand persons working in microwave-irradiated workshops, as well as animal experiments. In the human subjects, three kinds of damage were found:

(1) Lymphocytosis and monocytosis.
(2) Granulocytopenia, monocytosis, and eosinophilia frequently accompanied by absolute lymphocytosis.
(3) Moderate neutrophilia.

The degree of changes in the blood could be correlated with exposure and/or duration of working period. This determination was based on the relative changes as a function of period of employment, which was felt to indicate a cumulative effect of microwaves in the human body. The type and intensity of the exposure was not documented.

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(U) Blood coagulation indices of dogs subjected to high intensity super-high frequency fields were studied at intervals of ten minutes to thirty days after irradiation. Initially the coagulation time was prolonged, but two hours after irradiation it was accelerated as a result of protective compensatory changes in neurohumoral factors. The protective reaction was, however, of short duration; the irradiation-induced prolongation of coagulation time reappeared and the animals' clotting times did not return to normal until at least fifteen days after exposure. Another study showed that long-term exposure to microwaves at a power density of 10mW/cm^2 decreased the overall activity of butyrylcholinesterase in the blood serum of rats. Under conditions of whole-body exposure, the microwaves did not exert a consistent effect on the enzyme molecule. The decrease in the overall activity of butyrylcholinesterase was correlated with a decrease in its concentration in the blood of the irradiated animals.

(U) The action of microwaves on human erythrocyte permeability to potassium and sodium ions was also investigated. The mechanism of action appears to be an inhibition of active transport and an altered diffusion through the pores in the membrane. The latter may be caused by the influence of UHF energy on the membrane itself or on the hydrated sodium cation and potassium cation. The microwaves either change the membrane structure thereby increasing the passive sodium cation and potassium cation diffusion and reducing the concentration gradient, or somehow block the mechanism of active ion transport.

(U) The question of stability of microwave-induced changes in blood components was addressed in chronic and acute tests using dogs and rabbits. The irradiation was at a frequency of 2375 MHz with a field strength of thirty microwatts per square centimeter. The rabbits were subjected to between one and ten irradiations of sixty minutes duration each, and the dogs were subjected to repeated irradiations over a period of more than a year. The changes in the blood and marrow of rabbits were found to be unstable and to pass after a period of five to ten days. Changes observed in the chronically exposed dogs were more stable, but became normalized over a period of twenty-five days. Investigation of chronic microwave irradiation on the blood-forming system of guinea pigs and rabbits was also reviewed. Both continuous wave (CW) and pulsed microwaves were utilized at an intensity of 3.5 mW/cm^2 and a wavelength of 10 cm. Increases in absolute lymphocyte counts in peripheral blood, abnormalities in nuclear structure, and mitosis in the erythroblastic cell series in the bone marrow and in lymphoid cells in lymph nodes and spleen were observed. The changes appeared to be a cumulative result of repeated irradiations and were attributed to nonthermal effects. There is limited evidence to support the belief that these cumulative effects are reversible upon cessation of exposure. It is still not quite clear if similar results could be observed in humans since wide species-variations have been observed by Soviet researchers working with animals.

(U) The primary concern of the present study was with electromagnetic field effects, but numerous reports regarding the effects of constant magnetic fields on the blood system were noted during the review. As with electromagnetic effects, effects on coagulation, biochemical properties, and formed elements were observed.

(U) To summarize the effects of electromagnetic radiation exposure on the blood, the following general changes emerge although conflicting reports are also present:

(1) General decrease in hemoglobin content.
(2) Generally reduced coagulation times.
(3) Decrease in leucocyte count.

These findings are based largely on animal experimentation. While detrimental in themselves, the extent of these changes would not be expected to be great enough to materially affect an individual's performance or general health, especially under stress conditions, where other factors such as physiological protective responses would be far more important.

PART 2 - CARDIOVASCULAR SYSTEM

(U) Heavy emphasis has been placed on investigations involving electromagnetic radiation on the cardiovascular system. Effects on hemodynamics include blood pressure variations and cardiac arrhythmias. Also included are reports of a slowdown of intraventricular and intra-atrial conduction, diffuse cardiac muscular changes, and ventricular extrasystole. As with other effects, animal studies are frequently reported and human reports are typically retrospective in nature. Many of the variations noted on the cardiovascular system result from central nervous system effects.

(U) Several reports concerning human cardiovascular effects from super-high frequency exposure were reviewed. Functional changes were noted, including a slight increase in the asynchronous contraction phase, a tension period, as well as other data indicative of moderate dystrophic changes of the myocardium accompanied by a disruption of its contractive capacity.

(U) Comparison of a group of engineers and administrative officials who were exposed to microwaves for a period of years and an unexposed control group revealed a significantly higher incidence of coronary disease, hypertension, and disturbances of lipid metabolism among the exposed individuals. Hereditary predisposition to heart disease was approximately the same in both groups, but overt disorders developed much more frequently in the previously exposed group. It was concluded that microwaves may act as a nonspecific factor which, under certain conditions, interferes with adaptation to unfavorable influences. Exposure may, therefore, promote an earlier onset of cardiovascular disease in susceptible individuals.

(U) Hemodynamic indices for thirty men in the 25-40 year age range who had been exposed to UHF exposures for from two to ten years were studied. These men showed a tendency to bradycardia, moderate decrease in the stroke and minute volumes, and a slowing of the rate of blood ejection from the left ventricle. Arterial pressure was essentially normal, but a compensatory constriction of the precapillary bed was noted in response to the decrease in cardiac ejection. There was also an increase in the tone of the large arteries. EKG changes indicated an intensification of vagotonic influences on the heart; possible fluctuations in the potassium-sodium balance were also postulated. In a similar study, it was concluded that hemodynamic changes resulted from disturbances occurring in the structural and functional state of the regulating system.

(U) Morphological changes in experimental mice exposed to short and ultrashort wavelengths were observed. Two series of experiments were conducted using 14.9 MHz and 69.7 MHz waves. In the first series, twelve animals were subjected to single lethal doses of the electromagnetic radiation. Very pronounced vascular dystrophic changes were found throughout the organism. In the second series, 37 mice were given daily 60-minute exposures to nonthermal intensities for five months. Morphological studies of these animals showed slight vascular disorders and compensatory proliferative processes in the internal organs as well as dystrophic changes in brain cells.

(U) In a group of patients suffering from "radio wave disease," cerebral hemodynamic changes were observed. These included reduced intensity of the pulse blood volume and an increase in tonicity of the intra- and extracranial vessels. The changes did not, however, appear to be functional in nature.

Personnel exposed to microwave radiation below thermal levels experience more neurological, cardiovascular, and hemodynamic disturbances than do their unexposed counterparts. Some of the cardiac and circulatory effects attributed to exposure include bradycardia, hypotension, and changes in EKG indices (sinus arrhythmia, extrasystole changes in intraventricular and intra-atrial conduction, diminished amplitude of EKG deflections, etc.).

(U) The cardiovascular effects have always been of primary interest, therefore, it is likely that research in this area will continue. It is not apparent if cardiovascular effects were first observed in animals or in patients suffering from the so-called "radiowave disease." It is probable that further research will more accurately establish hemodynamic variations in both animals and humans. Greater emphasis will be placed on animal studies which will allow for more precise dose-response quantitations.

PART 3 - CELLS

(U) Histological techniques have been used extensively for evaluating the effects of electromagnetic radiation on cellular systems. Such studies have included in vivo investigations of the cellular effects resulting from whole body irradiation and in vitro studies employing cell cultures.

(U) The most popular cells for study appear to be those of rat or mouse liver. Nonthermal effects on subcellular structures include the formation of binuclear cells and irregular thickening of the nuclear membrane. Invagination of cytoplasm into the nucleus has also been observed, frequently accompanied by breaks in the nuclear membrane. Marked changes in the endoplasmic reticulum and the mitochondria have also been noted. The available data, although still insufficient and inconclusive, seem to indicate that the magnitude of these effects is frequency dependent.

(U) The liver cells of rats exposed for three hours to a 1.625 MHz field showed damage to the protein synthesizing structures. Distinct changes were seen in the nucleoli or ribosome synthesizing apparatus. The ultrastructure of mouse liver cells was investigated after exposure to the same frequency. The mitochondria became swollen and underwent lysis. Some giant mitochondria also appeared. The cellular reactions observed were largely the same as those observed after the action of many other environmental factors.

(U) Phagocytic function has reportedly been increased by exposure to an electromagnetic radiation field and induction of colicin synthesis has been observed in E. coli irradiated with a nonthermal intensity.

(U) In many cases, electromagnetic radiation effects occur at the cellular level, therefore tissue culture techniques provide a well controlled and accurate method for study of those effects. Ultrahigh frequency exposure of cultures of rat fibroblasts, monkey kidney cells, and human embryo fibroblasts led to degeneration of the culture in four to six days. The earliest degeneration occurred in primary cell cultures. Studies are now under way on cell permeability, cell interfaces, cell stimulation, and the electrical characteristics of nerve cells. Other Bloc research will include study of microwave effects on mitosis, cell differentiation, and subcellular deoxidation potentials. The data obtained from these studies of cellular and subcellular responses to electromagnetic stimulation will be highly significant, since they may lead to the eventual understanding of basic mechanisms underlying biological changes which occur during and after microwave radiation.

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PART 4 - CENTRAL NERVOUS SYSTEM

(U) Research on the effects of radiowaves and microwaves on the central nervous system of humans was relatively widespread. A number of reports are discussed in this section, as well as research results regarding central nervous system effects on animal models and isolated nerves.

(U) Subjects exposed to microwave radiation exhibited a variety of neurasthenic disorders against a background of angiodystonia (abnormal changes in tonicity of the blood vessels). The most common subjective complaints were headache, fatigue, perspiring, dizziness, menstrual disorders, irritability, agitation, tension, drowsiness, sleeplessness, depression, anxiety, forgetfulness, and lack of concentration.

(U) Various neurological disorders were investigated by studying the vestibular and visual analyzer functions in persons exposed to radio waves of varying types for various periods. Elevation of the threshold of excitability was also accompanied by a lengthening of the time required for dark adaptation. The magnitude and intensity of the changes tended to increase with length of exposure. Similar studies showed increases in the threshold of olfactory sensitivity. EEG automatic frequency analysis was performed on 80 persons exposed to one meter wavelength radiation and 80 healthy controls. No differences were found between the exposed group and the controls regardless of length of the exposure, intensity of the field, or frequency. Presumably, all of these exposures were of a nonthermal nature. Conversely, thirty-seven persons occupationally exposed to a superhigh frequency microwave field (10 $\mu W/cm^2$) over periods of two to eight years, were studied; symptoms of asthenic and autonomic vascular disturbances, endocrine shifts, and abnormal EEG's were observed in half of the patients. Their reflexes in response to light and sound were weak, distorted, or nonexistent and their skin galvanic reaction to flashing light was abnormally intense and prolonged. Additional data will be required in order to assess the significance of these human studies.

(U) Long-term experiments conducted on rabbits demonstrated that irradiation with intermittent or continuous low intensity microwave fields elicits qualitatively and quantitatively different changes in the EEG. Intermittent radiation had a more pronounced effect on the recovery time. It has also been observed that long-term exposure of humans to microwave radiation results in extremely flattened EEG patterns.

Exposure of rabbits to low levels of microwave radiation resulted in alteration of brain electrical activity, but caused no detectable macroscopic or microscopic histological changes. Examination of the brains of rabbits sacrificed immediately after exposure to 10 centimeter microwaves at power densities of 20 to 30 mW/cm^2 revealed hyperemia of the meninges, distension of superficial vessels, and small extravasations of blood in deeper brain areas. Some, or all of the observed changes, could have been thermal rather than nonthermal effects, since the power density employed in the experiment was powerful enough to have caused a fairly great temperature rise. The effects noted immediately after exposure were apparently reversible, since no changes in the condition of the brain tissue were found in animals sacrificed on the day following exposure.

(U) Study of the rabbit visual cortex after a one minute exposure of the head to 40 $\mu W/cm^2$ at a wavelength of 12.5 cm revealed changes in the frequency of the background activity of 52 percent of visual cortical neurons. Chronic irradiation (two weeks) of rabbits caused the development of a prevalence of slow, irregular biological currents; this was interpreted as evidence of progressive establishment of an inhibitory state in the cortex of the cerebral hemispheres. Normalization of the electrical shifts required up to two months in some cases. Similar studies with rats indicated apparent decrease in cholinesterase activity in the central nervous system.

(U) Histological examination of the cerebral cortex cells from rats exposed to UHF at 5 to 15 $\mu W/cm^2$ revealed the onset of sclerosis and the formation of vacuoles in some of the cells.

(U) Some excellent studies using biopotential recordings were performed to determine the effect of microwaves on the kinetics of nerve impulse conduction. Frog sciatic nerves were irradiated with 12.5 cm wavelength microwaves for one minute and parallel temperature measurements were made. Calculations showed that the absorption of one calorie of microwave energy per gram of material per minute gave a temperature rise of 1.1 degrees C in the experiment. The effects of microwaves and of direct contact heating (from three to nine degrees) on nerve impulse parameters (the rate of excitation conduction (EC) and the biopotential amplitude (BA)) were measured and compared. For thermal effects alone, one degree increased the values of EC and BA about five percent. Changes in EC were characterized by rapid increases as absorption of microwave energy increased, followed by a fairly sharp drop upon switching off the microwave irradiation and normalization within three minutes. These increases in EC values (higher than values obtained by thermal effects alone) were especially pronounced in a study where the samples were heated three and six degrees. In a series where $\Delta t = 9.1$ degrees, EC was lower, although the temperature did not exceed physiological normal limits. Changes in BA

during microwave irradiation were also characterized by a much faster increase, followed by a sharp drop to below the original level after irradiation and essential recovery in three minutes. In a series where the temperature increased to 31°C, the microwave effect at first was the same as the thermal effect; after thirty seconds the BA value was even lower than for the thermal effect alone, possibly due to overlap of ionic currents at such high temperature. This was followed by a substantial drop after irradiation, and very little recovery in three minutes. The differences in results in this series were attributed to different initial conditions of the preparations.

(U) These experiments indicate that microwaves may have a specific effect of a nonthermal nature on EC and BA, causing sharp and reversible changes in these functional parameters of nerve impulse. Further experimentation will be needed before extrapolations of similar functional changes to in vivo conditions, or to humans, are attempted. It is expected that Soviet research on these and other CNS responses will continue during the next five years.

PART 5 - DIGESTIVE SYSTEM

(U) A number of alterations in the function of the gastrointestinal system were observed. Reportedly, exposures of subjects working for long periods of time in the presence of low intensity centimeter and decimeter waves resulted in numerous disorders. These included dyspeptic disorders, edema of the gums, bleeding gums, alteration of the gastric acidity, and a reduction of the tonus and evacuator functions of the stomach.

(U) Numerous animal studies have been conducted on the motor function of the gastrointestinal tract and the secretory function of the stomach. Non-thermal intensities were reportedly used. In general, suppression of the stomach's evacuatory function, with signs of adaptation upon repeated exposure, was found. After partial denervation of the stomach, the opposite occurred. It was concluded that the waves have a dual effect - a mediated action through changes in the function of the CNS and a direct effect on the organ or its local innervation. In general, gastric juices increased and little change in acidity was noted. This work tends to support observations of functional changes in humans and indicates that they may actually result from a CNS interaction. Other animal results are discussed below, but do not relate to the human observations.

(U) The effects of high frequency radiowaves on the content of nucleic acids in the digestive organs of rabbits were studied. The total nucleic acid content and the individual levels of DNA and RNA were assayed in the liver, pancreas, stomach, small intestines, and blood. It was found that the content of nucleic acids in the organs was a function of the power and duration of exposure. Low doses were found to considerably stimulate the nucleic acids, while higher doses reduced their content. Significant shifts in DNA content required very high level exposures. In a similar study on frogs exposed to microwaves (2307 MHz), the highest nucleic acid content was found in the pancreas and the lowest in the stomach. Again, low doses increased the total nucleic acid content while higher doses induced insignificant increases or reductions in their content.

(U) The effects of microwaves (2307 MHz) on radiophosphorus resorption in the stomach, duodenum, ileum, and colon were studied in rabbits. Simultaneously, absorbed radiophosphorus distribution in the liver, lungs, kidney, and spleen was investigated. It was found that rates of radioactive phosphorus resorption by sections of the alimentary canal differ. Under microwave exposure, resorptive activity of the stomach is somewhat decreased, while in the small and large intestines, it is increased. Lower intensity exposure accelerated the intestine resorptive function to a greater extent than large doses of lower frequency waves. Radiophosphorus deposition in the viscera is also a function of the dosage.

PART 6 - GLANDS

(U) Investigations of the effects of radiowaves and microwaves on the glandular system have been concentrated mainly on the adrenal, pituitary, and the thyroid. The glandular effects, however, do not appear to be a high priority area when compared to other systems currently under investigation.

(U) The functional status of the adrenal cortex in shipboard specialists subjected to the effects of a UHF field was reviewed. Thirty-eight men were exposed to the field for periods of 24 to 1800 hours and ketosteroids and oxycorticosteroids (which reflect androgenic function) were monitored. The results indicated that androgenic, glucocorticoid, and mineral corticoid functions of the adrenal gland cortex do not deviate from the normal. Microwave exposure also increased thyroid function in these subjects. The increase was attributed to secondary effects of the radiation and was felt to result from disturbances of the sympathetic nervous system in the hypothalmic region. In guinea pigs, the weight of the adrenal glands increased after continuous exposure at low levels for fourteen days, but decreased in animals exposed to interrupted exposures. Modification of lipid metabolism appears to be the mechanism of action. Similar exposure

using chicks resulted in increased ascorbic acid content in the cytoplasm of the adrenal cortex, but other work has produced conflicting results regarding the effects on the adrenal cortex.

(U) A quantitative assay of the gonadotropic hormones and growth hormones in the pituitary body of rats exposed to microwave radiation indicated that for a certain time after exposure, blocking or inactivation of gonadotropin-releasing agents occurs in the hypothalamus. Both neural-hormonal and pituitary gonadotropic hypofunctional effects resulted from whole-body microwave irradiation.

(U) The general conclusion that can be drawn from various (both animal and human) studies of the anterior pituitary and adrenal cortex is that exposure to radiowaves and microwaves of thermal intensities results in suppression of the hormone producing functions but exposure to nonthermal intensities tends to enhance production.

(U) An increase of the thyroid function indices was found in animals undergoing microwave irradiation for four months at a power density of 5 mW/cm^2. In histological sections of the cylindric epithelium covering the thyroid, follicles were seen and electron microscopy revealed reticulum.

PART 7 - METABOLISM

(U) Electromagnetic radiation exposure has been found to produce disturbances in carbohydrate energy and nitrogen metabolism in the brain, liver, and muscles. It appears that under electromagnetic exposure, macroergic compounds become deficient due to disjunction of the oxidative phosphorylation processes and deranged metabolism of carbohydrates. With respect to nitrogen metabolism, radiation causes an intensification of the ammonia formation processes in the absence of correspondingly more vigorous processes for its elimination.

(U) Exposure of rats to various intensities of electromagnetic fields with a frequency of 48 KHz produced an increase of lactic and pyruvic acids and a decrease in glycogen content in brain tissue. The changes depended on the field intensity and exposure duration and one month after cessation of the exposure the titer of lactic acid in the rat brain had not returned to normal.

(U) The role of metabolic disturbances of the heart in development of functional and structural changes under the influence of low frequency impulse electromagnetic fields was studied. Test animals were rats and it was found that exposure decreased ATP and creatinphosphate by

causing disturbances of the oxidative changes of carbohydrates and divergence of conjugation of oxidation and phosphorylation processes. It was concluded that changes in carbohydrate energy and nitrogen metabolism preceded the inception of structural changes in the myocardium.

(U) While these animal studies indicated an upset of some metabolic pathways, the degree of functional impairment was relatively small and probably not a significant factor. No human metabolic variations were noted and meaningful extension of these animal studies to the human is not possible. Research in this area is likely to remain low key and will be conducted mostly on animals.

PART 8 - REPRODUCTION

(U) The effects of electromagnetic radiation on reproductive systems have been the subject of numerous animal studies. Experiments with female white mice revealed changes in the estrus cycle. During the five-month study, the mice were irradiated twice daily for one hour, using a 10 cm wavelength of low intensity (10 mW/cm^2). Although the average number of normal cycles was unchanged, normal cycle duration increased. Prolonged diestrus and metestrus, along with a shortened estrus period, resulted in a decrease in the reproductive function of the ovaries. A weight loss was found to occur starting at about two weeks, reaching a maximum loss after four months.

(U) The fertility of female white mice was also investigated. The animals, irradiated as above, were mated during proestrus or early estrus with nonirradiated males. Conception in fifty-eight control animals was 94 percent, but only 75 percent in irradiated animals. Long-term non-thermal microwave irradiation of male mice evoked diffuse changes in the testes. Subsequent mating of the animals resulted in reduction in the size of litters.

(U) Microwave radiation at 10 and 50 mW/cm^2 intensity was administered for twenty and fifteen minutes respectively at various stages of the twenty day gestation periods. The progeny showed reduced viability, poor development, and anomalies. Changes in rate of postnatal development and disturbances of higher nervous system activity were also observed.

(U) Female white mice were irradiated twice daily for one hour with 10 cm waves of low intensity (10 mW/cm^2) up to the eighteenth day of pregnancy. There were stillbirths, a significant number of weak newborn, and a general retardation of body weight gain and growth. Other researchers found similar effects in litters from females which had been exposed twice daily for one hour to a 10 cm wavelength at an intensity of 10 mW/cm^2 for five months prior to mating.

(U) Genetic effects of electromagnetic radiation were observed in other studies. Male rats, irradiated with microwaves at 50-55 mW/cm^2, were mated with nonirradiated females. Litters displayed reduced viability and abnormal development, reduced rate of development and nervous disorders.

(U) Although researchers noted a certain degree of specificity in the pathological changes induced by microwave irradiation of mice, they concluded that the pathological processes occurring in male or female animals resulted from different mechanisms of action.

(U) Both sexes of the fruit fly, Drosophila melanogaster, were exposed to microwaves to study the effects of radiation-induced mutation. Group A, exposed for five seconds to 38 MHz, showed an increased frequency of mutation when bred five to nine days after irradiation. The results were not statistically conclusive, however. Group B, exposed for ten minutes to 2375 MHz, showed no effect on frequency of mutations.

(U) A strain of Staphylococcus aureus, known to be resistant to penicillin, was exposed to an electromagnetic field. A mutant was found to be sensitive to penicillin, probably due to a change in lipid content.

(U) In summary, a large amount of research has been done on the reproductive effects of EMR. However, effects on human reproduction, especially on male fertility, have not been demonstrated.

PART 9 - VISUAL SYSTEMS

(U) The role of microwaves in cataract formation and visual damage has been studied extensively in the past and is reasonably well understood. Primary attention in many studies has been directed at the biological effects of superhigh frequency electromagnetic radiation on the crystalline lens of the eye. Biomicroscopic techniques have been used to study cataract development in persons regularly exposed to microwave fields. A four-year study involving 600 workers and 300 controls revealed no significant difference between the two groups. Cataracts were discovered in only one percent of those persons exposed to such radiation; most of these cases resulted from safety violations. Cataracts which occurred were characterized in their early stages by turbidity of the lens and changes in form and color.

(U) In another study, thirty-five workers regularly exposed to microwave fields and having pronounced congenital lenticular cataracts were examined over a one to three year period; the results of their examinations were compared to those of twelve persons with similar cataracts who had no history of exposure to radiation. No progression was noted in any of the exposed individuals; changes were slow and probably attributable solely to natural aging of the lens.

(U) Combined wavelengths over the range of the millimetric spectrum were used in an animal study involving nine rabbits exposed for 35-70 minutes. Although the radiation used was of considerable intensity (120-495 mW/cm^2), no damage occurred in the deeper media of the eye, in particular the lens, during the 2 to 2½ months observation period. However, erosion of the epithelium of the cornea did occur along with damage to the conjunctiva and its vessels. Multiple tiny hemorrhages in the mucosa and submucous tissue were also evident.

(U) The Soviets have reported the occurence of "acute attacks" (sic) of glaucoma (1304 cases) which were correlated with geomagnetic disturbances. Moreover, recurring "acute attacks" came primarily on days when the mean value of the horizontal component of the geomagnetic field varied significantly. The significance of this report is questionable, but it indicates that the Soviets are examining all aspects of magnetic and electromagnetic radiation which might cause changes in vision.

(U) Although a growing body of evidence suggests that the microwave power density required to produce cataracts is incompatible with life, the Soviets will continue to investigate the visual effects of EMR but their effort will be reduced from its previous level.

PART 10 - INTERNAL SOUND PERCEPTION

(U) Perception of modulated microwave signals which seem to be originating intracranially as characteristic sounds is a phenomenon which was first reported in the US open literature more than thirteen years ago. To produce sounds, peak power densities of up to 80 mW/cm^2 may be required, but the average power density usually is 5 $\mu W/cm^2$. The Soviets have studied this phenomenon in order to determine the underlying physiological mechanism(s) and to define the optimum irradiation parameters needed to evoke the response. They found that when the fundamental frequency of the electromagnetic stimulus was raised from 2050 to 2500 MHz, the reaction threshold rose significantly, but at a frequency of 3000 MHz there was no reaction in the auditory centers. The average intensity of electromagnetic radiation required to evoke the response was less than 10 mW/cm^2; it was concluded that the fundamental signal frequency rather than the amount of energy constituted the primary stimulus and that the observed phenomenon was sensory in nature.

(U) The Soviets will continue to investigate the nature of internal sound perception. Their research will include studies on perceptual distortion and other psychophysiological effects. The results of these investigations could have military applications if the Soviets develop methods for disrupting or disturbing human behavior.

SECTION III

MISCELLANEOUS OBSERVATIONS

(U) Most of the reported biological effects from radiowaves and microwaves result from exposure to the higher frequency ranges. Many of the observed physiological changes probably occur as a result of thermal effects arising from the vibration of ions and dipoles of water molecules in tissues; the vibrations are set into motion more efficiently by the shorter wavelength (high frequency) waves. For example, a radiowave of ten centimeters wavelength converts about fifty percent of its energy into heat in this manner, whereas a three-centimeter wave converts nearly ninety-eight percent of its energy into heat. A study of the biological activity of low frequency (seven KHz) impulse electromagnetic radiation of different intensities and durations was done on rats. It was found that the pathological changes were a function of dose; susceptibility to radiation was governed by metabolic processes and morphology and the organs and systems could be classified as to sensitivity in the following order: testicles, liver, kidneys, heart, and central nervous system. Another study indicated that relatively low frequency electromagnetic fields generated sonic and ultrasonic oscillations in living organisms which in turn produced elastic deformations. If the frequency of the source field corresponded to the oscillation frequency of the cells (the resonance frequency most likely), the cells deteriorated as a result of the mechanical resonance.

(U) Clinical studies were done on thirty subjects, aged 25 to 40 years, exposed to industrial ultrahigh frequency centimeter waves at power densities of 10 to 500 mW/cm^2 for periods of time ranging from 4 to 13 years. Subjective complaints included generalized weakness, afternoon and evening apathy, fatigue, headache, sleep disorders, and nonradiating precordial pain suggestive of asthenia or neurasthenia with autonomic dystonia. Electroencephalography revealed periods of absence of alpha wave activity alternating with low R waves, increased frequency of potentials, dysrhythmia, periodic low peak potentials, and reactions to afferent stimuli. Peripheral blood studies revealed lymphocytosis or monocytosis in eight subjects; increased alpha and gamma globulins were found in 18 subjects. Erythrocyte potassium was within the lower limits of normal, while urine potassium was within the upper limits of normal. Adrenal cortex function was evaluated by urine levels of 17-ketosteroids, which were elevated to 22 to 40 mg in 11 subjects; average levels were 20.5 mg. Urine levels of epinephrine and norepinephrine were elevated in some subjects. Thyroid function was evaluated by rate of radioiodine uptake. Average uptake within two hours was 11.3 percent, and in four hours 16.9 percent. The 24 hour uptake did not differ from normal values. Electrocardiography revealed changes in the heart conduction system in six subjects; the $T_{v1}>_{v6}$ syndrome was found in ten

subjects and a U wave was registered in lead V_3 in eight subjects. Hemodynamic and myocardial function parameters were studied by tachooscillography and polysphygmography. Arterial pressure was usually within normal limits, although it was of a labile nature. Bradycardia was present in 14 subjects and decreased minute volume was observed in eight; increased peripheral resistance was found "in a significant number" of subjects. Autonomic-vascular changes and emotional lability and reactivity were attributed to CNS changes and increased pituitary-adrenal gland function. It was also noted that such shifts in neuroendocrine function could lead to circulatory disorders manifested by changes in the hemodynamic indices and electrical activity of the heart.

(U) A second study was done on two groups of workers occupationally exposed in the radio industry. The first group consisted of 100 subjects who had worked for several years under conditions of periodic exposure to microwaves of considerable intensity (up to several mW/cm^2). The second group consisted of 115 subjects who had begun work after the introduction of protective measures and had been exposed to microwave intensity levels approximately the same as those to which the first group was exposed. A control group of 100 subjects not exposed to the action of microwaves was also continuously examined. The study showed adverse effects, primarily on the nervous and cardiovascular systems, in both exposed groups. These effects were more pronounced in the first group. They were manifested by more frequent complaints of asthenic syndrome and vegetative vascular dysfunction.

(U) A lack of standards for measuring power levels represents a problem which probably accounts for conflicting reports regarding the effects of a given frequency and intensity. Other problems with dosimetry and experimental technique also exist. Such differences make comparison of results from one investigator to another, as well as from one country to another, extremely difficult.

(U) Only a few studies involving electromagnetic interaction with the immunological system have been reported. In one, rabbits were employed to study the body immunological reactivity under long-term irradiation. The rabbits were immunized with typhoid antigen and divided into two groups. One group was exposed to waves of 50 and 10 mW/cm^2 intensity for four hours a day over a four-month period. Analysis of the data obtained indicated that chronic exposure to the effects of low intensity high frequency radiowaves can influence the immunoreactive state of the body as evidenced by differences in phagocytic activity of neutrophils, blood serum complement level, and specific antibody titers.

(U) Soviet investigators have conducted studies on the effects of microwave frequencies in combination with ionizing radiation, magnetic fields, drugs, and nonionizing electromagnetic radiation of other wavelengths. Generally, synergistic effects have been observed. Continued work in this area is expected, and possibly new safety standards for these combined effects will be developed.

(U) In summary, this section shows the rather broad front on which Soviet researchers are investigating the biological effects of EMR. It is apparent that their interest covers all body systems which could reasonably be expected to display responses to such radiation. As with Western researchers, they have concentrated their efforts on the higher frequency spectrum which would be expected to produce more thermal responses. However, they also continue to be interested in nonthermal effects, which, by Western standards, they have yet to conclusively demonstrate.

SECTION IV

DISCUSSION OF RESEARCH METHODOLOGIES

The Soviet interest in the nonthermal effects of microwave radiation is evident both from the standards established and the many low intensity irradiation experiments conducted by their researchers.

The results of the research have encouraged the Soviets to investigate methods for exploiting microwaves and radiowaves to produce controllable psychophysiological effects. Laboratory facilities for investigating the combined effects of several microwave frequencies have been established at various institutes. Other research involves examining the pathological effects of UHF radiation from 300 to 3,000 MHz on man. This work supports the view, contested by some non-Soviet authors, that there are nonthermal modes of action. While no specific research results are reported, it appears that on the basis of results obtained the Soviets will not alter their standards. Part of this effort apparently involves development of prophylactic procedures against nonthermal UHF radiation as well as development of therapeutic techniques for those exposed. Beneficial effects of exercise and nutrition in increasing body resistance to radiation have been postulated. Physiotherapy, vitamins, and stimulants are recommended for the treatment of this type of radiation sickness.

Recently, US and other Western scientists have been quite concerned with the vast difference between the two standards. So far, there has been no serious attempt to reconcile or explain these dissimilarities. However, two interesting possibilities presented below may partially explain the lack of agreement:

a. Soviet researchers are using batch exposure techniques. They expose a number of animals in compartmented cages to the same radiation dose. Western experience with batch exposure has shown that such a practice tends to exaggerate or perturb the field. This exaggeration is due to reflected energy and the phenomenon of standing waves. What the exaggeration means in terms of comparison to the exposure of a single animal is that one is likely to be dealing with higher power levels than he realizes. This may, to some extent, explain the different findings at supposedly identical dosage levels.

b. Much of the difference between US and Soviet thermal and nonthermal positions may exist because of a definition problem. The Soviet definition of "thermal" means a measurable increase in body temperature measured rectally.

"Nonthermal" means that no increase in rectal temperature is measurable. Therefore, it appears that if a change or an effect is noted without an increase in rectal temperature it is a nonthermal effect explainable as an energy coupling. This definition does not take into account localized temperature increases which may not be reflected in rectal temperatures.

It has been reported that some European Communist countries have established two standards - one for military and one for the civilian sector. Although the civilian standards are lower, some researchers feel that they are not low enough. Reports also indicate that a number of female workers in industry may have aborted as a result of exposure to microwave radiation ostensibly within the safety standards.

The extent to which microwaves and other nonionizing radiation causes chromosome aberrations is somewhat of a controversial subject as is the question of the reversibility of any possible injury. It has been suggested that studies on the surface properties and perméability of cell membranes could supply some answers to these questions.

SECTION V

SAFETY PRECAUTIONS AND STANDARDS

(U) Safety precautions and standards have been established in both the US and USSR to protect not only persons who are occupationally exposed but also to protect the health of persons living or working near powerful generating or transmitting facilities. Significant differences in these standards exist and appear to be primarily due to different viewpoints on nonthermal effects in the two countries. Both nations' standards take into account the potentially lethal thermal effects resulting from high-intensity exposure, but the biological effects of nonthermal irradiation are not well defined or documented. In addition, some research has indicated the possibility of a cumulative effect on humans, but this is also very poorly defined.

Soviet research has produced guidelines which were used to establish a value of 10 $\mu W/cm^2$ per working day as the maximum admissible value for microwave irradiation. Higher exposures, at values of 0.01 to 0.1 mW/cm^2, are permissible for up to two hours per day or 1 mW/cm^2 for 15 to 20 minutes per day. Protective glasses are required in the latter case. The Czechoslovakian standards for frequencies above 300 MHz allow a maximum of 0.025 mW/cm^2 in the continuous wave mode for eight hour exposures. The standard for pulsed operation for the same exposure period is 0.01 mW/cm^2. In June 1973, Poland revised its exposure safety standards for nonionizing radiation in the frequency range of 0.3 to 300 GHz. The new standard permits unlimited exposure of humans to field intensities of 0.01 mW/cm^2. Eight hours per day exposure is permitted for intensities up to 0.2 mW/cm^2 for fixed fields and 1.0 mW/cm^2 for rotating fields. Exposures of up to 10 mW/cm^2 are permitted for limited periods of time without safety equipment. Exposures greater than 10 mW/cm^2 are prohibited without approved safety equipment. Prior to June 1973, the maximum radiation exposure level for all nonionizing radiation was 0.01 mW/cm^2 for up to eight hours per day, which is the same as the safety standard for the USSR. The 0.1 mW/cm^2 limit remains in effect for 0.1 MHz to 300 MHz, but revised standards for this frequency range are under consideration. The East German maximum permissible exposure to microwaves is 10 mW/cm^2, but neither the exact frequency range or duration for this exposure is specified. By comparison, the United States Standards Institute recommends 10 mW/cm^2 as averaged over any 1/10 hour period. The US Army and Air Force use the following equation to determine permissible exposure time (T_p).

$$T_p = \frac{6000}{W2}$$

where T_p = permissible exposure time in minutes during any one hour period and
W = the power density in the area in mW/cm^2.

Potential problem areas for exposure to excessive electromagnetic radiation which were found in the Communist literature included a wood processing plant, coastal radiotransmitting centers, radio equipment on ships, and flight communications equipment in the crew cabins of aircraft. Open feeder lines were identified as major sources of exposure.

(U) Protective devices described for use in working near unacceptable intensity fields include protective (metal-coated) eye glasses and clothing and shielding of the source with special absorbers or sheet metal or wire mask shields. A small semiconductor indicator instrument used to warn workers of dangerous conditions from electromagnetic fields has been developed. It rings an alarm when the field intensity exceeds the allowable level. An indicator paper for visual determination of the intensity of an electromagnetic field has also been developed. The indicator is prepared by impregnating a filter paper with a thermosensitive chemical compound.

(U) In an animal study, it was reported that oral administration of caffeine in doses of 20 mg per kg lowered the duration of resistance against hyperthermia caused by microwave irradiation. Caffeine did not influence the temperature at which the animals died, but it shortened the time to death. The reason for the lowered resistance of rats to microwaves was attributed to caffeine's exciting effect on the CNS which caused increased metabolic activity and consumption of oxygen. Although caffeine might exert similar effects on the human CNS, any lowering of resistance to hyperthermia would be insignificant; trained personnel working with properly operating, adequately serviced microwave equipment would probably almost never be exposed, even accidentally, to the tremendous radiation intensity required to induce heating of the human body. Nevertheless, monitoring of Soviet research on the action of drugs in combination with microwave radiation should continue, since such studies may eventually result in the detection of nonthermal safety hazards resulting from the mutually potentiating effects of radiation fields and pharmacological compounds.

Should subsequent research result in adoption of the Soviet standard by other countries, industries whose practices are based on less stringent safety regulations could be required to make costly modifications in order to protect workers. Recognition of the .01 mW/cm^2 standard could also limit the applications of new electronic technology by making the commercial exploitation of some products unattractive because of increased costs imposed by the need for additional safeguards.

SECTION VI

TRENDS, CONCLUSIONS, AND FORECAST

(U) A significant amount of research continues to be performed in the Eurasian Communist countries to establish the effects of radiowaves and microwaves on biological systems. It is often difficult to evaluate the reported results, however, because details of the exposure in terms of frequency, duration, and intensity are quite variable, and sometimes poorly reported. This, coupled with problems of measurement encountered in such studies, creates a rather confusing body of data from which to draw objective and absolute conclusions regarding the significance of the research. The Eurasian Communist investigators tend to place greater importance on the potential nonthermal effects than do their counterparts in the West, but information regarding the precise nature of the exposure under consideration is often difficult to establish. A move toward improved statistical analysis of data and standardization of dosimetry can be expected as Eastern Bloc researchers react to criticism of their work by Western scientists.

(U) The types of responses reportedly exhibited by the various biological organs, processes, or functions are in line with what has been reported by Western investigators. Again, most of the responses which are reported can be linked with the thermal action of the radiation. Studies which report on nonthermal effects deal largely with subjective responses, relying on reports of headache, sleepiness, loss of appetite, etc. The presence of nonthermal effects, in addition to thermal effects at higher intensities, has also been postulated by Eurasian Communist investigators, but no detailed investigative support for this possibility was noted. Accordingly, it is difficult to establish whether or not a trend toward this type of research will begin. It is safe to say that research on nonthermal effects at thermal intensities will be exceedingly difficult since another dimension to an already formidable problem will have been added.

No Eurasian Communist research activity has been identified which can be clearly or directly related to any military offensive weapons program. However, Soviet scientists are fully aware of the biological effects of low-level microwave radiation which might have offensive weapons application. Their internal sound perception research has great potential for development into a system for disorienting or disrupting the behavior patterns of military or diplomatic personnel; it could be used equally well as an interrogation tool. The Soviets have also studied the psychophysiological and metabolic changes and the alterations of brain function resulting from exposure to mixed frequencies of electromagnetic radiation. One physiological effect which has been demonstrated is heart seizure. This has been accomplished experimentally in frogs by synchronizing a pulsed ultrahigh

frequency microwave signal of low average-power density with the depolarization of the myocardium and beaming the signal at the thoracic area. A frequency probably could be found which would provide sufficient penetration of the chest wall of humans to accomplish the same effect. Another possibility is alteration of the permeability of the blood-brain barrier. This could allow neurotoxins in the blood to cross. As a result, an individual could develop severe neuropathological symptoms and either die or become seriously impaired neurologically.

The above study is recommended reading material for those consumers who have an interest in the application of microwave energy to weapons. A discussion of weapons is not within the scope of this study.

SECTION VII

INFORMATION GAPS

(U) Little information regarding the effects of relatively low frequency radiowaves was available. These frequencies produce few thermal effects, but although Eurasian Communist research frequently investigates nonthermal effects, few reports of studies at these low frequencies could be found.

(U) A limited amount of information regarding the effects of environmental conditions on susceptibility to damage from radiowave exposure was reviewed. In fact, the few articles available on these factors present conflicting results. In addition, a few reports on the effects of the very complex fields encountered in the near field situation (i.e., very close to the source) were found.

(U) The effects of relatively low level exposure to radiowaves (such as might be encountered by persons living in the vicinity of high powered radio stations) are not well documented. One report suggests a statistical evaluation of the health of persons living in such areas as compared to persons living in areas with a more normal electromagnetic level. This would be a very difficult study to undertake if statistically significant data were to be obtained.

(U) No official safety standards have been identified for Albania, Bulgaria, Hungary, Yugoslavia, and the Asian Communist countries.

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

(U) This study was undertaken to provide a review and evaluation of the current Eurasian Communist country state-of-the-art in the area of the effects of radiowaves and microwaves. It generally covers the 1968-1975 period. The major topics include discussions of the effects on humans and animals. The study provides information on the general trends of research with special attention to possible military applications. Where appropriate, information on safety standards and research personalities and facilities is provided.

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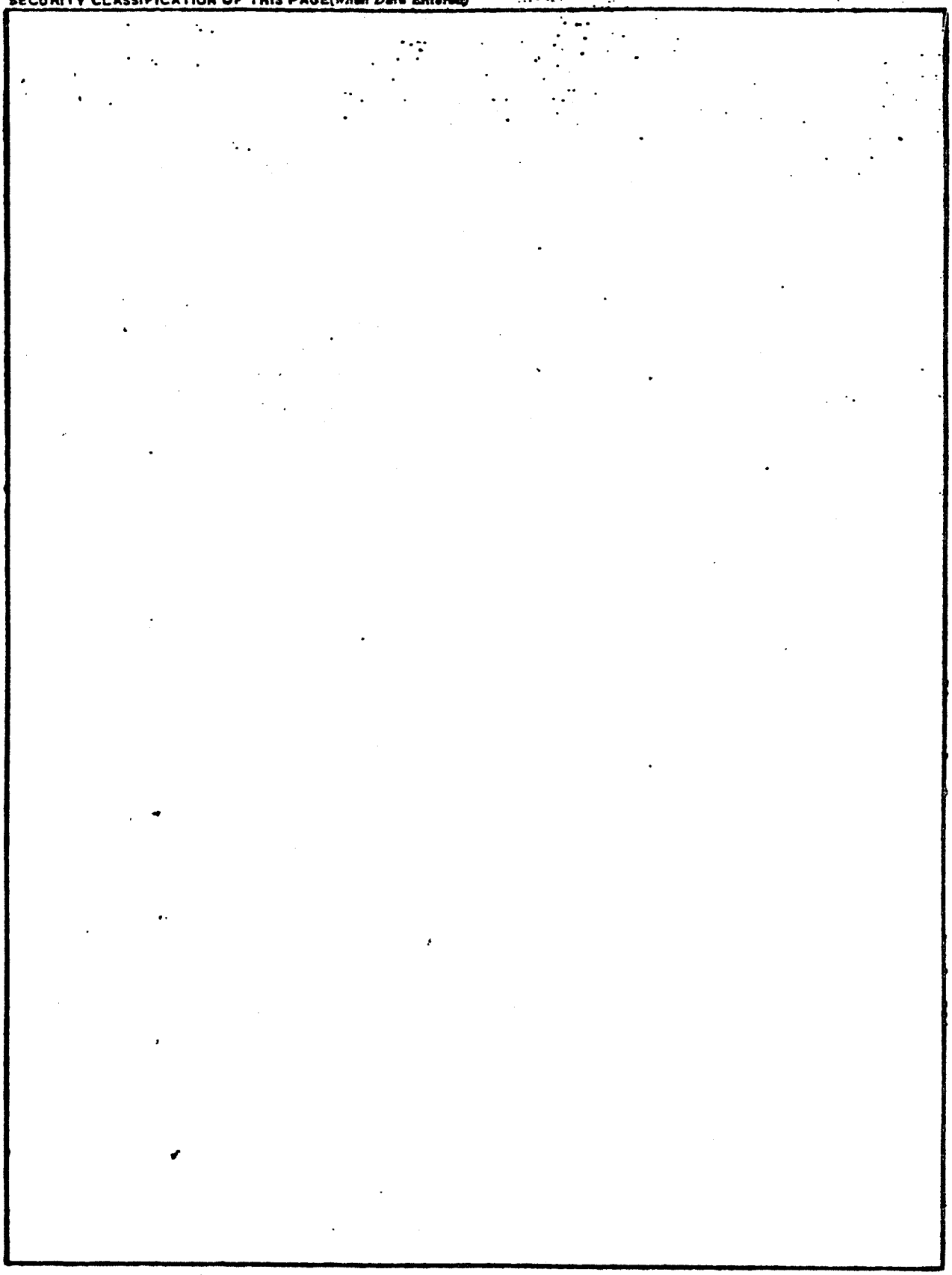

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The road to digital success in pharma

By David Champagne, Amy Hung, and Olivier Leclerc
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Pharmaceutical companies can play a central role in the digital revolution of healthcare. But capturing this opportunity requires identifying the right initiatives.

Pharmaceutical companies are running hard to keep pace with changes brought about by digital technology. Mobile communications, the cloud, advanced analytics, and the Internet of Things are among the innovations that are starting to transform the healthcare industry in the ways they have already transformed the media, retail, and banking industries. Pharma executives are well aware of the disruptive potential and are experimenting with a wide range of digital initiatives. Yet many find it hard to determine what initiatives to scale up and how, as they are still unclear what digital success will look like five years from now. This article aims to remedy that. We believe disruptive trends indicate where digital technology will drive the most value in the pharmaceutical industry, and they should guide companies as they build a strategy for digital success.

Trends reshaping healthcare

Outcomes-based care is moving to center stage

Payors and governments have an ever sharper focus on managing costs while delivering improved patient outcomes, putting an even greater onus on pharma companies to demonstrate the value of their drugs in the real world—not just in randomized controlled trials—if they are to retain market access and premium pricing. In this environment, digitally enabled "beyond the pill" solutions, which include not just drugs but also sensors to collect and analyze data to monitor a patient's condition between visits to healthcare providers, are becoming critical to serving both parties' needs. These solutions help drive the adherence to treatment and outcomes that payors and governments seek, and they generate the data that pharma companies need to demonstrate their drugs' superior efficacy.

Patients are becoming more engaged

In a digital age, patients are much less dependent on their doctors for advice, increasingly able and willing to take greater control of their own health. They feel empowered by the vast amount of health information available online and on apps, and by the array of health and fitness wearables such as FitBit and Apple Watch. In one survey, more than 85 percent of patients said they were confident in their ability to take responsibility for their health and knew how to access online resources to help them do so.[1] In addition, patients are becoming keener to evaluate different healthcare products and services given that they bear a growing proportion of the costs. In a digital world, the ability to engage with patients as they make such evaluations could be key to the success of a pharma company's commercial model.

New competitors are moving in

Information and insights into patients' histories and clinical pathways are no longer the preserve of the traditional healthcare establishment. Where once health providers' paper-based medical records were the main source of patient health data, and drug research and development data were kept within the walls of the pharma companies, today, technology companies such as Apple, IBM, and Qualcomm Technologies are moving into healthcare. They are able to engage with patients through apps, health and fitness devices, and online communities, for example. And they are able to collect petabytes of data from these and other sources, such as electronic medical records and insurance claims, capturing valuable insights. For example, the IBM Watson Health platform—recently at the center of a partnership with Apple and its HealthKit health-sensor data platform—is using advanced analytics and natural-language-processing capabilities to deliver clinical decision support. Pharma companies will need to decide soon how to position themselves to compete or collaborate with these new players, or build complementary capabilities.

More information is available about product performance

Historically, pharma companies have controlled both the generation and dissemination of information about their products. Digital technologies have weakened that control, opening an array of new, independent information channels. There are online communities for sharing and discussing patients' experiences, apps and sensors to monitor the impact of therapy on a patient's daily life, and advanced data aggregation and analysis to link disparate, complex data sets and generate new insights into drug safety and efficacy. In response, pharma companies will have to build the capabilities to anticipate or react rapidly to these new sources of evidence, and remain the main source of authority on the performance of their products.

Process efficiency and agility is improving dramatically

Advanced analytics, sensors, and the automation of complex decisions are capable of delivering a step change in the efficiency, speed, quality, and responsiveness of business processes in all industries. The pharmaceutical industry is no exception. To thrive in a digital world, pharma companies will need to deploy next-generation technologies to streamline their business processes. They need to achieve near real-time transparency of their clinical-trials portfolio in R&D, for example, and frictionless sales and operations planning in the supply chain, as well as meet new expectations in efficiency and agility from customers, employees, patients, and suppliers.

Four areas of digital opportunity

Against this backdrop, we believe there are four main areas where digital developments will drive value for pharma companies, building on what we see as the key components of digital success—an ability to deliver more personalized patient care, engage more fully with physicians and patients, use data to drive superior insight and decision making, and transform business processes to provide real-time responsiveness.

Companies do not have to become leaders in all four areas across the enterprise—some will deliver more value than others in relation to any given disease, depending on market dynamics and their portfolio. But to decide where to concentrate their efforts, they do need to develop a point of view on each area's potential to transform their commercial and innovation models. To help in these decisions, we sketch here a picture of how we believe successful pharma companies will operate in each area in the near future.

Personalized care: Sensors and digital services for tailored, 24/7 treatment

The ability to personalize interactions with stakeholders is a key value driver from digital technology in any industry. In pharma, this value will be realized in large part through the use of sensors and digital services to provide tailored care around the clock.

Within five to seven years, a significant proportion of the pharmaceutical portfolio will create value through more than just drugs. Many drugs will be part of a digital ecosystem that constantly monitors a patient's condition and provides feedback to the patient and other stakeholders. This ecosystem will help improve health outcomes by tailoring therapy to a patient's clinical and lifestyle needs and enable remote monitoring by health professionals of a patient's condition and adherence to treatment. There is already a plethora of wireless sensors on the market to measure a patient's biophysical signals. Combining these with other data about patients as they go about their daily lives—nutritional information collected by a smart refrigerator, for instance, or exercise information from smart gym weights—will allow real-time alerts to be issued to caregivers and physicians when there is a need for intervention.

For example, a care plan for a Parkinson's patient might include a medication regimen with "chip on a pill" technology to monitor drug taking along with a smartwatch that monitors the patient's condition, sends him or her reminders to adhere to the prescribed treatment, and sends the neurologist compliance and health-status reports. The neurologist can then coach patients on lifestyle changes or even customize therapy remotely. Such digitally enabled approaches to patient care are likely to improve outcomes to the extent that they could become a condition of reimbursement, particularly for expensive specialty drugs.

Several companies already offer integrated products and services. WellDoc, for example, has launched BlueStar, the first FDA-approved mobile app for managing type 2 diabetes, while AliveCor has built a smartphone-based electrocardiogram. Patients take their own readings, which can be reviewed by a remote expert without the cost and delay associated with seeing a specialist. Many more of these kinds of products have recently been approved or are in development.

Medication itself will of course still be important. But it will be more personalized, targeting the needs of each patient with greater precision than before. Advanced data analytics that mine electronic medical records, including diagnostic results, medication history, and genomic, proteomic, and gene-expression data will help identify optimal therapies and predict how individual patients will respond to treatment.

Fuller engagement: Omnichannel conversations with physicians and patients

Digital-engagement technologies open up a whole new world for marketing, the exchange of information, and recruitment for trials. Pharmaceutical sales reps, medical-science liaisons, and patient-service teams can inform and influence patients, physicians, and caregivers in person or via mobile phones, the Internet, apps, or social media. Patients are already starting to use patient portals for their medical records and to communicate with their physicians, and they use apps to fill scripts and online patient communities to speak to other patients with the same disease.

Anytime-anywhere virtual care will become increasingly commonplace. Specialist virtual-care apps already exist. NeoCare Solutions, developed by Aetna, gives new parents returning home with infants from the intensive care unit on-demand coaching from a neonatal nurse. The US Department of Defense is testing robots to engage and screen soldiers for posttraumatic stress disorder,[2] while in the United Kingdom, political parties are making promises to enable patients to use Skype to call their general practitioners by 2020.

All of these interactions offer pharma companies the opportunity to derive value. To realize it, they will have to build advanced digital marketing and engagement capabilities similar to those deployed by leading retailers, airlines, telecom companies, and consumer-goods companies.

Data-driven insight: Advanced analytics to increase pipeline and commercial value

Pharma companies sit on a wealth of data, usually locked away in different technical and organizational silos. Some are already linking and mining their data sets to improve their pipelines, products, and strategies. But there remains a huge opportunity to create further value from data and analytics using internal and external data sources to drive superior results. A few examples follow:

- *In R&D*, digital discovery and the testing of molecules with advanced modeling and simulation techniques will be commonplace. For instance, physiological simulation will accelerate product development, and 3-D tissue modeling will help assess potential toxicity using computer simulation. In late development, sensor-data streams from in vivo clinical trials captured by wearables will be factored into registration filings and value dossiers to give an early indication of real-world effectiveness.
- *Marketing and sales forces* will deploy advanced analytics to understand prescribing behavior and potential patient profiles, enabling more precise targeting of providers and increasing the number of prescriptions filed. For example, a “patient finder” technology that mines electronic medical records to identify sufferers from specific rare diseases will enable sales forces and medical science liaisons to focus on providers caring for patients likely to have those diseases, although they are as yet undiagnosed.
- *Pharma companies* and other healthcare players link and analyze data from insurance claims, clinics, laboratories, sensors, apps, social media, and more in order to generate real-world evidence about a drug's efficacy, guiding reimbursement and clinical practices. We envisage a world in which most care is "protocolized"—that is, in which clinical decisions on the best treatment options are suggested to physicians by an automated decision algorithm informed by advanced analytics. In this environment, winning pharmaceutical companies will be those able to influence the algorithm. Payors, meanwhile, will be able to develop new approaches to contracting and risk sharing for specialty drugs. Payment based on adherence or cure-rate data, or even "micropricing" based on the daily measurement of specific outcomes and quality of life, are some of the possibilities.

Real-time responsiveness: Automated processes to improve cost, reactions, and agility

Cloud and mobile technology, sensors, and next-generation business intelligence will bring about a new wave of automation in business processes—that is, streamlined, automated work flows with few handovers and end-to-end, real-time transparency on progress, costs, and business value. This will drive a step change in the efficiency, responsiveness, and agility of a wide range of complex, often cross-functional, processes, be they in the back office, the supply chain, R&D, or commercial. Banks have shown that the processing time and costs associated with opening an account or mortgage origination can be reduced by up to 99 percent and 70 percent respectively, with a clean-slate redesign of these cross-functional processes and state-of-the-art digital technology enablement.

In pharmaceuticals, employee on-boarding, sales and operations planning, launch monitoring, and marketing-content approval would especially benefit from streamlined, automated work flows and increased transparency. Clinical-trial management, from recruitment to submission, is another area that will see dramatic change with advanced automation. Targeted online recruitment and remote-monitoring technology (sensors, connected devices, and apps) will increasingly enable clinical trials to take place in "real world" settings so that patients can go about their lives with very minor changes in habits, while participating in a trial. Greatly reducing interventions in clinics or trial sites during the trial of a drug will reduce the burden on patients and make trial conditions more akin to a patient's life when he or she is prescribed the drug outside a trial setting. Increased connectivity and automation in

trial-management processes will also enable advanced trial design and monitoring approaches. For example, sites and sponsors can be connected in order to support the data management and analytics required for adaptive trial designs.

Capturing the value

Most pharma companies have started to build some digital capabilities, but talent and resources for their efforts can be fragmented, often across hundreds of small initiatives. Without clear strategic direction and strong senior sponsorship, digital initiatives often struggle to secure the funding and human resources required to reach a viable scale, and they cannot overcome barriers related to inflexible legacy IT systems. Talent and partnerships are also critical issues—many companies realize they need to form partnerships to acquire digital capabilities and specialist skills but are often unclear about what kinds of partnerships to set up and how to extract value from them.

We believe there are three strategic actions pharma companies should take to overcome these obstacles and start on a path that will capture value from digital.

- *Focus on two or three flagship initiatives.* It is important to place a few big bets that will each be sponsored by a senior executive, made highly visible to the organization throughout design and pilot phases, and lauded when early wins start coming in. These flagships will need to be properly resourced from the start and supported by partnership initiatives that complement a company's existing capabilities. The objective is to secure early success, which in turn generates the buy-in and momentum required to drive the next wave of initiatives. The choice of flagship initiatives needs to be based on a company's pipeline, product portfolio, and business strategy. Companies should therefore identify the distinctive sources of value that digital technologies and capabilities can create in the disease areas in which they operate, and then define the flagship initiatives to develop solutions for two or three specific use cases. For example, a flagship initiative could be building a digital ecosystem (a solution combining sensors, apps, and services) for patient adherence to an upcoming oncology blockbuster launch drug (the use case).
- *Run collaborative experiments, and then scale what works.* Companies cannot be expected to know in detail up front what a winning solution looks like for any particular set of assets in any particular market. For example, it is not possible for a company to design from A to Z a digital medical-affairs ecosystem on paper without experimenting with different channel platforms and content types to understand how key opinion leaders prefer to interact with the company. Hence, companies need to set up the right environment for collaborative experimentation within the initiative: for example, by putting the right people from IT, business compliance, and outside partners in a "war room" to run quick test-and-learn cycles. When results are positive—patient awareness of a disease and a particular drug increases, for instance—efforts can be scaled up. Technology prototypes can become enterprise solutions, and new ways of working become formalized and integrated into business processes.
- *Develop the organization for new business models.* Digital talent may be scarce to begin with, but a digital center of excellence can help bring together what capabilities there are, concentrating them into a critical mass and avoiding duplication of resources across commercial and R&D. It can also run the portfolio of digital partnerships, ring-fence funding for digital initiatives, and codify and export learnings from pilots across markets. In this new world, it will be vital that IT evolves to be able to manage faster experimentation cycles, while still managing the legacy estate for cost and reliability. This should lead to a two-speed IT function,[3] where “fast domains" operate with different skills, architecture principles, budgeting, and planning cycles to those that exist in "legacy domains" that remain focused on enterprise resource planning and traditional business applications.

We have outlined the four areas in which we believe digital will drive the most value for pharma companies. The areas leverage digital innovation to make products and services more personalized, physicians and patients more engaged, decisions and product evidence more data driven, and business processes more immediate. To capture this value, each company will need to consider how its businesses are set to be affected by the digital changes under way, and then chart its own course accordingly. A better understanding of what digital success looks like will help companies get to their destination: improved innovation and commercial models for pharma companies and better care for patients.

About the author(s)

David Champagne is an associate principal in the London office, **Amy Hung** is a specialist in the New Jersey office, and **Olivier Leclerc** is a director in the Southern California office.

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The road to digital success in pharma

By David Champagne, Amy Hung, and Olivier Leclerc
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Most pharma companies have started to build some digital capabilities, but talent and resources for their efforts can be fragmented, often across hundreds of small initiatives. Without clear strategic direction and strong senior sponsorship, digital initiatives often struggle to secure the funding and human resources required to reach a viable scale, and they cannot overcome barriers related to inflexible legacy IT systems. Talent and partnerships are also critical issues—many companies realize they need to form partnerships to acquire digital capabilities and specialist skills but are often unclear about what kinds of partnerships to set up and how to extract value from them.

We believe there are three strategic actions pharma companies should take to overcome these obstacles and start on a path that will capture value from digital.

- *Focus on two or three flagship initiatives.* It is important to place a few big bets that will each be sponsored by a senior executive, made highly visible to the organization throughout design and pilot phases, and lauded when early wins start coming in. These flagships will need to be properly resourced from the start and supported by partnership initiatives that complement a company's existing capabilities. The objective is to secure early success, which in turn generates the buy-in and momentum required to drive the next wave of initiatives. The choice of flagship initiatives needs to be based on a company's pipeline, product portfolio, and business strategy. Companies should therefore identify the distinctive sources of value that digital technologies and capabilities can create in the disease areas in which they operate, and then define the flagship initiatives to develop solutions for two or three specific use cases. For example, a flagship initiative could be building a digital ecosystem (a solution combining sensors, apps, and services) for patient adherence to an upcoming oncology blockbuster launch drug (the use case).
- *Run collaborative experiments, and then scale what works.* Companies cannot be expected to know in detail up front what a winning solution looks like for any particular set of assets in any particular market. For example, it is not possible for a company to design from A to Z a digital medical-affairs ecosystem on paper without experimenting with different channel platforms and content types to understand how key opinion leaders prefer to interact with the company. Hence, companies need to set up the right environment for collaborative experimentation within the initiative: for example, by putting the right people from IT, business compliance, and outside partners in a "war room" to run quick test-and-learn cycles. When results are positive—patient awareness of a disease and a particular drug increases, for instance—efforts can be scaled up. Technology prototypes can become enterprise solutions, and new ways of working become formalized and integrated into business processes.
- *Develop the organization for new business models.* Digital talent may be scarce to begin with, but a digital center of excellence can help bring together what capabilities there are, concentrating them into a critical mass and avoiding duplication of resources across commercial and R&D. It can also run the portfolio of digital partnerships, ring-fence funding for digital initiatives, and codify and export learnings from pilots across markets. In this new world, it will be vital that IT evolves to be able to manage faster experimentation cycles, while still managing the legacy estate for cost and reliability. This should lead to a two-speed IT function,[3] where “fast domains" operate with different skills, architecture principles, budgeting, and planning cycles to those that exist in "legacy domains" that remain focused on enterprise resource planning and traditional business applications.

We have outlined the four areas in which we believe digital will drive the most value for pharma companies. The areas leverage digital innovation to make products and services more personalized, physicians and patients more engaged, decisions and product evidence more data driven, and business processes more immediate. To capture this value, each company will need to consider how its businesses are set to be affected by the digital changes under way, and then chart its own course accordingly. A better understanding of what digital success looks like will help companies get to their destination: improved innovation and commercial models for pharma companies and better care for patients.

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Do You Have Microwave/EMR Sickness?

Your Cell Phone (i.e. Electromagnetic Weapon) May –Insidiously – Be Making Us Sick!

by Paul Raymond Doyon

All truth passes through three stages. First, it is ridiculed. Second, it is violently opposed. Third, it is accepted as being self-evident. - Arthur Schopenhauer

In the beginner's mind there are many possibilities. In the expert's mind there are few. - Shunryu Suzuki

The intuitive mind is a sacred gift and the rational mind is a faithful servant. We have created a society that honors the servant and has forgotten the gift. - Albert Einstein

A good student answers questions but does not question answers. - Ira Shor

Many people have a hard time fathoming that something that they cannot see, touch, smell, taste or hear - sense with the five senses - can harm them so much. But if people did really know the facts regarding the dangers of cell phones and WiFi (wireless networks) and the masts (cell phone towers) that emit an ever-increasing and pervasive level of microwave radiation, would they still be willing to use them? Would they still be willing to allow the antennas to be built in the vicinity of their homes, work places, schools, and hospitals? The fact of the matter is that there are about eighty immune system disorders that we didn't have twenty-five years ago before we really started microwaving the planet. Research is showing that this electrosmog may very likely be playing a role in a host of illnesses including autism, ADHD, CFS, Alzheimer's, allergies, heart disease, stroke, diabetes[1], insomnia, depression, infertility, leukemia, breast cancer, brain tumors, miscarriages, birth defects, and a plethora of other illnesses – not to mention electrosensitivity (ES)[2].

Footnotes

[1] Dr. Magda Havas's ground-breaking research has found a link between EMR and diabetes - and also among other illnesses like MS: "Havas has done studies showing that not only is the problem real, but otherwise serious medical conditions can be helped by using the Graham-Stetzer filter. In a study presented at the International Scientific Conference on Childhood Leukaemia in 2004, Havas found that the filters were associated with fewer and less severe headaches, more energy, lower blood sugar levels for diabetics, and improved balance for those with multiple sclerosis. 'I was stunned with the results we got,' Havas said. The lower the dirty electricity in a room the lower the symptoms expressed in patients. Some of the startling results included putting people with diabetes in a room with the filter, and blood sugar levels began to normalize instantly. The results with Multiple Sclerosis patients was even more remarkable. 'People who were in wheelchairs and using walkers, we put the filters in and we have videotapes of people who couldn't walk, walking,' Havas said. 'I actually think some percentage of the population that have MS are already responding to dirty electricity. Maybe it would work with Parkinson's, Alzheimer's, depression, asthma?' Further results of a study Havas reported to the World Health Organization on Electrical Hypersensitivity included a study of a private school in Toronto that had 50 filters installed. The study was single-blind (the teachers knew nothing about what the researchers were studying), and 50% of teachers showed some improvement in at least one of their symptoms. Other subjective results included teachers reporting that students were less disruptive in the classroom. Could dirty power be causing or exacerbating the rise in ADD/ADHD in kids? No one really knows because no one is studying the issue" (Henderson 2006).

[2] More and more people are becoming electrosensitive every day and yet many people who are electrosensitive may not be aware of their own electrosensitivity. People who are extremely electrosensitive will even feel ill when in a room with people who have their cell phones on standby mode and also when they are close to cell phone towers. The former Director-General of the WHO, Dr. Gro Harlem Brundtland – a medical doctor – became electrosensitive and was able to detect when someone

Dr. George Carlo[3], who ran a multi-million dollar research program for the cell phone industry and went public regarding the dangers posed by cell phones, uses the analogy of putting a frog in water. If you put a frog in boiling water, it will jump out. However, if you put a frog in cold water and gradually heat the water, you can cook the frog because the frog's body will adjust to the slight changes in temperature and it will not notice it is being cooked. Well, the same thing might be happening to an unsuspecting public - a public that has not been informed about the real dangers of microwave radiation from cell phones, WiFi and other high-frequency-radiation emitting devices and antennas.

The truth of the matter is that your cell phone and your WiFi might very well be making you and those close to you sick! Please read on!

I. Symptoms known to be caused by exposure to electromagnetic radiation - depending on frequency, duration, and exposure levels - in the early stages (and/or at lower exposure levels) can be decreased stamina, memory problems, fatigue, sleep disturbances, headaches, eye sensitivities, increased allergies and other sensitivities, dizziness, irritability, concentration problems, nausea, and restlessness. At the latter stages (and/or at higher exposure levels), unexplained anxiety, insomnia, swollen lymph nodes, depression, loss of appetite, hypoxia (lack of oxygen getting to the tissues), hyperactivity, dry eyes, vision problems, weakened immune system, frequent urination, night sweats, extreme thirst, weight gain or weight loss, testicular pain and so on (Becker[4] 1985, Levitt 1995, Cherry 1996, Kolodynski & Kolodynski 1996, Santini et al 2002, Al Khlaiwi & Meo 2004, Radio Wave Sickness, Selsam 2005, Bortkiewicz et al 2005, Sage 2006). These symptoms very often suddenly appear in people who have had a cell phone tower installed nearby their home.

II. Microwave exposure induces oxidative damage[5] leading to depletion of the body's natural production and store of a number of antioxidative enzymes[6] and antioxidants like super oxide

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in the same room was carrying a cell phone.

[3] Dr. Carlo, also a lawyer, is the director of the Washington-based non-profit *Safe Wireless Initiative* http://www.safewireless.org/ and has been fighting the cell-phone industry ever since he went public with the dangers of cell phones and was hence relieved of his position working for the cell phone industry.

[4] "In 1971, Zinaida V. Gordan and Maria N. Sadchikova of the USSR Institute of Labor Hygiene and Occupational Diseases described a comprehensive succession of symptoms, which they identified as Microwave Sickness. The initial symptoms are low blood pressure and slow pulse. The second stage includes headaches, dizziness, eye pain, sleeplessness, irritability, anxiety, stomach pain, nervous tension, inability to concentrate, hair loss, which are eventually followed by adrenal exhaustion and ischemic heart disease" (Becker, 1985, pp. 314-315).

[5] Actually, it was shown by a Dr. Dewhem Harmam in 1954 – hired by the US Government during the cold war to come up with a cure for radiation poisoning – that exposure to radiation would release a deluge of lethal hydroxyl radicals in the body due to the ionization of water in the body by the radiation (McLeod and White 2002). Gugkova, et al (2005) have shown that the reactive oxygen species hydrogen peroxide forms in aqueous solutions when exposed to "high peak-power pulsed electromagnetic radiation of extremely high frequencies." Alam & Ohgaki (2002) have shown that ferrous iron can bind with hydrogen peroxide to produce the hydroxyl free radical under exposure to ultraviolet radiation. We can only speculate that the same might happen with other forms of radiation exposures combined with the electromagnetic damage to erythrocytes with the possible release of iron into the extracellular blood.

[6] In studies conducted by Cremer-Bartel (1983) [cited in Levitt] weak ELF fields were shown to alter a particular enzyme

dismutase (SOD), catalase, glutathione, CoQ10, and melatonin (Wei 1999, Campanella et al 2003, Gautier & Santini 2003, Ilhan et al 2004, Ozquner et al 2005, Regoli et al 2005, Zwirska-Korczala et al 2005, Goldberg G. 2006, Jelenkovi et al 2006, Kalns et al 2006, Ozquner et al 2006,Yurekli et al 2006, Carlo[7] 2007). When the body becomes depleted in antioxidants, what are known as free radicals - aka reactive oxygen species (ROS) - will wreck havoc on the body's cellular systems (e.g. cell wall, mitochondria, DNA) causing oxidative damage which can thus lead to premature aging, a weakened immune system, and sticky blood, among other serious problems. With a depressed level of antioxidants in the blood, for example, not only low-density lipoproteins (LDL)[8] will bind with free radicals (oxidants) leading to the gooey stuff

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necessary for the synthesis of melatonin. Interestingly, a number of researchers (Ishikawa et al. 1982, Ikarashi et al 1984, 1985), for research purposes, have applied microwave radiation in order to inactivate brain enzymes to prevent postmortem changes - and which also result in changes in neurotransmitter levels. For example, it was shown by Ikarashi et al (1985) that "microwave irradiation at 10 kW rapidly inactivated brain enzymes" while exposure of a .5 second 5 kW burst of microwave radiation on rat brains (Ishikawa et al 1982) reduced noradrenaline, dopamine, and 5-hydroxytryptamine. (On the other hand, a 1.5 second exposure increased the monamine levels and was recommended for complete enzyme deactivation before brain dissection.) Moreover, it has been shown that exposure to microwave radiation can cause a diffusion of dopamine from some high-level dopamine areas of the brain to other areas which usually contain low levels (Kant et al 1979). In short what we are seeing here is an imbalance of dopamine in the brain induced by microwave radiation – and one can only speculate as to what the consequences will be of incessant exposure to microwave radiation due to the brain hormone imbalances it is producing in the general population. Moreover, since brain enzymes act as catalysts in promoting biochemical reactions, which include the production or metabolism of neurotransmitters - which affect behavior - we can only speculate what long-term consequences (e.g. increases in psychological illness, criminal behavior, etc.) the current - and unceasing - modern-day exposure to ambient microwave radiation is producing in the general population - especially on those who use cell phones on a regular basis.

[7] "We understand that these information-carrying radio waves trigger protein membrane responses at the cell membrane level leading to disruption of intercellular communication and build up of free radicals inside the cell. Understanding of this mechanism is very important because it now explains the wide diversity of symptoms that we are seeing in patients who are reporting electrohypersensitivity and also other conditions such as headaches and unexplained anxiety that henceforth from this point forward now we'll know will be associated with these information-carrying radio waves" (Carlo 2007).

“Dr. Carlo explained in detail his theory of how cell phones cause brain damage. It begins with the wave. The signals use carrier waves of around 1,900 megahertz (MHz), which are so high in frequency that they pass right through us, and our houses, unnoticed. But harmful information-carrying waves are packed into the carrier waves. These information waves, which carry signals that can be decoded by our computers and mobile phones, are low-frequency waves in the range of one hertz (Hz). That's slow. So slow that our cells can feel them as an aggravating, physical jolt at their surfaces. Within 30 seconds or so of bombardment, our cells temporarily shut down their surface transport and intercellular communication functions, to resist further damage from threatening invaders. Normally, small threats to cells cause them to send out chemical signals to neighbouring cells that tell them to protect themselves from invaders, and they signal for help from our immune system's T-cells. But bombardment from mobile phone waves causes whole areas of cells and tissues to shut down their surfaces, stopping the active transport of good and bad stuff in and out of the cell, without time to signal a warning to other cells. Further, the shut down of gap junction communication pathways compromises tissue and organ functions, including the immune system.

Free radicals build up inside the cells so they eventually die and spill toxins and fragmented DNA into the space between cells. There, micronuclei form as a result of membranes becoming organized around broken bits of DNA. These micronuclei wreak havoc, disrupting cell function and allowing cancers to form. That is how, as Dr. Carlo explains, both benign and malignant tumours are caused by wireless signals. He suggests a similar process occurs at the blood-brain barrier that protects our delicate neurons and their tiny sophisticated chemical signals from contaminants in our blood. Once cells in the barrier are shut down by mobile phone waves, all kinds of big, toxic molecules enter our neural spaces where they can cause many problems, among them "autism spectrum disorders," which include some types of anxiety attacks, hyperactivity, ADD, problems with focusing, mild and severe autism, hyper-irritability and others” (Brown 2006).

[8] Low-density lipoproteins (LDL) are responsible for carrying cholesterol from the liver to the body's cells where they are used in the construction of the cellular walls. High-density lipoproteins (HDL) are responsible for carrying cholesterol away from the body's organs and to the liver where it is processed and excreted as bile. Low-density lipoproteins have been dubbed the bad cholesterol because they are more easily oxidized than the HDLs. When a LDL is oxidized it will be engulfed by

that forms plaque on arterial walls, but evidence is showing that this can also happen with the high density lipoproteins (HDL) as well (Hurtado, et al 1996). This leads to arteriosclerosis and more viscous blood, which in turn can cause blood clots leading to strokes and heart attacks.

III. Microwaves, depending on their frequencies, have been known to effect an abnormal flux of calcium into or out of cells[9] (Nair 1989, Cleary 1999, Dorothy 1999[10], Amara 2004). When there is an abnormal influx of calcium into mast cells, for example, they release their store of histamine (Chakravarty 1986, 1987). This is just one of the ways in which microwave exposure has been known to trigger or aggravate allergic reactions.[11]

IV. Microwave exposure has been known to induce mitochondria dysfunction (Dutto et al 1984, Xie et al 2004, Goldberg G 2006, Buchachenk et al 2006). The mitochondria are the powerhouse of the cell. Dysfunctional mitochondria are unable to produce sufficient cellular energy, resulting in fatigue - and very possibly even causing obesity.[12]

V. Microwaves have been shown to depolarize the body's red blood cells (Tomson). This will cause the red blood cells to clump together substantially diminishing the amount of oxygen transported to and carbon dioxide transported away from the brain cells and the body's other organs' cells leading to hypoxia and acidosis. This can cause symptoms similar to altitude sickness: nausea, dizziness, inability to concentrate, headaches and so on. Microwaves have also been shown to induce protein-shedding from the cellular membranes of red blood cells (Liburdy et al 1984, 1987, 1988). This would naturally weaken the red blood cell leaving it more susceptible to attack by free radicals and hence to oxidative damage.

VI. Microwave exposure has been shown in studies to induce a decrease in the numbers of Natural Killer (NK) cells (Smialowicz et al 1983, Yang et al 1983, Nakamura et al 1997, 1998,

macrophages, which in turn becomes what are called foam cells. Foam cells have a penchant for sticking to arterial walls and causing arteriosclerosis.

[9] "Moreover, Nair and Cleary have reported, that the flux of positively charged sodium, calcium and potassium ions across cell membrane can also be affected by radio-frequency exposure, over a wide range of frequencies (27 MHz to 10 GHz)" (Amara, et al, 2004)

[10] "Dr. Blackman has conducted far more experiments in his laboratory on this influx/efflux than anyone else. They have shown that calcium ion alteration occurs at particular carrier frequencies, particular signal strengths, particular modulation frequencies and in particular temperature ranges, but not in others which lie between them. After summarising these hundreds of experiments Carl Blackman stated that EMR must be treated as chemicals (plural) because we have made the mistake of treating it as a single chemical looking for single effects across the whole spectrum, when it is clear that the effects are very significant and occur at particular combinations of variables, but do not occur at a nearby different combination" (Dorothy 1999).

[11] "Attempting to explain a 25% increase in asthma and a 5% increase in asthma-related death rates throughout rapidly mobilizing metropolitan Sydney, Franch found that the production of histamine, which triggers bronchial spasms, is nearly doubled after exposure to mobile phone transmissions. Cell phones also reduce the effectiveness of anti-asthmatic drugs, and retard recovery from illness" (Thomas 2005).

[12] Researchers (Takahashi, et al 1994) in Japan have been able to induce obesity in rats by producing microwave-induced lesions to an area of hypothalamus (called the ventromedial hypothalamic nucleus or VMH). They noted a drop in the hypothalamic contents of norepinephrine and dopamine and a decrease in adrenal epinephrine concluding that a drop in these hormones may be related to the VHM-induced obesity.

Dmoch & Moszczynski 1998), which is a form of white blood cell (lymphocyte) and is the body's first line of defense against pathogens. This leads to the body's weakened ability to recover from viral and other types of infections. Therefore, people exposed to microwave radiation would take longer than normal to recover from your day-to-day infections.

VII. Exposure to long-term microwave radiation has been shown to change a particular form of white blood cell (lymphocyte) ratio - known as the T-helper/T-suppressor (T4/T8) cell ratio - from normal to abnormal (Dmoch & Moszczynski 1998). Abnormalities in this T-lymphocyte ratio have been shown to lead to an increased susceptibility to viral, fungal, and bacterial infections. Symptoms include "sore throats, low-grade fevers, weakness, persistent fatigue, and swollen lymph glands" (Braverman).

VIII. In fact, research has shown that exposure to microwaves and other electromagnetic radiation not only weakens the immune system,[13] but also effects an increase in viruses, bacteria, mold, parasites, and yeast in the blood of the human host.[14]

IX. Microwave exposure has been shown in studies to induce what is known as "subliminal" stress (Becker[15] 1985, Levitt[16] 1995), (since the body does not know it is being stressed)

[13] "[Dr. Coghill's] latest research suggests the microwaves generated by mobile phones may damage the ability of white blood cells to act as the 'policemen' of the body, fighting off infection and disease. Mr. Coghill took white blood cells, known as lymphocytes, from a donor, keeping them alive with nutrients and exposed them to different electric fields. He found that after seven-and-a-half hours, just 13% of the cells exposed to mobile phone radiation remained intact and able to function, compared with 70% of cells exposed only to the natural electromagnetic field produced by the human body" (BBC News Online Network). http://news.bbc.co.uk/1/hi/health/194065.stm

[14] Dr. Robert Young states in an interview on a British news program that "when we are exposed to lower frequencies ranging between 10 hertz and 100 hertz, those particular frequencies have a tendency to disturb cells significantly that they start disorganizing, breaking apart, and giving birth to perceived viruses, bacteria, yeasts, and molds" (Qlink World).

[15] "Initially, the stress activates the hormonal and/or immune systems to a higher than normal level, enabling the animal to escape danger and combat disease. If the stress continues, hormone levels and immune reactivity gradually decline to normal. If you stop your experiment at this point, you're apparently justified in saying, 'The animal has adapted; the stress is doing no harm.' Nevertheless, if the stressful conditions persist, hormone and immune levels decline further, well below normal. In medical terms, stress decompensation has set in, and now the animal is now more susceptible to other stressors, including malignant growth and infectious diseases. In the mid-70s, two Russian groups found stress hormones released in rats exposed to microwaves, even if they were irradiated only briefly by minute amounts of energy. Other Eastern European work found the same reaction to 50-hertz electric fields. Several Russian and Polish groups have since established that after prolonged exposure the activation of the stress system changes to a depression of it in the familiar pattern, indicating exhaustion of the adrenal cortex...Soviet biophysicist N. A. Udintsev has systematically studied the effects of one ELF magnetic field (200 Gauss at 50 hertz) on the endocrine system. In addition to the slow stress response we've been discussing, he found activation of the 'fast' fight-or-flight hormones centering on adrenaline from the adrenal medulla. This response was triggered in rats by just one day in Udintsev's field, and hormone levels didn't return to normal for one or two weeks. Udintsev also documented an insulin insufficiency and rise in blood sugar from the same field. One aspect of the syndrome was very puzzling. When undergoing these hormonal changes, an animal would normally be aware that its body was under attack, yet, as far as we could tell, the rabbits were not. They showed no outward signs of fear, agitation, or illness. Most humans certainly wouldn't be able to detect a 100-gauss magnetic field, at least not consciously. Only several years after Friedman's work did anyone find out how this is happening. In 1976 a group under J. J. Noval at the Naval Aerospace Medical Research Laboratory at Pensacola, Florida, found the slow response in rats from very weak electric fields, as low as five thousandths of a volt per centimeter. They discovered that when such fields vibrated in the ELF range, they increased levels of the neurotransmitter acetylcholine in the brainstem, apparently in a way that activated a distress signal subliminally, without the animal's becoming aware of it. The scariest part was that the fields Noval used were well within the background levels of a typical office, with its overhead lighting, typewriters, computers, and other equipment. Workers in such an environment are exposed to electric fields between a hundredth and a tenth of a volt per centimeter and magnetic fields between a hundredth and a tenth of a gauss" (Becker, pp.

causing the adrenal glands to excrete an abnormally greater amount of cortisol and adrenaline. Excretion of adrenaline, for one, can lead to irritability and a feeling of hyperactivity - the latter now very common in children with Attention Deficit Hyperactivity Disorder (ADHD). In a continuous state, excessive cortisol release will lead to adrenal exhaustion, where the adrenal glands just stop functioning - a common abnormality found in Chronic Fatigue Syndrome (CFS).

X. Microwave exposure has been shown to alter levels of 5-HT (5-hyroxytriyptamine) in the blood (Wang 1989) of workers exposed. 5-HT is a precursor to the production of the brain hormone serotonin. Low levels of serotonin have been linked to anxiety and depression (Gorman et al 2002, Goldberg G 2006). An increase in anxiety and depression can in turn be very well linked to growing numbers of suicides.

XI. Microwave exposure has been shown to induce a decrease in levels of the brain hormone norepinephrine (Takahashi et al 1994). This hormone is essential for control of the autonomic nervous system, and lack of it can lead to autonomic nervous system disorders. For example, if the autonomic nervous system is not working properly, the body will have trouble regulating its temperature - i.e. cooling itself when it is warm and heating itself when it is cold (Gandhi & Ross 1987). This could lead to cold or heat intolerance, i.e. feeling colder than one would normally when it is cold and feeling warmer than one would normally when it is warm (Way et al 1981). In fact, people with Chronic Fatigue Syndrome (PWC) have been found to have a disturbed circadian Core Body Temperature (Tomoda et al 1997). An abnormal decrease in norepinephrine levels has also been connected to short-term memory disturbances (Clinton et al 2006), ADHD (Arnsten & Li 2005) and depression (Charney 1988, Meyer et al 2006).

XII. Production of the brain hormone melatonin has also been shown to be altered by exposure to microwaves (Yellon 1994, Altpeter et al 2006). This brain hormone and antioxidant is necessary for proper sleep. 42 million (approximately one in five) Americans in 2006 took sleep medication for insomnia, up 60% from 2000 (Saul 2006), while others often experience sleep disturbances due to exposure to electromagnetic radiation (EMR) (Hubert et al 2002). A drop in melatonin levels has also been connected with increases in breast cancer (Blask et al 2005).

XIII. Changes in the levels of the brain hormone, dopamine (or dopamine transporters), has also been shown to be connected with microwave radiation and other EMF exposure (Mausset-Bonnefont et al 2004, Sieron et al 2004). A drop in dopamine levels has also been linked with depression (Brown & Gershon 1993) and restless leg syndrome (RLS) (Allen 2004).

277-278, 1985).

[16] "...Test animals appear not to know they are stressed, yet blood tests show high levels of cortisone, a substance released in the body under conditions of long-term disease, as opposed to adrenaline, which is released in a fight-or-flight response. Monkeys exposed to a 200 gauss magnetic field for four hours a day showed a generalized stress response for six days, which then declined, suggesting that animals had adapted to the exposure. Researchers who stop the experiment at that point can reasonably conclude that there has been no long-term damage. However, in subsequent experiments, it has been found that when the exposure continues, hormone and immune levels will fall far below normal and remain there. The immune system becomes exhausted and unable to rebound, opening the body to infectious diseases and an inability to fight malignancies" (Levitt, 1995, pp. 128-129).

XIV. Exposure to electromagnetic radiation has been shown to effect an abnormal drop in the levels of the neurotransmitter acetylcholine (Modak et al 1981, Dutta et al 1992, Omura & Losco 1993, Testylier et al 2002, Gautier et al 2003). A drop in the levels of this neurotransmitter has been linked to a number of neurological and neuromuscular disorders - including Alzheimer's disease.

XV. Some electromagnetic frequencies have been shown to induce restlessness (Cherry 1996, Rajendra et al 2004, Shtemberg et al 2004, Selsam[17] 2005). This suggests a possible connection between EMR and restless leg syndrome (RLS) since dopamine has been shown to be affected by EMR and dopamine agonists are used to treat RLS (Weimerskirch & Ernst 2001, Aramideh & de Weerd 2006).

XVI. Electromagnetic fields - like those emitted by cell phones - have been shown to alter regional cerebral blood flow (Huber et al 2002, Huber et al 2005, Haarala et al 2003, Goldberg G 2006, Aalto et al 2006). In conditions like autism and chronic fatigue syndrome (CFS) it has been shown via SPECT (Single Proton Emission Computed Tomography) scans that there is an altered flow of blood in the brain (Tomoda et al 2000, Goldberg MJ[18] 2000, Miike[19] et al 2004).

XVII. Numerous studies are now connecting microwave and other electromagnetic radiation exposure to an increase in allergies (Kimata 2002 [see also Ingels], Kimata 2003, Kimata 2005). Microwave exposure has been shown to turn on mast cells to produce more histamine[20] - the chemical responsible for allergic reactions - and other electromagnetic fields have been shown to actually increase the number of mast cells in the body[21] (Johansson & Liu 1995, Johansson et

[17] "These reports show that the people for years have been ill due to pulsed high frequency electromagnetic fields, without the treating doctors recognising the cause. For that reason, people who are receiving the high frequency at home or at work have suffered and are suffering and they receive no therapy. The deciding [effective] therapy is to end the exposure. The continually repeated assertion in the media by the Radiological Protection Commission (Strahlenschutzkommission), that there is no proof for health risks under the present valid limits, has had the consequence that most doctors, (including myself until a year ago) have not drawn a relationship between the many unexplained illness patterns and high frequency radiation. The doctors do not know that at not one single mobile phone base station have investigations into the health-state of the people been carried out. Thus, the evaluation of the Strahlenschutzkommission in 2001 has no scientific basis" (Selsam 2005).

[18] Dr. Michael Goldberg was able to find commonalities in the bloodwork - and the blood flow in the brain (via SPECT) - of people with CFS, autism, and ADHD. He states “While there is ongoing controversy regarding past brain biopsy findings and their implications, if any, to this generation of children, we do have NeuroSPECT Scans, which show reproducible, quantifiable blood flow in the brain. Blood flow corresponds directly to function. When NeuroSPECT Scans of children diagnosed as autistic/PDD have been correlated with MRI's and CAT Scans, the combination consistently shows no pre-existing damage to the brain, but rather points toward an immune shutdown consistent with that found in adults with Chronic Fatigue Syndromes and other adult dementias and with children diagnosed as quiet ADD and mixed ADD” (Goldberg MJ 2000).

[19] Dr. Miike and his colleagues determined that the phenomena of school phobia in Japan had actually physiological causes and is actually what they term Childhood Chronic Fatigue Syndrome (CCFS). There were approximately 10,000 school phobia cases in Japan in 1990. This number increased to approximately 140,000 in 2004 – an increase of 1400 percent in just fourteen years.

[20] “A doctor, John Holt, in Australia has written to us saying that when working with microwaves (to irradiate cancer cells) he has observed that the microwaves from cell phones cause a doubling of histamine (which are released from mast cells) and that such electrosmog from mobile phones could be the cause of the ever-increasing asthma and other allergies" (FEB 2001).

[21] "Professor Johansson: 'We are right now in the process of examining a larger number of facial skin samples, and from them the most common finding is a profound increase of mast cells….Furthermore, increases of similar nature have now been

al 1996, Johansson et al 2001). Microwaves have also been found to increase immunoglobulin antibodies in the body (Bergier et al 1990, Dmoch & Moszczynski 1998, Moszczynski et al 1999, Yuan et al 2004, Kimata 2005). Immunoglobulin antibodies are responsible for triggering an allergic reaction to a particular substance or protein. Could it be that the EMR confuses the body into making antibodies to the wrong things? Many researchers and scientists were - and still are - puzzled by the fact that the East German population had so few allergies in comparison to the West German population when the two countries unified (Hermann-Kunz 1999a & 1999b, Heinrich et al 2002, Kramer et al 2002). But what they failed to examine is the simple fact that East Germany had much stricter regulations regarding ambient radiation levels than West Germany. Since East Germany adopted West Germany's standards, allergies in former East Germany have since reached par with the levels of former West Germany.

XVIII. Microwave exposure has also been shown to adversely affect the heart (Becker, 1985, pp. 314-315; Ozquner et al 2005) and could very well be linked to heart irregularities and responsible for triggering heart attacks in a number of cases.

XIX. Exposure to microwave radiation has also been shown to effect an abnormal increase in nitric oxide (NO) (Jelenkovic et al 2006). An abnormal increase in cellular calcium can also lead to an abnormal increase in cellular NO (Kitamura et al 1997, Li et al 2003), which in excess combines with the superoxide (O2-) to produce a damage-producing free radical or oxidant called peroxynitrite (Henmani & Parihar 1998). Peroxynitrite has been linked with chronic fatigue syndrome (Pall).

XX. Microwave exposure has been shown in numerous studies to open the blood brain barrier (BBB) (Albert & Kerns 1981, Williams et al 1984, Quock et al 1986, Quock et al 1987, Neubauer et al 1990, Schirmacher et al 2000). The BBB protects the brain from foreign substances like viruses, bacteria, and chemical toxins in the blood, which would otherwise injure the brain. Thus, exposure to microwave radiation could very well open people up to viral and bacterial infections of the brain that would not normally occur otherwise.

XXI. There has been a dramatic increase in brain tumors (Bleyer 1999) and other cancers in the past twenty years - especially with the advent of the cell phone. After 1984 (the year the first cellular phone networks were set up in most major cities in the USA) there was a notable jump in children's brain tumors (see video[22]), though according to the National Cancer Institute (NCI) this is due to better diagnostics (1998). Brain tumors are now the number one cause of death in children surpassing leukemia in 2002. Just last year seven people in Melbourne at RMIT University working in a building on the top two floors underneath a cell phone mast suddenly were diagnosed with brain tumors (Macnamara 2006). They had been working under the mast for ten years.

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demonstrated in an experimental situation employing normal healthy volunteers in front of visual display units, including ordinary house-hold television sets' " (FEB 2001).

[22] <http://www.youtube.com/watch?v=PVhggyXD5co&mode=related&search =>

XXII. There has been an exponential increase in autism[23], ADHD, Chronic Fatigue Syndrome[24], and Alzheimer's[25] since 1984, the year the first commercial cell phone networks started to spread across the USA. These rates increased even further with the switchover from analog (1G) to digital (2G) in the early 90s (Marshall[26] 2001, Weatherall 2007).

XXIII. There have been numerous confirmed cases of deformities in animals (Animal Study) and plants (Kato 2004) near cell phone towers – and the worldwide disappearance of frogs (Balmori[27] 2006), birds (Mukherjee[28] 2003) and insects (most recently bees[29] - see Barrionuevo

[23] Though often only attributed to mercury in vaccines, "In the 1990s, reported autism cases among American children began spiking, from about 1 in 10,000 in 1987 to a shocking 1 in 166 today" (Studies in the News 2006).

[24] "I stumbled into the field of autism somewhat by accident. My wife had had Chronic Fatigue Syndrome for over ten years. Jokingly, my son asked me "Why are you sending Mom all over the country to doctors? Why don't you just fix her? That began my journey into clinical research. It rapidly became apparent we were dealing with some component of the immune system, an autoimmune like reaction. During that time, as I was investigating all options for my wife, a few Autistic children were referred to my practice. Much to my surprise, these children had blood work comparable to that of my wife and other adults with this undiagnosed disorder, and to that of children I had been seeing diagnosed with quiet ADD and mixed ADHD I remember thinking then, 'What could the immune system have to do with autism?' Paralleling this, beginning in the 1980's was the initially slow, now epidemic incidence of disorders in children labeled as Autism/PDD and the increase of reports of autoimmune diseases in the animal literature, of altered ecological balance, immune system abnormalities in various species. We either have to assume that this increase of disorders in the human population is mass-hysteria, mass-psychosis, schizophrenia, and/or behavioral developmental disorders in children or we must step back and realize that maybe we have a large number of adults and children suffering from a disease process that is affecting how their brain and nervous system functions, in ways that physicians had never understood (or had the technology to understand). I have family after family within my new practice in which there is a mother or father with Chronic Fatigue Syndrome, an older child with ADD/ADHD, and a younger child or two with Autism/PDD. As noted, unless we assume this is all random, there is unfortunately a logical connection between the above disorders and their rapid emergence as a crisis" (Goldberg MJ 2000).

"By 1986, she was seeing more than 300 patients with the now-familiar symptoms, and cluster outbreaks had been reported in cities and towns across the country, including a well-publicized one at Lake Tahoe. She consulted with UCSF virologist Jay Levy, who was then working to discover the HIV virus. She and Levy wondered whether they were seeing a new virus or something related to AIDS in a milder form. Somehow, they felt, the immune system in these patients had been disrupted. When we get sick with a flu, the fever, achiness and fatigue are not caused by the virus itself but by the immune response, the chemicals released to fight infection. Perhaps Jessop's patients had an immune system stuck in the "on" position, creating persistent flu-like symptoms. But what virus was causing the disruption? After investigating a number of potential culprits - human herpesvirus 6 (HHV-6) and Epstein-Barr virus (EBV), among others - Jessop and Levy, like other investigators, came up empty. In 1988, the Centers for Disease Control and Prevention (CDC) named the puzzling illness chronic fatigue syndrome (CFS), as if this illness were about nothing more than being a little extra tired. The moment the name was set in print, patients lambasted it for trivializing a devastating illness and inviting psychiatric stigma. By 1991, Jessop was seeing 1,500 patients with CFS, marking the Bay Area as one of the largest clusters of the nationwide epidemic" (Wall 2005).

[25] "Just ten years ago, Alzheimer's was considered an obscure and rare condition, but today it is the nation's fourth leading cause of death. What happened?" (Levitt, 1995, p. 200).

[26] "The incidence of ME/ICD-CFS is known to be rising: in April 1994, the insurance company UNUM (one of the largest disability insurers) reported that in the five years from 1989-1993, mens' disability claims for CFS increased 360%, whilst womens' claims for CFS increased 557%. No other disease category surpassed these rates of increase. In order of insurance costs, ME/ICD-CFS came second in the list of the five most expensive chronic conditions, being three places above AIDS. At the Fifth American Association of Chronic Fatigue Syndrome International Research and Clinical Conference held in January 2001 in Seattle, the Associate Director of the University of Washington's CFS Research Centre (Dr N Afari) confirmed that the incidence is indeed rising" (Marshall et al 2001).

[27] "A bibliographical review on the possible effects of radiofrequency radiation (RFR) from wireless telecommunications on living organisms and its impact on amphibians is presented. The technical characteristics of this new technology and the scientific discoveries that are of interest in the study of their effects on wild fauna and amphibians are described. Electromagnetic pollution (in the microwave and in the radiofrequency range) is a possible cause for deformations and decline

2007) is being connected with these levels of ambient background radiation (Sandu 2007)[30]. Also, sardines (or pichard) in Australia (Gov. of Australia[31]), carp in Japan (CBS News[32] 2003), and lobster in Florida (Schneider[33] 2003) have been found to be infected with forms of the herpes virus. One study has even shown that electromagnetic fields can actually stimulate the genome of the Epstein-Barr Virus (Grimaldi et al 1997), the herpes virus responsible for *mononucleosis* in the US or aka *glandular fever* in the UK, Australia, and New Zealand. A number of herpes-family viruses (e.g. CMV, EBV, HH6V) are usually found to infect people with CFS, autism, ADHD, and Alzheimer's.

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of some amphibian populations. Keeping in mind that amphibians are reliable bio-indicators, it is of great importance to carry out studies on the effects of this new type of contamination. Finally, some methodologies that could be useful to determine the adverse health effects are proposed" (Balmori 2006).

[28] **"**THE wireless telecom revolution is catching on at the expense of a tiny winged creature - the house sparrow. The tiny birds are fast disappearing from cities 'contaminated' with electromagnetic waves arising out of increased number of mobile handsets. According to Dr S. Vijayan, Director of the Salim Ali Centre for Ornithology and Natural History (SACON), 'A number of studies has been conducted to find out the relationship between the increase in electromagnetic waves and the decrease in the number of sparrows. A positive correlation has been found between them.' 'There have been studies in Spain which showed that sparrows disappear from cities where electromagnetic contamination is very heavy,' Dr Vijayan added" (Mukerjee 2003).

[29] **"**In 24 states throughout the country, beekeepers have gone through similar shocks as their bees have been disappearing inexplicably at an alarming rate, threatening not only their livelihoods but also the production of numerous crops, including California almonds, one of the nation's most profitable. 'I have never seen anything like it,' Mr. Bradshaw, 50, said from an almond orchard here beginning to bloom. 'Box after box after box are just empty. There's nobody home.' The sudden mysterious losses are highlighting the critical link that honeybees play in the long chain that gets fruit and vegetables to supermarkets and dinner tables across the country. Beekeepers have fought regional bee crises before, but this is the first national affliction. Now, in a mystery worthy of Agatha Christie, bees are flying off in search of pollen and nectar and simply never returning to their colonies. And nobody knows why. Researchers say the bees are presumably dying in the fields, perhaps becoming exhausted or simply disoriented and eventually falling victim to the cold. As researchers scramble to find answers to the syndrome they have decided to call "colony collapse disorder," growers are becoming openly nervous about the capability of the commercial bee industry to meet the growing demand for bees to pollinate dozens of crops, from almonds to avocados to kiwis. Along with recent stresses on the bees themselves, as well as on an industry increasingly under consolidation, some fear this disorder may force a breaking point for even large beekeepers. A Cornell University study has estimated that honeybees annually pollinate more than $14 billion worth of seeds and crops in the United States, mostly fruits, vegetables and nuts. "Every third bite we consume in our diet is dependent on a honeybee to pollinate that food," said Zac Browning, vice president of the American Beekeeping Federation. The bee losses are ranging from 30 to 60 percent on the West Coast, with some beekeepers on the East Coast and in Texas reporting losses of more than 70 percent; beekeepers consider a loss of up to 20 percent in the off-season to be normal" (Barrionuevo 2007).

[30] **"**A study conducted by three departments of Panjab University has found that cell phone towers are the dominating source of electromagnetic radiations in environment in the city and this could lead to diseases in plants and animals" (Sandu 2007).

[31] "In 1995, a massive 'kill' of adult pilchards occurred over their entire distribution in Australia, from Carnarvon (WA) to Noosa Heads (Qld). After examining several possible causes, including sudden temperature changes caused by upwelling of deep water, a herpes virus has been found to be the cause of the deaths. The cause of the virus has not been determined conclusively" (Gov. of Western Australia).

[32] "A herpes virus that has decimated Japan's carp farms is spreading, officials said Thursday, as they battled to contain the country's first known outbreak of the fish disease. Since October, farm-bred carp in Lake Kasumigaura and Lake Kitaura in eastern Japan have died en masse, threatening the lakes' annual catch. On Sunday, fisheries officials in Ibaraki prefecture (state), where the lakes are located, had estimated the amount of dead fish at 860 metric tons (946 short tons), equivalent to 150 million yen (US$1.4 million) of losses for fishermen" (CBS News 2003).

[33] "A herpes-like virus has infected up to 10 percent of baby lobsters in the Florida Keys, leading some fisheries experts to wonder whether the disease explains recent dips in lobster catches. Biologists doubt the disease can be transferred to humans, but have alerted the national Centers for Disease Control and Prevention just in case" (Schneider 2003).

Now, in heavily electropolluted Japan it has been reported that it is very common for women to have miscarriages in their last trimester of pregnancy. Usually, the fetus is deformed.[34] One Japanese study (Nagaishi et al 2004) has shown chromosome abnormalities in the fetuses of miscarriages; and another has shown an increasing male/female ratio in fetal deaths since the 1970s (Mizuno 2000). Cell-phone use has also recently been shown to lower sperm count in men the longer they use the phone (Hope 2006).

The cell phone industry makes hundreds of billions of dollars in profits every year. They have the money and the power to influence politicians, the media, and even the research. Unethical researchers receive mass funding from this industry and are pressured to tell you it is safe while the researchers who inform us of its true dangers have consistently had their funding cut.[35]

At present there are approximately 40,000 signatories to *The Freiburger Appeal*[36] drafted after a number of German doctors recognized a connection between many of the symptoms listed above and exposure to microwave radiation and other EMR - and after the German government had failed to act to protect its citizenry. In some countries like Israel and Ireland there have been cases where citizens have taken their health and the law into their own hands when they realized that their governments would not protect them or their children from this danger.[37]

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[34] "Prof. Ogino then presented a graph which showed a drastic increase in miscarriages and SIDS in Japan in recent years, with no corresponding increase in Germany. An article on risk assessment (Science 165:1232 (1969)) compared Japan's wild forward push with America's more cautious approach. It brought up the idea of the Precautionary Principle" (Ormsby 2004).

[35] "Grants were not given to look for low-level hazards, and scientists who did find such effects were cut down to size. Funds for their work were quickly shut off and vicious personal attacks undermined their reputation.... when nonthermal dangers were documented in America, military and industrial spokespeople simply refused to acknowledge them, lying to Congress and the public. Many scientists, who naturally wanted to continue working went along with the charade" (Becker, 1985, p.306).

Many of the researchers I have contacted personally have told me that they have virtually no funds and others have mentioned that they have to search for obscure journals in which to publish their research since it seems the word is out and pressure is being applied on journals not to publish EMF studies.

[36] **"**In the Freiburger Appeal [6], initially 50 doctors in Germany reported reduced therapeutic efficiency of prescribed drugs correlated with the use of pulsed microwaves, such as those from Mobile Telephone Masts. Some 40,000 signatories have now supported the appeal, including 1,200 doctors. Alongside the Freiburger Appeal there are now similar appeals from Lichtenfelser, Hofer, Bamberger and Helsinki. In the Irish Republic, the IDEA group of Doctors has its own reports relating to Mobile Telephone Masts [10] which confirm the findings of the Freiburger Appeal doctors" (JerseyMastConcern).

[37] "In November 2003 something or somebody pulled the mast from its base and left it lying on its side. Eileen said: 'When I went to see what had happened I cried with delight. Even to this day nobody in Wishaw seems to know how the mast came down.' Naturally the phone company wanted their broken mast back - but they hadn't bargained with the Siege of Wishaw. Residents surrounded the downed mast with a posse of volunteers and camped on the site 24 hours a day determined there would be no mast replacement. The stand-off lasted for almost 18 months until finally the mast owners admitted defeat" (The Irish Post 2006).

"Israel- On the 28.9.06 , 200 people from the neighbourhood, Neve Horesh, in Dimona, decided to take their health and the law into their hands and destroyed a cellular antenna. Two weeks ago they found out that one of the villa owners in the area installed cellular antenna on the roof for $1200 a month, they asked him to remove it, because it risked them and their children. Their next step was to ask the city engineer to order to destroy it. The cellular company applied to court and claimed it had all the necessary approvals. On the 27.9.06, 200 people arrived to the house and destroyed the cellular antenna, the owner of the villa and his family saw the people and ran away and the residents destroyed the technical equipment that was used to operate the antenna. 'We didn't care that the police would arrest us', told Nissim Ben Yakar, one of the residents. 'It was about our

Naturally, we all have a right not to be exposed to this radiation which is affecting our health and making us and our families sick. Unfortunately, it seems like our governments favor the corporations and of course their money over our rights. We should expect to be seeing lawsuits in the future with regards to second-hand RF radiation.[38]

children lives. The villa owner's luck was that the angry residents didn't burn his house, because the rage against him was very big'" (Ifargan 2006). (Translation by Iris Atzmon)

[38] "Radiofrequency radiation emissions from cellular towers and handsets hold the potential for increased incidence of long-term medical effects, but of equal importance are the immediate effects of exposure to the radiation. Unlike second-hand cigarette or cigar smoke, exposure to which has been linked to life threatening and debilitating diseases, radiofrequency radiation exposure has, to date, successfully avoided the issue of passive personal exposure. It is extraordinary that absorption of unwanted radiation is never cited as an objectionable byproduct of the wireless communication craze. The reason may be that radiofrequency radiation, being tasteless, odorless and invisible, just isn't considered. But, in fact, recent research has demonstrated that even short-term exposure to radiation power densities emanating from a nearby cellular telephone is sufficient to modify brainwave patterns, affect short-term memory, and modify an individual's ability to perform physical tasks such as driving an automobile. These effects are all well and good for those who are willing to accept the risk of modified brain functions and cancer but they are not well and good for the innocent victim of the insidious radiation - radiation that an innocent non-participant cannot even be aware is being deposited into his or her body. Radiation emanating from a portable cellular telephone does not discriminate. It propagates through the entire environment surrounding the radiating antenna of the phone" (Kane 2007).

The only way the cell phone industry gets its power is because consumers pay them their money. They have created an imaginary need or addiction. But if you heed the information above, then you will hopefully realize that you do not really need this "unnecessary evil" - or rather you need it like you need a hole in your head or rather a brain tumor. Consumers need to become aware that they *do* have the power to affect change. Hence, the consumer is either part of the problem or part of the solution! The consumer can decide. The consumer has a choice - that is - unless they are Unconscious!

The forces of greed, selfishness, conformity, ignorance, apathy, obedience, fear, blind skepticism, and denial are powerful forces in our societies, which industries hence use to manipulate a populace. However, they are all still forms of Unconsciousness. And only an Unconscious person, aware of the severe damage that this technology is leveling, would pay an industry to cause them, their family and others harm. Only an Unconscious person would be a willing partner in a grave crime being committed against other human beings, plants, insects, and animals living on this planet.

Social psychologists have shown that it is much easier for people to harm other people when they do so under the orders of an authority figure - and further if done so indirectly and incrementally. When you add in the unconscious elements of conformity (everyone else is doing it so it must be OK), convenience, selfishness, greed, and denial, well you naturally have the ingredients for a disaster. If someone kills you directly and immediately, they go to jail; however, if someone kills you indirectly and incrementally, well they get away with murder. What should eventually come to light is that the Weapons of Mass Destruction (WMD) are not in Iraq, but rather in our front pockets, and we are not only committing mass genocide with these EM WMDs but also a slow mass suicide.

What can we do to protect ourselves (and our families) from this unconsciousness? One thing would be to limit one's and one's family's exposure to the electrosmog as much as possible. This can be done by relocating – (though finding a place without this radiation is becoming more and more difficult), and if this is not possible - shielding one's home. There was recently a building built in Budapest which is designed to block residents' exposure to EMR (All Hungary News 2007) - evidence that people are indeed starting to take this problem seriously.

More and more people are looking into creating EMR-free communities (see EMF-Refugee at http://health.groups.yahoo.com/group/emfrefugee/ and we can expect in the future that doctors will start sending patients to these areas. Meters and shielding materials can be purchased at www.lessemf.com and other companies like it.

Numerous studies are now showing that a number of antioxidants have an ability to protect one against the negative consequences of exposure to electromagnetic radiation. However, each antioxidant works differently in the body with some offering more protective effects to specific organs (e.g. milk thistle has been shown to offer the liver specific protection) while a number work in conjunction with each other. Therefore, it is useful to think of a "football team" analogy when taking antioxidants with each one performing a specific function while also working together as a team. The following are recommended with many already being shown in studies to offer protection against EMR: Alpha Lipoic Acid (ALA), Acetyl-L-Carnitine, Vitamin C, Vitamin A, Vitamin E, the B vitamins, Carotene, Cryptoxanthin, Lutein, Zeazanthin, Lycopene, Flavanoids, Gingko Biloba, Pycnogenol, Grape Seed Extract, Quercetin, Isoflavones, Milk Thistle, Bilberries, Blueberries, Hawthorn, Glutathione (from whey powder), N-Acetyl-L-Cysteine, Super Oxide Dismutase (SOD), Selenium, Catalase, Bee Propolis and Coenzyme Q10. Many of these products can be bought at discount supplement companies like www.iherb.com. Also, products like Noni Juice, Blueberries, Bee Propolis, Snake Venom, certain Chinese herbs, Inositol, Transfer Factor – plus the acupuncture point ST36 (Zusanli) – have been shown to stimulate NK cell production in the body. For people suffering from mycoplasma infections, the product Myco from Raintree Nutrition - www.raintreenutrition.com has been shown to be effective against this pathogen.

Acupuncture and Qigong are also helpful in balancing and strengthening the body's own natural electromagnetic field. These are however, all short-term solutions. In the long-term, the only solution will be to drastically reduce this dangerous and unacceptable level of ambient background electromagnetic radiation.

Since it is premature to expect civilization to wake up from its unconsciousness anytime in the near future, the only feasible alternative now is to look at fiberoptics – which has been proposed by the late New Zealand biophysicist Dr. Neal Cherry and is also now being promulgated by Dr. George Carlo. So rather than radiating the whole planet with high frequency microwaves, it would be much safer to have fiberoptic cables everywhere with ubiquitous outlets in which to plug in electronic devices including cell phones and computers. One can also envision umbrella cell-phone and WiFi usage areas – similar to cigarette smoking areas – having an extremely

limited range, where those who would like to go and fry their brains with microwaves can do so without harming those who would rather not.

"All that is necessary for evil to triumph is for good people to do nothing."

P.S. The cell phone industry has been buying up the patents on inventions that help protect cell phone users from the harmful radiation emitted by cell phones. Unfortunately, it is a catch-22 situation for them since if they use them, they are hence admitting what they have been denying all along - that cell phones are actually dangerous. This would open them up to a plethora of possible lawsuits. Either way, the consumer loses.

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International Experts' Perspective on the Health Effects of Electromagnetic Fields (EMF) and Electromagnetic Radiation (EMR).

June 11, 2011 (updated as of July 2014). Below are some of the key **resolutions, appeals,** and **declarations** released by expert scientific groups around the world since 1998, regarding the **biological and health effects** of both low frequency electromagnetic fields (**EMF**) associated with electricity and radio frequency (**RF**) electromagnetic radiation (**EMR**) generated by wireless devices.

Anyone who reads these cannot be left with the illusion (or delusion) that this form of energy is without adverse biological and health consequences at levels well below existing guidelines. Children are particularly vulnerable. It is irresponsible of governments to maintain the status quo in light of thousands of studies that have been published and statements by these experts.

Here are the resolutions/appeals/reports in reverse chronological order. **Note**: this page is update with new appeals/resolutions as they become available. Last updated July 12, 2014.

22. July, 2014: Canadian Physician's Declaration July 9, 2014.

There is considerable evidence and research from various scientific experts that exposure to microwave radiation from wireless devices; Wi-Fi, smart meters and cell towers can have an adverse impact on human physiological function. Many recent and emerging studies from university departments and scientific sources throughout the world support the assertion that energy from wireless devices may be causatively linked to various health problems including reproductive compromise, developmental impacts, hormonal dysregulation and cancer. In fact, in 2011 the World Health Organization listed microwave radiation as a Class 2B possible carcinogen and subsequent research strengthened the evidence that a stronger designation may be justified.

Physicians Call for Health Canada to Provide:

i) Wireless safety standards that are more protective of the health of Canadians; and

ii) Guidelines and resources to assist Canadian physicians in assessing and managing health problems related to microwave radiation.

To view document with 22 signature click here.

21. July, 2014: International Scientists Declaration July 9, 2014

Scientists call for Protection from Radiofrequency Radiation Exposure.

According to this international group of 53 scientists from 18 countries who do research dealing with electromagnetic fields and/or electromagnetic radiation, Canada's Safety Code 6 Guideline is fundamentally flawed and does not protect people

This expert group urgently calls upon Health Canada . . .

i) to intervene in what we view as an emerging public health crisis;

ii) to establish guidelines based on the best available scientific data including studies on cancer and DNA damage, stress response, cognitive and neurological disorders, impaired reproduction, developmental effects, learning and behavioural problems among children and youth, and the broad range of symptoms classified as EHS; and

iii) To advise Canadians to limit their exposure and especially the exposure of children.

Click here for pdf of this document with signatures as of July 9, 2014.

20. November, 2012: International Doctors' Appeal 2012 is a 10-year follow-up to the Freiburg Appeal of 2002 (see #5 below). In this appeal, physicians recognize that radio frequency radiation poses a serious health risk and they demand that precaution be exercised to protect public health. Click here for pdf.

19. March, 2012: Guideline of the Austrian Medical Association for the diagnosis and treatment of EMF related health problems and illnesses (EMF syndrome) provides information on how to proceed if patients exhibit EMF-related health problems. It includes taking history of health problems and EMF exposure; examination and findings; measurement of EMF exposure; prevention or reduction of EMF exposure; diagnosis; and treatment. Click here for pdf.

18. May 31, 2011: International Agency for Research on Cancer (IARC) and World Health Organization (WHO) reclassified radio frequency electromagnetic fields as a Class 2B carcinogen (possibly carcinogen to humans). This applies to all forms of radio frequency radiation (and not just cell phones as some inaccurately claim). Click here for press release. Final report will be published in the July 1st issue of The Lancet Oncology.

17. May 2011: The Parliamentary Assembly Council of Europe (PACE) released Resolution 1815 on the *Potential Dangers of Electromagnetic Fields and their effect on the Environment.* This document has some excellent recommendations regarding cell phones, cordless phones, wireless baby monitors, WiFi, WLAN, WiMax, power lines, relay antenna base stations; with special concerns expressed for the protection of children and those who are electrosensitive. Click here for document.

16. May 2011: Multiple Chemical Sensitivity (MCS) and Electrohypersensitivity (EHS), Summary of meeting at the WHO headquarters Geneva, May 13, 2011. Click here for report. Some statements from this meeting are quoted below:

We need to include these illnesses [MCS and EHS] in the WHO International Classification of Diseases (ICD), because what makes it more difficult for legal recognition is precisely the lack of code for these diseases in the ICD.

The adverse reactions to chemicals or electromagnetic radiation vary in duration according to each patient, and the manifestations differ too. When the patient is again exposed, symptoms usually worsen or result in the appearance of new symptoms.

The process of these diseases (MCS and EHS) is chronic and the patient's situation is exacerbated if he/she lives in a toxic environment, such as near Tarragona petrochemical industry or subjected to electromagnetic radiation: emissions in the neighborhood, mobile phone antennas , etc. The patient has to avoid re-exposure.

We are facing very high numbers of people already diagnosed . . . between 12% and 15% of the population has some kind of disturbance in the presence of a chemical substance. In the EHS, figures of affected people are between 3 and 6% of the population, but these numbers are growing continuously.

Each country can recognize these diseases and include them in their ICE, independently of WHO, since according to the WHO countries have sovereignty on this issue.

15. April 2011: The **Russian National Committee on Non-Ionizing Radiation Protection** (RNCNIRP) released their Resolution entitled "*Electromagnetic fields from Mobile Phones: Health Effect on Children and Teenagers*". *Click* here for report.

The Committee presents some startling statistics [references provided in original document].

In April 2008, the RNCNIRP reviewed the short-term and long-term effects of mobile phone use for children. In particular, it reviewed possible decrease of intellectual abilities and cognition together with possible increases in susceptibility to epileptic fits, "acquired dementia" and degeneration of cerebral nervous structures. The results of clinical studies have shown that chronic exposure to RF EMF may lead to borderline psychosomatic disorders. In 2010, a number of papers published in Russian and foreign peer-reviewed journals showed a response to RF EMF exposure from the immune system.

. . . since 2000 there has been a steady growth in the incidence of childhood diseases identified by RNCNIRP as "possible diseases" from mobile phone use. Of particular concern is the morbidity increase among young people aged 15 to 19 years (it is very likely that most of them are mobile phone users for a long period of time). Compared to 2009, the number of CNS [central nervous system] disorders among 15 to 17 year-old has grown by 85%, the number of individuals with epilepsy or epileptic syndrome has grown by 36%, the number of "mental retardation" cases has grown by 11%, and the number of blood disorders and immune status disorders has grown by 82%. In group of children aged less than 14 years there was a 64% growth in the number of blood disorders and immune status disorders, and 58% growth in nervous disorders. The number of patients aged 15 to 17 years old having consultations and treatment due to CNS disorders has grown by 72%.

Because of this the RNCNIRP considers it important to conduct a scientific study to determine whether the growth in morbidity resulted from EMF exposure from mobile phone use or whether it was caused by other factors.

14. 2010: Seletun Statement, Norway: The International Electromagnetic Field Alliance (IEMFA) released their report entitled *Scientific Panel on Electromagnetic Field Health Risks: Consensus Points, Recommendations, and Rationales* following a scientific meeting at Seletun Norway November 2009. The summary/abstract is provided below. Click here for publication. Click here for report and short video of Dr. Olle Johansson.

Summary: *In November, 2009, a scientific panel met in Seletun, Norway, for three days of intensive discussion on existing scientific evidence and public health implications of the unprecedented global exposures to artificial electromagnetic fields (EMF). EMF exposures (static to 300 GHz) result from the use of electric power and from wireless telecommunications technologies for voice and data transmission, energy, security, military and radar use in weather and transportation. The Scientific Panel recognizes that the body of evidence on EMF requires a new approach to protection of public health; the growth and development of the fetus, and of children; and argues for strong preventative actions. New, biologically-based public exposure standards are urgently needed to protect public health worldwide.*

Conclusions in this report build upon prior scientific and public health reports and resolutions documenting the following consensus points:

a) Low-intensity (non-thermal) bioeffects and adverse health effects are demonstrated at levels significantly below existing exposure standards.

b) ICNIRP and IEEE/FCC public safety limits are inadequate and obsolete with respect to prolonged, low-intensity exposures.

c) New, biologically-based public exposure standards are urgently needed to protect public health world-wide.

d) It is not in the public interest to wait.

13. 2009: EU Parliament Electromagnetic Report and Resolution entitled: *European Parliament Resolution on health concerns associated with electromagnetic fields,* was adopted February 17, 2009 with 29 recommendations. Click here for report.

12. 2009: Porto Alegre Resolution, Brazil. Scientists and doctors recognize electrohypersensitivity and are concerned that exposure to electromagnetic fields may increase the risk of cancer and chronic diseases; that exposure levels established by international agencies (IEEE, ICNIRP, ICES) are obsolete; and that wireless technology places at risk the health of children, teens, pregnant women and others who are vulnerable. Click here for document.

11. 2008: Venice Resolution, Italy. International Commission for Electromagnetic Safety (ICEMS) Scientists recognize biological effects at non-thermal levels, that standards are inadequate, that electro-sensitivity exists and that there is a need to research mechanisms. Click here for Venice Resolution.

Three key statements are provided below:

We take exception to the claim of the wireless communication industry that there is no credible scientific evidence to conclude there a risk. Recent epidemiological evidence is stronger than before, which is a further reason to justify precautions be taken to lower exposure standards in accordance with the Precautionary Principle.

We recognize the growing public health problem known as electrohypersensitivity; that this adverse health condition can be quite disabling; and, that this condition requires further urgent investigation and recognition.

We strongly advise limited use of cell phones, and other similar devices, by young children and teenagers, and we call upon governments to apply the Precautionary Principle as an interim measure while more biologically relevant standards are developed to protect against, not only the absorption of electromagnetic energy by the head, but also adverse effects of the signals on biochemistry, physiology and electrical biorhythms.

10. 2007: BioInitiative Report, USA. In response to statements that there are no scientific studies showing adverse biological effects of low level electromagnetic fields and radio frequency radiation, a group of researchers produced the BioInitiative Report that documents 2000 studies showing biological effects of extremely low frequency (ELF) electromagnetic fields and radio frequency (RF) radiation and calling for biologically based exposure guidelines. This document was criticized for not having been peer-reviewed even though most of the studies cited in this document were peer-reviewed. Click here for pdf.

Since then some of the BioInitiative papers as well as ones by other authors have appeared in a special issue of the peer-reviewd journal Pathophysiology (Volume 16 Issues 2-3, 2009). The papers in this journal document EMF effects on DNA, EMF effects on the brain, EMF in the environment, and science as a guide to public policy. Click here for abstracts.

9. 2006: Benevento Resolution, Italy. The International Commission for Electromagnetic Safety (ICEMS) organized a conference entitled: *The Precautionary EMF Approach: Rationale, Legislation and Implementation.* Scientists at this conference signed the Benevento Resolution (click here for pdf) that consists of 7 major statements. Among those statements are the following:

1. . . . there are adverse health effects from occupational and public exposures to electric, magnetic and electromagnetic fields, or EMF, at current exposure levels. What is needed, but not yet realized, is a comprehensive, independent and transparent examination of the evidence pointing to this emerging, potential public health issue.

4. Arguments that weak (low intensity) EMF cannot affect biological systems do not represent the current spectrum of scientific opinion.

6. We encourage governments to adopt a framework of guidelines for public and occupational EMF exposure that reflect the Precautionary Principle– as some nations have already done.

8. 2005: Helsinki Appeal, Finland. Physicians and researchers presented the Helsinki Appeal to the European Parliament. Click here for document. They state that:

The present safety standards of ICNIRP (International Commission of Non-Ionizing Radiation Protection) do not recognize the biological effects caused by non-ionizing radiation except those induced by the thermal effect. In the light of recent scientific information, the standards recommended by ICNIRP have become obsolete and should be rejected. Especially children and other persons at risk should be taken into account when re-evaluating the limits regarding the harmful effects of electromagnetic fields and radiation. Call for new safety standards, reject International Commission on Non-Ionizing Radiation Protection (ICNIRP) guidelines.

7. 2005: Irish Doctors' Environmental Association (IDEA)**, Ireland.** Members of IDEA wrote a position paper on electromagnetic radiation. Doctors recognize electrohypersensitivity (EHS) is increasing and request advice from government on how to treat EHS. Click here for document. Below is a quote from this document.

The Irish Doctors' Environmental Association believes that the Irish Government should urgently review the information currently available internationally on the topic of the thermal and non-thermal effects of exposure to electro-magnetic radiation with a view to immediately initiating appropriate research into the adverse health effects of exposure to all forms of non-ionising radiation in this country, and into the forms of treatment available elsewhere. Before the results of this research are available, an epidemiological database should be initiated of individuals suffering from symptoms thought to be related to exposure to non-ionising radiation. Those claiming to be suffering from the effects of exposure to electro-magnetic radiation should have their claims investigated in a sensitive and thorough way, and appropriate treatment provided by the State.

The strictest possible safety regulations should be established for the installation of masts and transmitters, and for the acceptable levels of potential exposure of individuals to electro-magnetic radiation.

6. 2002. Catania Resolution, Italy. This resolution was signed by scientists at the international conference "State of the Research on Electromagnetic Fields-Scientific and Legal Issues". Click here for resolution. Three of their statements are provided below:

1. Epidemiological and in vivo and in vitro experimental evidence demonstrates the existence of electromagnetic field (EMF) induced effects, some of which can be adverse to health.

4. The weight of evidence calls for preventive strategies based on the precautionary principle. At times the precautionary principle may involve prudent avoidance and prudent use.

5. We are aware that there are gaps in knowledge on biological and physical effects, and health risks related to EMF, which require additional independent research.

5. 2002 : Freiburg Appeal, Germany. Physicians request tougher guidelines for radio frequency exposure. This document was endorsed by thousands of healthcare practitioners. Click here for pdf. Below is a quote from this report.

We have observed, in recent years, a dramatic rise in severe and chronic diseases among our patients, especially:

· Learning, concentration, and behavioural disorders (e.g. attention deficit disorder, ADD)
· Extreme fluctuations in blood pressure, ever harder to influence with medications
· Heart rhythm disorders
· Heart attacks and strokes among an increasingly younger population
· Brain-degenerative diseases (e.g. Alzheimer–s) and epilepsy
· Cancerous afflictions: leukemia, brain tumors

Moreover, we have observed an ever-increasing occurrence of various disorders, often misdiagnosed in patients as psychosomatic:

· Headaches, migraines
· Chronic exhaustion
· Inner agitation
· Sleeplessness, daytime sleepiness
· Tinnitus
· Susceptibility to infection
· Nervous and connective tissue pains, for which the usual causes do not explain even the most conspicuous symptoms

Since the living environment and lifestyles of our patients are familiar to us, we can see especially after carefully-directed inquiry a clear temporal and spatial correlation between the appearance of disease and exposure to pulsed high - frequency microwave radiation (HFMR), such as:

· Installation of a mobile telephone sending station in the near vicinity
· Intensive mobile telephone use
· Installation of a digital cordless (DECT) telephone at home or in the neighbourhood

We can no longer believe this to be purely coincidence, for:

· Too often do we observe a marked concentration of particular illnesses in correspondingly HFMR-polluted areas or apartments;
· Too often does a long-term disease or affliction improve or disappear in a relatively short time after reduction or elimination of HFMR pollution in the patient's environment;
· Too often are our observations confirmed by on-site measurements of HFMR of unusual intensity.

4. 2002: Salzburg Resolution, Austria. The *Salzburg Resolution on Mobile Telecommunication Base Stations* makes four recommendations including preliminary guidelines 0f 0.1 microW/cm2 for sum of all emissions from mobile phone stations. This is well below the current ICNIRP guidelines and those in Canada and the US (1000 microW/cm2) and is slightly lower than guidelines in Switzerland, Italy, Russia, China (10 mciroW/cm2). Click here for document.

3. 2000: Stewart Report, UK. The Independent Expert Group on Mobile Phones (IEGMP) produced a report, *Mobile Phones and Health,* that is commonly referred to as the Stewart Report, named after its Chairman Sir William Stewart. Click here for pdf. A quote from the foreward shows how much our understanding of this issue has changed since 2000.

The report points out that the balance of evidence does not suggest mobile phone technologies put the health of the general population of the UK at risk. There is some preliminary evidence that outputs from mobile phone technologies may cause, in some cases, subtle biological effects, although, importantly, these do not necessarily mean that health is affected. There is also evidence that in some cases people's well-being may be adversely affected by the insensitive siting of base stations. New mechanisms need to be set in place to prevent that happening.

The report goes on to state that:

1.17. The balance of evidence to date suggests that exposures to RF radiation below NRPB and ICNIRP guidelines do not cause adverse health effects to the general population.

1.18 There is now scientific evidence, however, which suggests that there may be biological effects occurring at exposures below these guidelines . . .

1.19 . . . We conclude therefore that it is not possible at present to say that exposure to RF radiation, even at levels below national guidelines, is totally without potential adverse health effects, and that the gaps in knowledge are sufficient to justify a precautionary approach.

1.20 In the light of the above considerations we recommend that a precautionary approach to the use of mobile phone technologies be adopted until much more detailed and scientifically robust information on any health effects becomes available.

2. 1998: Vienna EMF Resolution, Austria. At a *Workshop on Possible Biological and Health Effects of RF Electromagnetic Fields*, the scientists agreed on the following:

The participants agreed that biological effects from low-intensity exposures are scientifically established. However, the current state of scientific consensus is inadequate to derive reliable exposure standards. The existing evidence demands an increase in the research efforts on the possible health impact and on an adequate exposure and dose asses.

Base stations: How could satisfactory Public Participation be ensured?

The public should be given timely participation in the process. This should include information on technical and exposure data as well as information on the status of the health debate. Public participation in the decision (limits, siting, etc.) should be enabled.

Cellular phones: How could the situation of the users be improved?

Technical data should be made available to the users to allow comparison with respect to EMF-exposure. In order to promote prudent usage, sufficient information on the health debate should be provided. This procedure should offer opportunities for the users to manage reduction in EMF-exposure. In addition, this process could stimulate further developmentlow-intensity emission devices

Regarding legal aspects . . .

there is protection deficit in the public and private laws which is unsatisfactory. The legislator is requested to solve the conflict of interests between the industries commission on one side and the neighbours involvement and their interests on protection of life and health on the other side. Because of the constitutionally determined objectives of the state to comprehensively protect the environment, there is a demand of acting precautionary on the polititcal and legal level.

The Vienna declaration on electromagnetic fields recommended 13 detailed action items for parliament to consider. Click here to read those items and to download pdf.

1. 1997: Boston Physicians' and Scientists' Petition. We the undersigned physicians and scientists call upon public health officials to intervene to halt the initiation of communication transmissions employing ground level, horizontally transmitted, pulsed microwaves in Boston. This form of transmission is scheduled to begin June, 1997, by the Sprint Corporation for personal communications systems (PCS). Given the biological plausibility of negative health impacts, particularly to the human nervous system, as well as anecdotal evidence of illness and death from such exposures in cities where transmission has already been implemented, and voluminous medical studies indicating human and ecological harm from microwaves, we urge the suspension of that implementation pending full public notification of its potential hazards and the full review and determination of its safety by the scientific community.

With 97 signatures sent to ENHALE (Environmental Health Advocacy League], Box 425 Concord MA, 01742.

*****

Based on these resolutions and appeals from international groups of physicians and scientists immediate action is required to protect public health from continued increasing exposure to radio frequency radiation and electromagnetic fields.

I call on . . .

1. ***regulators*** *around the world to reexamine existing guidelines for both EMF and EMR and to reduce them to the lowest possible levels to protect the public and workers. Values above 4 milliGauss (low frequency magnetic fields); above 0.1 microW/cm2 (power density for radio frequency radiation) and above 40 GS units (dirty electricity) have been associated with adverse health effects in peer reviewed scientific publications!*
2. ***government agencies*** *responsibility for the location of both base stations and power lines to keep distances at least 400 meters (base stations) and 100 meters (transmission lines) from residential properties as well as school and health care facilities.*
3. ***utilities*** *(water, gas, electricity) to reconsider the use of wireless smart meters and provide wired options for those who are sensitive, for those who do not want to be exposed, and for those in densely populated settings.*
4. ***manufacturers*** *who are providing technology that uses electricity and/or emits radio frequency radiation to re-engineer their products to provide the minimum radiation possible. This includes light bulbs, computers, wireless home devices like baby monitors and cordless phones, cell phones, smart meters, plasma TVs, among others.*
5. ***architects, builders, electricians,*** *and* ***plumbers*** *to design and construct buildings that are based on principles of good electromagnetic hygiene. This includes using materials that absorb or shield building interiors from microwave radiation especially near external sources of this radiation and in multi-unit buildings; to provide wired alternatives to wireless devices; to properly wire and ground buildings to minimize low frequency electromagnetic fields and to eliminate ground current problems; and to install filters on electrical panels and/or throughout the building to ensure good power quality.*
6. *local, state, federal* ***health authorities*** *to educate medical professions about the potential biological effects of both low frequency and radio frequency electromagnetic energy; about the growing number of people who have electrosensitivity (ES) or electrohypersensitivity (EHS) and to alert them on how they can help their patients in terms of minimizing their exposure and promoting their recovery.*
7. ***hospitals*** *and*
8. ***school boards*** *should choose wired internet access over WiFi (wireless technology) and not allow towers/antennas within 400 meters of their school property.*
9. ***parents*** *to practice good electromagnetic hygiene especially in the bedroom and especially for their children. This involves using wired rather than wireless devices in the home, keeping electric appliances away from the bed, turning off/unplugging devices when not in use.*
10. *the* ***media*** *to provide information to the public about the health and safety of using this technology; to rely on "independent experts" who do not receive funding or other benefits based on the outcome of research studies; and to identify experts funded by the industry as "industry representatives". The integrity of many of these scientists leaves much to be desired.*

Dr. Magda Havas

http://pulse.ncpolicywatch.org/2015/04/13/watchdog-report-highlights-huge-duke-energy-contributions-to-gop-guvs/

Watchdog report highlights huge Duke Energy contributions to GOP guvs

By Rob Schofield
April 13, 2015
In News

Print This Post

The good people at Democracy NC released the following this morning:

Duke Energy Gives $3 Million to Committee Tied to Gov. Pat McCrory as He Guides Coal Ash Response

A new analysis of government records reveals that Duke Energy – the world's largest private electric utility – began writing unusually large checks to the national Republican Governors Association while Gov. Pat McCrory and Republican lawmakers debated how to respond to the company's giant spill of coal ash sludge into the Dan River.

In four payments from June to December 2014, Duke sent the Republican Governors Association a total of $3,050,000 – more than 10 times its previous record donation to the RGA. Duke's contributions made it the top corporate donor to the RGA in 2014 and the second largest donor, behind the $3.5 million given by billionaire Sheldon Adelson, owner of the Las Vegas Sands.

In 2012, the RGA spent $5 million to boost the election of Pat McCrory as governor, and it is expected to be a major financial backer of his 2016 bid for reelection. Records show McCrory has attended numerous RGA events and helped the association raise funds.

"Duke Energy's large donations raise questions about the governor's ability to serve the public interest more than his own political interest," said Bob Hall, executive director of the nonpartisan watchdog group Democracy North Carolina. "Critics say the coal ash regulation law passed in 2014 was too soft on Duke. Is this money the reason why?"

RGA's website says its "primary mission is to help elect Republican governorships throughout the nation." As a "527 political organization," it can receive and spend unlimited donations from corporate and other donors to elect candidates, without directly coordinating with the candidate.

The organization files relatively obscure reports with the Internal Revenue Service. Democracy North Carolina's analysis shows that Duke Energy and Progress Energy gave RGA a total of only $40,000 in the five years from Jan. 1, 2003 to Dec. 31, 2007, an average of $8,000 a year.

In January 2008, Pat McCrory, a long-time Duke Energy executive and former Charlotte mayor, announced his campaign for governor. Within weeks, Duke and Progress Energy began sending checks of $10,000 or more to the RGA, according to the IRS disclosure reports.

In October 2008, candidate McCrory hosted a fundraiser for the RGA in Charlotte. As the invites circulated, Duke Energy stepped up with a gift of $100,000 – its first six-figure RGA donation. (See the event invitation at: http://www.scribd.com/doc/240852146/101308-Event-Invite).

Duke and Progress Energy gave a total of $155,000 during 2008 – or 10 times their previous record of $15,000 in 2007. The two companies, now merged, increased their giving after 2008, reaching a high of $275,000 in 2013 before the new high of $3,050,000 in 2014.

The companies also increased their donations to other 527 partisan committees. Duke Energy gave $200,000 to the Democratic Governors Association in 2012 and another $200,000 in 2014. Progress Energy donated $200,000 to the DGA in 2013.

Duke also donated a total of $235,000 during 2012-2014 to the Republican State Leadership Committee, which its website says promotes "the election of state Republican candidates."

Hall pointed out that Duke may be donating significant amounts of money to other electioneering committees that do not file disclosure reports – including Renew North Carolina, a nonprofit set up by Pat McCrory's supporters to help his political career, and NC House Legislative Partners, which supports Republican General Assembly candidates.

"The public has a right to know who is donating to our lawmakers and their reelection efforts, directly and through shadow committees," Hall said. "Duke Energy should lead the way by voluntarily disclosing its contributions to these committees."

* * * * *

Here are the donations from Duke and Progress Energy and to the Republican Governors Association disclosed (form 8872) at: http://forms.irs.gov/app/pod/basicSearch/search?execution=e1s2

DONATIONS TO REPUBLICAN GOVERNORS ASSOCIATION

Duke Energy 12/12/2014 $ 275,000
Duke Energy 10/21/2014 $ 2,000,000
Duke Energy 09/30/2014 $ 500,000
Duke Energy 06/17/2014 $ 275,000 2014 Total $3,050,000

Progress Energy 09/17/2013 $ 175,000
Progress Energy 04/24/2013 $ 100,000 2013 Total $ 275,000

Duke Energy 11/09/2012 $ 900
Duke Energy 11/02/2012 $ 450
Duke Energy 06/22/2012 $ 175,000
Progress Energy 05/22/2012 $ 25,000 2012 Total $ 201,350

Duke Energy 12/28/2011 $ 25,000
Duke Energy 11/16/2011 $ 450
Progress Energy 11/16/2011 $ 25,000
Progress Energy 10/25/2011 ($ 15,000)
Progress Energy 09/26/2011 $ 15,000
Progress Energy 09/08/2011 $ 15,000
Duke Energy 06/13/2011 $ 75,000
Duke Energy 06/13/2011 $ 25,000
Progress Energy 02/15/2011 $ 10,000 2011 Total $ 175,450

Duke Energy 09/29/2010 $ 50,000
Duke Energy 09/16/2010 $ 50,000
Duke Energy 04/12/2010 $ 25,000
Duke Energy 02/25/2010 $ 25,000 2010 Total $ 150,000

Duke Energy 12/14/2009 $ 25,000
Duke Energy 05/05/2009 $ 15,000
Duke Energy 03/16/2009 $ 50,000
Progress Energy 01/27/2009 $ 10,000 2009 Total $ 100,000

Duke Energy 09/09/2008 $ 100,000
Progress Energy 08/27/2008 $ 20,000
Duke Energy 03/06/2008 $ 25,000
Progress Energy 01/29/2008 $ 10,000 2008 Total $ 155,000

Duke Energy 06/19/2007 $ 5,000
Progress Energy 01/30/2007 $ 10,000 2007 Total $ 15,000

Progress Energy 03/16/2006 $ 10,000 2006 Total $ 10,000

EFFECT OF GSM MOBILE PHONE RADIATION ON BLOOD-BRAIN BARRIER

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ABSTRACT

Some animal studies have suggested that mobile phone radiation may cause increase in blood-brain barrier permeability. We have hypothesized (Leszczynski et al. Differentiation, 70, 2002, in press) that the mobile phone radiation-induced increased expression and phosphorylation (activity) of stress protein hsp27 might be the molecular mechanism regulating blood-brain barrier permeability and, possibly, cell apoptosis. Here we present evidence suggesting that mobile phone radiation indeed affects hsp27-dependent cytoplasmic distribution of F-actin and stability of stress fibers. This observation supports our hypothesis that mobile phone radiation-induced changes in hsp27 expression/activity might eventually lead to increase in the permeability of blood-brain barrier.

BACKGROUND

The question whether microwave radiation, that is emitted by mobile phones (radio-frequency modulated electromagnetic fields: RF-EMF), might exert any detrimental health effects remains unanswered. Several recently conducted reviews of the to-date published research have concluded that there is significant and credible scientific evidence to the fact that RF-EMF induces biological effects [1,2,3,4]. However, it still remains to be determined whether these biological responses could cause health hazard.

The possibility of the induction of cellular stress response by the non-thermal levels of mobile phone radiation has been shown just recently. In vivo, Daniells et al. [5] and de Pomerai et al. [6] have shown that overnight irradiation of nematode worms with RF-EMF (750MHz) at SAR of 0.001W/kg causes increase in expression of heat shock protein. Fritze et al. [7], using rat model, have shown increase in expression of stress protein hsp70 in brains of animals exposed for 4 hours to RF-EMF (890-915MHz) at SAR of 1.5W/kg. In vitro, Kwee et al. [8] have shown induction of stress protein hsp70, but not hsp27, in transformed human epithelial amnion cells exposed for 20 min. to RF-EMF (960MHz) at SAR of 0.0021W/kg. Thus, because of the known broad spectrum of physiological processes that are regulated by stress proteins [9], it is possible to suggest that mobile phone radiation-induced activation of cellular stress response might affect variety of physiological processes, among them brain tumor development and blood-brain barrier permeability. Having this in mind, French et al. [10] have put forward hypothesis suggesting that repeated exposures of cells to mobile phone radiation over a long period of time might affect tumor development due to the hypothesized chronic up-regulation of the expression levels of cellular stress proteins. However, occurrence of such chronic stimulatory effect on the expression of stress proteins induced by mobile phone radiation, as suggested by French et al. [10], still remains to be experimentally demonstrated.

PREVIOUS STUDY

In our earlier study [11] we have demonstrated that the 1-hour non-thermal exposure of human endothelial cell line EA.hy926 to SAR of 2W/kg (900MHz GSM signal) leads, among others, to: (i) changes in phosphorylation status of a large number of proteins, (ii) among them, transient increase in phosphorylation of hsp27 stress response protein, which was prevented by SB203580, a specific inhibitor of p38 mitogen-activated protein kinase (p38MAPK), (iii) transient changes in protein expression levels of hsp27 and p38MAPK.

Over-expression and phosphorylation of hsp27 has been shown to regulate polymerization of F-actin and formation and stability of stress fibers. This, when occurring in endothelial cells lining brain's capillary blood vessels, might be of importance for the functioning of blood-brain barrier. Stabilization of stress fibers and cytoplasmic distribution of F-actin was shown to cause: (i) cell shrinkage, that might lead to opening of spaces between cells, (ii) increase in the permeability and pinocytosis of endothelial monolayer, (iii) increase in formation of the so called “apoptosis-unrelated” blebs on the surface of endothelial cells, which eventually might obstruct blood flow through capillary blood vessels, (iv) stronger responsiveness of endothelial cells to estrogen and, when stimulated by this hormone, to secrete larger than normally amounts of basic fibroblast growth factor (bFGF) which might, in endocrine manner, stimulate de-

differentiation and proliferation of endothelial cells and possibly led to the associated with cell's proliferative state - cell shrinkage and unveiling of basal membrane.

The possibility of the effect of RF-EMF exposure on blood-brain barrier permeability has been suggested earlier by in vivo [12] and in vitro [13] studies. However, there are also reports where authors claim that the non-thermal levels of RF-EMF radiation do not affect blood-brain barrier permeability [14,15]. The no-effect, which is claimed by Fritze et al. [14], is not so straight forward. The authors have observed stress response and increased permeability of the blood-brain barrier immediately after the end of irradiation. This effect was, however short lasting. Therefore, it remains unclear what would be the blood-brain barrier response to the repeated exposures to mobile phone radiation because the effect of repeated exposures was not examined. The increased blood-brain barrier permeability due to increase of pinocytosis was suggested by Neubauer et al. [16] who have demonstrated increase in pinocytosis of cerebral cortex capillaries that were exposed to 2.45 GHz microwave radiation. Finally, the recently reported study by Töre et al. [17] has shown that 2 hour exposure of rats to RF-EMF (900MHz) at SAR of 2W/kg (averaged over the brain) causes increase in the permeability of blood-brain barrier. The molecular mechanism and the cellular signaling pathways involved in the induction of blood-brain barrier permeability are still unknown.

Activated (phosphorylated) hsp27 has been shown to inhibit apoptosis by forming complex with the apoptosome (complex of Apaf-1 protein, pro-caspase-9 and cytochrome *c*), or some of its components, and preventing proteolytic activation of pro-caspase-9 into active form of caspase-9 [18,19]. This, in turn, prevents activation of pro-caspase-3 which is activated by caspase-9. Thus, induction of the increased expression and phosphorylation of hsp27 by the RF-EMF exposure might lead to inhibition of the apoptotic pathway that involves apoptosome and caspase-3. This event, when occurring in RF-EMF exposed brain cells that underwent either spontaneous or external factor-induced transformation/damage, could support survival of the transformed/damaged cells.

HYPOTHESIS

Based on the known cellular role of over-expressed/phosphorylated hsp27 we have proposed a hypothesis [11] that: the activation (phosphorylation) of hsp27 by mobile phone radiation might be the molecular mechanism (i) regulating increase in blood-brain barrier permeability, which would explain, observed in some animal experiments, increase in blood-brain barrier permeability, and (ii) regulating apoptosis through interference with the cytochrome c/caspase-9/caspase-3 pathway (Figure 1).

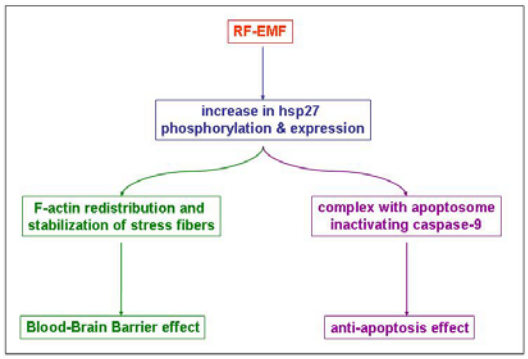

Fig. 1. Hypothetical flow of events that might occur in cells in response to mobile phone radiation.

OBJECTIVE

The present study was undertaken to determine whether physiological responses of endothelial cells, which are associated with the hsp27 expression and phosphorylation and might affect permeability of blood-brain barrier (stability of stress fibers, cell size/shape), occur in the mobile phone radiation exposed cultures of human endothelial cell line EA.hy926.

MATERIAL AND METHODS

Human endothelial cell line EA.hy926 cells, grown on microscope cover slides, were exposed for 1h to 900MHz GSM signal at an average SAR of 2W/kg (range 1.8 – 2.5 W/kg). Temperature of cell cultures remained throughout

irradiation period at 37±0.3°C thus the effects reported here are of non-thermal nature. Cells on cover slides were fixed either immediately or 1h after the end of irradiation. The expression of hsp27 was determined by indirect immunohistochemistry in order to confirm that the cells respond to irradiation in the same way as in the previous study [11]. The appearance of cells (size, shape) and cytoplasmic pattern of F-actin distribution (stabilization of stress fibers) was determined by staining of the cells with fluorescent-dye (AlexaFluor) labeled phalloidin.

RESULTS AND DISCUSSION

As expected, 1h exposure of cells to mobile phone radiation increased expression of hsp27. However, in order to increase hsp27 expression by heat shock was required 3h incubation of cells at 43°C (1h exposure had no effect). This observation, together with the measurements showing that temperature of medium was throughout RF-EMF exposure period at 37±0.3°C, suggest that the observed here effects are of non-thermal nature.

The stability of stress fibers, as determined by the pattern of staining with phalloidin-AlexaFluor, increased after 1h irradiation and did not decline during the 1h of post-irradiation incubation. Induction of the stability of stress fibers caused cells to shrink. In cells expressing high levels of hsp27, the cell edges were brightly stained with phalloidin-AlexaFluor, what indicates re-localization of F-actin to cell ruffles. These cells rounded-up and cells contacted in-between only through thin pseudopods. In cells expressing lower levels of hsp27, network of stress fibers was seen throughout the cytoplasm but not in the ruffles.

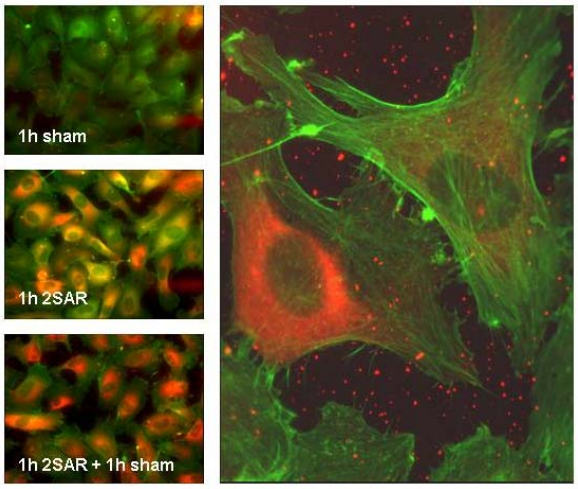

Fig. 2. Expression pattern of F-actin in EA.hy926 cells detected using phalloidin-AlexaFluor staining (green fluorescence) and hsp27 using indirect immunofluorescence (red color). Left panel: cells exposed for 1h to sham, cells exposed for 1h at 2W/kg (2SAR), and cells exposed for 1h at 2W/kg followed by 1h exposure to sham. Right panel: cell expressing high level of hsp27 has F-actin in cell ruffles whereas cell expressing low level of hsp27 has F-actin in form of stress fibers distributed throughout cytoplasm (notice difference in stress fiber density over the nuclear region in both cells).

The observed here, hsp27-related changes in cytoplasmic distribution of F-actin are apparently outcome of two phenomena: hsp27 over-expression and hsp27 phosphorylation. These observed changes support the hypothesis that the hsp27/p38MAPK stress signaling pathway might be the molecular mechanism regulating mobile phone radiation-induced permeability of blood-brain barrier.

CONCLUSIONS

The proposed above intra-cellular mechanism for the mobile phone radiation-increased permeability of the blood-brain barrier is a hypothesis but as such it is reasonably supported by the evidence concerning both effects of microwaves on stress response and effects of hsp27 (increased expression and activity) on cell physiology. Furthermore, it appears that the physiological changes caused by hsp27 phosphorylation indeed take place in endothelial cells (stress fibers' expression, cell size/shape changes). These events, when occurring repeatedly (on daily basis) over the long period of time (years) might become health hazard because of the possible accumulation of brain tissue damage.

ACKNOWLEDGEMENTS

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OncoTargets and Therapy

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ORIGINAL RESEARCH

Effects of electromagnetic radiation exposure on bone mineral density, thyroid, and oxidative stress index in electrical workers

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Background: In the literature, some articles report that the incidence of numerous diseases increases among the individuals who live around high-voltage electric transmission lines (HVETL) or are exposed vocationally. However, it was not investigated whether HVETL affect bone metabolism, oxidative stress, and the prevalence of thyroid nodule.

Methods: Dual-energy X-ray absorptiometry (DEXA) bone density measurements, serum free triiodothyronine (FT3), free thyroxine (FT4), RANK, RANKL, osteoprotegerin (OPG), alkaline phosphatase (ALP), phosphor, total antioxidant status (TAS), total oxidant status (TOS), and oxidative stress index (OSI) levels were analyzed to investigate this effect.

Results: Bone mineral density levels of L1–L4 vertebrae and femur were observed significantly lower in the electrical workers. ALP, phosphor, RANK, RANKL, TOS, OSI, and anteroposterior diameter of the left thyroid lobe levels were significantly higher, and OPG, TAS, and FT4 levels were detected significantly lower in the study group when compared with the control group.

Conclusion: Consequently, it was observed that the balance between construction and destruction in the bone metabolism of the electrical workers who were employed in HVETL replaced toward destruction and led to a decrease in OPG levels and an increase in RANK and RANKL levels. In line with the previous studies, long-term exposure to an electromagnetic field causes disorders in many organs and systems. Thus, it is considered that long-term exposure to an electromagnetic field affects bone and thyroid metabolism and also increases OSI by increasing the TOS and decreasing the antioxidant status.

Keywords: bone mineral density, electromagnetic radiation, electrical workers, thyroid, RANK, RANKL

Introduction

Electromagnetic field (EMF) is a space of mobile and electric-loaded particles affected by power and appears as a result of spinning of the electrons inside atoms around the atomic core and themselves.[1] Human body acts like an electromagnetic machine where each cell has a specific electric circuit.[2] Therefore, human being has a magnetic field. The magnetic field in the human body appears by the movements of bioelectrical loads, and the magnetic field signals of the substances creating human to intercommunicate are consistent with each other. Alongside the internal and external magnetic field existing in the nature, human beings are exposed to some magnetic fields such as cell phones, computers, electrical household appliances, and high-voltage transmission lines. The electromagnetic balance of the human body is disrupted by these magnetic fields.[2]

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EMFs reach into the tissues, causing cellular dysfunctions.[3] They lead to disorders such as insomnia, headache, and stress. These fields negatively affect blood biochemistry, digestive and circulatory systems, and increase the risk for cancer.[4–8] High-voltage transmission lines were detected as a cause for leukemia and brain cancer in children; and a close relation between childhood cancers, especially leukemia and living in close proximity to high-voltage electric transmission lines were observed.[8,9] Studies conducted in the USA and Finland determined that Alzheimer's disease is observed four times more in men and three to four times more in women among the workers (radio operators, industrial equipment workers, data processing device mechanics, phone-line workers, those working in electric plants, and substations) who are frequently exposed to EMFs.[2]

Since a magnetic field is not visible, not directly sensed, and the effects are observed cumulatively after a long period, it is not regarded enough. Although, it is still problematic whether a poor magnetic field is harmful for human health, studies carried out on animal cells revealed that poor magnetic field causes many biological effects such as changing hormone and enzyme levels, preventing motion of tissue chemicals.[10–15] In the literature, some articles report that the incidence of numerous diseases increases among the individuals who live around high-voltage electric transmission lines (HVETL) or are exposed vocationally.[16–18] However, it was not investigated that whether HVETL affect the bone metabolism, prevalence of the thyroid nodule, and oxidative stress levels in electrical workers. Furthermore, since biological effects of EMF are observed after a long period, the electrical workers are an appropriate group to search this effect. In the present study, we examined the effects of exposure to an EMF on bone mineral density (BMD), thyroid nodule formation, serum free triiodothyronine (FT3), free thyroxine (FT4), RANK, RANKL, osteoprotegerin (OPG), alkaline phosphatase (ALP), phosphor (P) levels, total antioxidant status (TAS), total oxidant status (TOS), and oxidative stress index (OSI) of electrical workers.

Patients and methods

The study group included 47 electrical workers employed in Electricity Generation Company (EGC) Transmission-Operation Facility 6, Kütahya and their ages varied between 29 and 52 years (mean 38.4 years). Mean working period of the study group was determined as 15.9±6.72 years. The control group was created from 47 healthy individuals with a similar socio-economical status with an age range between 28 and 52 years (mean 39.1 years) who were not exposed to ionizing and non-ionizing radiation for diagnostic and therapeutic purposes and who complied with the study group in terms of smoking and exercise habits. Consent of Clinical Researches Ethics Committee of Afyonkarahisar with a consent number of 2012/15-123 was obtained on July 6, 2012. This study was supported by Afyon Kocatepe University Scientific Research Projects Unit (Project no: 12.TIP.11).

The participants of the study were informed and their written consent was obtained. Individuals who work as electrical workers at least for 10 years were enrolled for this study. Individuals working for less than 10 years were excluded. Individuals without diseases that may affect the bone metabolism (thyroid/parathyroid disorders, kidney failure, autoimmune or tumoral diseases) and those who do not have the aforesaid conditions in their medical history were enrolled for this study. The participants were investigated for osteoporosis factors such as body mass index, smoking, alcohol use, nutritional status, familial medical history, and exercise and exposure to EMF including use of cell phones, computer, and hair dryer. The participants did not expose to any radiation such as magnetic resonance imaging (MRI) for diagnosis and treatment purposes. Furthermore, all the participants were informed about the study and told the minimal risk of radiation absorption related to the dual-energy X-ray absorptiometry (DEXA) scans and, included in the study after their consent was received. The data about the familial and personal medical history, dietary habits, exercise and physical activity status, and the conditions such as fatigue, anxiety, and headache after work were obtained through a face-to-face survey including 34 questions. Furthermore, the measurements of EMF and body temperatures of the electrical workers were performed in their units. Blood analyses, ultrasound scan (USS) of the thyroid gland, and bone DEXA scan of the participants were used as a tool for data collection.

USS of the thyroid gland

USS of the thyroid gland was performed in the control and the study group. The scan was performed with a LOGIQ 7 (General Electric Medical System, Milwaukee, WI, USA) ultrasonography device through a 7.5–10 MHz linear probe. The procedure was applied after positioning the patient's neck to extension by placing a lifter under the patient's shoulder. During the scan, images on the coronal, horizontal, and sagittal planes were obtained and thyroid gland size, homogeneity of the thyroid parenchyma echo, the presence of the nodule (present–absent), and vascularity through Doppler ultrasonography were assessed.

DEXA measurements

BMD of the lumbar area and hip of the individuals in both groups were measured by using the DEXA method (DXA.

Hologic QDR 4500) and the lowest t-score value was used for statistical evaluation. Baltas et al mentioned that the DEXA method was approved by WHO (World Health Organization), NOF (National Osteoporosis Foundation), and IOF (International Osteoporosis Foundation) for diagnosis and follow-up of osteoporosis,[19] and it is an essential tool to measure the BMD. The measures of the lumbar vertebra and femur are accepted as general measurement areas for the diagnosis of osteopenia and osteoporosis. It is a routine method for BMD. In the present study, the DEXA method was utilized to measure BMD and measures of the lumbar vertebrae and femur were performed.

T-score shows the difference of BMD scores between the patient and young adults who have the same sex and ethnicity with the patient. T-score values of the groups were used in the study.

(Hip) BMD measurement: While the patient was lying on supine position on the table, her/his feet were positioned on internal rotation by 25° with a 30 cm gap between the feet and fixed in a foot positioner. Hip joint, femur head, and femur neck were included into the screening.

(L1–L4) BMD measurement: The patient was positioned on supine position and full contact of the waist was provided by placing a support under the knees. Vertebrae between L1 and L4 were taken into the shot.

Biochemical analyses

Analyses of bone metabolism parameters (OPG, RANK, RANKL)

Blood analyses were performed by collecting venous blood samples of the patients with an empty stomach; and serum levels of three different parameters including OPG (e-Bioscience, Vienna, Austria), RANK (Cusabio, Wuhan, Hubei, People's Republic of China), and RANKL (BioVendor, Shenzhen, People's Republic of China) were analyzed by an ELISA device (Biotek ELx800) in accordance with human-specific kit protocols. During the ELISA analysis, the standards procured with the kits were thawed, then diluted. Eight standards were prepared to create the calibration curve required for calculating the concentrations in ELISA device automatically by using the absorbance of the samples. Standards and samples were analyzed twice, and the mean value of each standard and sample was used for statistical calculations.

The kits used include OPG (e-Bioscience), Ref no: BM2021INST, Lot no: 74889021; RANK (Cusabio) Catalog no: CSB-E13539h, Lot no: F15069918; RANKL (BioVendor) Ref no: RD193004200R, Lot no: E12-054.

Analysis of thyroid functions

All tests were analyzed in the same laboratory. Serum concentrations of thyroid-stimulating hormone (TSH), FT3, and FT4 were analyzed with the original kits of Abbott Architect 1600 Chemiluminescence method.

Analysis of TAS and TOS

Methods such as TAS to measure the antioxidant status in a medium are generally calibrated by using a standard antioxidant solution called Trolox Equivalent which is analogous of vitamin E; the TAS levels measured were read as mmol Trolox Equiv/L. TAS measurements were performed by kinetic reading in the spectrophotometer 5 minutes after the sample and reagent were mixed. TOS measurements were done by reading at end-point 560 nm in the spectrophotometer 3–4 minutes after mixing the samples and reagents, and the results were expressed in hydrogen peroxide liter (μmol H_2O_2 equiv/L).

Calculation of OSI

After TAS and TOS measurements, the OSI levels, which allow us to make an exact comment on the oxidant and antioxidant balance, were calculated according to the following formula specified in the catalog of the kit (rel assay diagnostics). OSI = (TOS μmol/L)/(TAS [mmol Trolox Equiv/L] ×100).

Statistical analysis

The data of the individuals who were exposed to the magnetic field and consisted of healthy individuals as the control group were analyzed by SPSS for Windows 15.0 package program of statistics. Compliance of the data to normal distribution was investigated by the Kolmogorov–Smirnov test. The analysis of the data compliant to the normal distribution was performed by independent sample *t*-test and one-way analysis of variance (ANOVA) for comparisons between the groups. The Least Significant Difference (LSD) test was used to determine the source of the statistically significant difference as a result of ANOVA test. Paired comparisons between the groups for the data that are not compliant with normal distribution were performed through Mann–Whitney *U*-test. The chi-square test was used for the comparison of the qualitative data. As a result of the analysis, *P*-values smaller than 0.05 were accepted as statistically significant.

Results

Age average and mean working period of the electrical workers were determined as 38.4 years and 15.9 years, respectively; age average and mean working period of the control group were 39.1 years and 17.2 years, respectively.

Table 1 The characteristics of the groups

Patient features and EMA exposure	Control Group (n=47)	Study Group (n=47)
Age (years)		
Average age*	39.05±5.85	38.37±7.53
Minimum/maximum age	28–52	29–52
Work experience (years)*	17.21±6.64	15.89±6.72
Smoking	11/47	18/47
Body Mass Index (kg/m^2)*	26.65±4.16	26.21±4.67
Body temperature measurements (°C)*	36.73±5.14	36.92±5.61
Fatigue, anxiety and headaches	16/47	34/47
The average measurement of HVETL exposure (μT)*	N/A	0.53±0.25
Mobile phone usage time* (minutes/month)	537.46±8.47	504.55±7.69
Hair dryer (times/week)*	1.6±0.61	1.1±0.77
Computer use (hours/week)*	23.33±5.61	21.82±4.22

Note: *The data is given as mean ± standard deviation.
Abbreviations: EMA, electromagnetic area; HVETL, high-voltage electric transmission lines; N/A, not applicable.

Age average and mean working period of the study and control group were consistent with each other. Smoking, exhaustion, anxiety, and headache were found lower, whereas the use of cell phone, computer, and hair dryer was found higher in the control group. Body mass indexes were comparable between both groups (Table 1).

No significant difference was observed between the groups in terms of the dietary habits and physical activity ($P>0.05$). In the evaluation of the nutritional habits in the participants, weekly consumption of protein, milk, yogurt, and vegetables were found to be similar. In addition, alcohol addiction, salt habits, and activity levels were found to be quite low, moderate, and low, respectively (Table 2).

Table 2 Nutrition and habits of the participants

Feature	Experimental group	Control group
Smoking	15/47	11/47
Alcohol consumption	5/47	5/47
Salt consumption		
Salt-free	0	0
Low salty	6	3
Moderate salty	43	37
High salty	0	0
Coffee consumption (cups/day) (n)		
None	0	4
1	44	39
2 and over	3	4
Milk consumption (glasses/week) (n)		
1–4	43	42
5–8	4	5
Type of Nutrition	Mixed	Mixed
Exercise and sports activity within the last 5 years;		
Sport such as walking and weight lifting at least 3 times per week on a regular basis.	3	5

In bone DEXA scans, mean BMD of L1–L4 was found −1.13 g/cm^2 in the study group and −0.16 g/cm^2 in the control group. Similarly, BMD of femur was found −63 g/cm^2 and 0.31 g/cm^2 in the study and control group, respectively. A significant difference was observed between BMD measurements of lumbar vertebrae L1–L4 and femur ($P<0.05$). Additionally, a significant difference was found between ALP and P levels ($P<0.05$). Mean ALP values in the control group and the study group were found as 76.00 versus 88.04 U/L, respectively. Blood phosphorus levels were in the control group, and the study group detected as 2.80 versus 3.43 mg/dL, respectively. RANK, RANKL, and OPG levels seem to support a possible increase for tendency to a severe osteoporosis in the individuals working around HVETL ($P<0.001$, $P<0.001$, and $P=0.004$, respectively) (Table 3, Figures 1–3).

Although thyroid function tests (FT3 and TSH) were lower in the study group, they were not statistically significant. The FT4 level was detected significantly lower in the study group than the control group. Furthermore, anteroposterior diameter measures of the thyroid gland of the study group increased when compared with the control group according to the morphometric measurement by USS; however, the result was not statistically significant. Left anteroposterior diameter measure of the thyroid gland was found significantly higher in the study group ($P<0.05$). There was not any significant difference between the groups in terms of nodule and parenchyma (Table 4).

Mean BMD values of L1–L4 and femur according to the age were detected lowest in 20–29 years of age and highest in 30–39 years of age in bone DEXA measurements. No significant difference was observed between BMD measurements of L1–L4 of the lumbar vertebrae and femur (Table 5).

Table 3 Comparison of bone mineral density and blood chemistry parameters between the study and control group

Measured parameters	Control group	Study group	*P*-value
RANK (pg/mL)	82.24 (4.63–263.27)	102.21 (48.63–294.84)	$P<0.001$*
RANKL (pmol/L)	322 (112–1,272)	408.06 (191–1,262)	$P<0.001$*
OPG (pg/mL)	51.98 (29.54–107.22)	45.06 (25.35–83.85)	$P=0.004$*
BMD (L1–L4)	−0.16±0.93	−1.13±0.99	$P<0.05$
BMD (FEMUR)	0.31±1.00	−0.63±0.84	$P<0.05$
ALP (U/L)	76.00±19.71	88.04±22.25	$P<0.05$
P (mg/dL)	2.80±0.41	3.43±0.37	$P<0.05$

Notes: *Mann–Whitney *U*-test was used for binary comparisons between groups in these data, and the values were given as median (minimum–maximum). *t*-test (independent samples *t*-test) for independent samples was applied in other data and values were given as mean ± standard deviation.
Abbreviations: OPG, osteoprotegerin; BMD, bone mineral density; ALP, alkaline phosphatase; P, phosphor.

Depending on the work experience, BMD values of L1–L4 and femur of the electrical workers with work experience of 20 years and over were found higher than those working for 10–19 years in both measurements. There was not any significant difference observed between BMD measurement levels of L1–L4 lumbar vertebrae, whereas a significant difference was observed between BMD levels of femur ($P<0.05$; Table 6).

Due to the work experience, Ca, ALP, RANK, and RANKL values of L1–L4 and femur of the electrical workers with work experience of 20 years and over were found higher than those working for 10–19 years. No significant difference was observed between values of Ca, RANK, and RANKL and a significant difference was detected between serum ALP values ($P<0.05$) (Table 7).

A significant elevation in the OSI and a significant reduction of total oxidative stress were found in the study group. These findings suggest that EMF increases the TOS, decreases the antioxidant status, and causes oxidative stress damage in the electrical workers ($P<0.05$) (Table 8).

Discussion

Electromagnetic waves (EMWs) damage tissues of the body through heating and changing chemical reactions.[20] High EMWs cause damage by heat; hazardous effects appear on the tissues by long-term exposure to low EMWs because of chemical changes. Some energy spreaded by EMW due to the heat effect is absorbed by the human body, and heat accumulation occurs inside the body. Such heat may cause undesired outcomes. The second effect is disruption of the molecules and atoms which are bonded to each other in a living organism.[20]

The limit of professional exposure is 500 μT for a magnetic field.[21] The highest exposure was found on electrical workers by a mean value of 0.161 μT in the studies conducted on different occupational groups.[22] Despite the fact that no measurements could be performed in the substation areas because of security measures and risk of accident, mean daily exposure was found 0.53 μT in the EMF measurements carried out on the workplaces and walking areas. Exposure to an EMF increases sodium, calcium, and magnesium levels in the plasma[23] and the oxidative stress.[15] Studies carried out with a Guinea pig showed that exposure to an EMF causes a significant increase in oxidant products and a decrease in antioxidant enzyme activity.[13] The studies assessing the exposure level generally detected that the exposure at 0.4 μT and above increases the risk of leukemia during childhood.[24,25] Similar studies revealed a relationship between electrical workers exposed to EMF and increased risk for leukemia.[26] In the blood analyses of the electrical workers

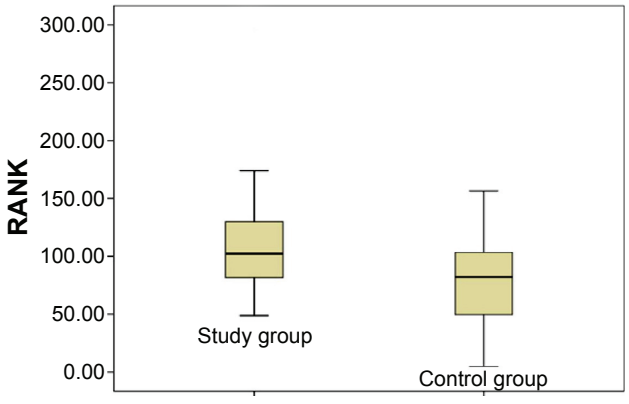

Figure 1 Distribution of RANK values in the study and control groups.

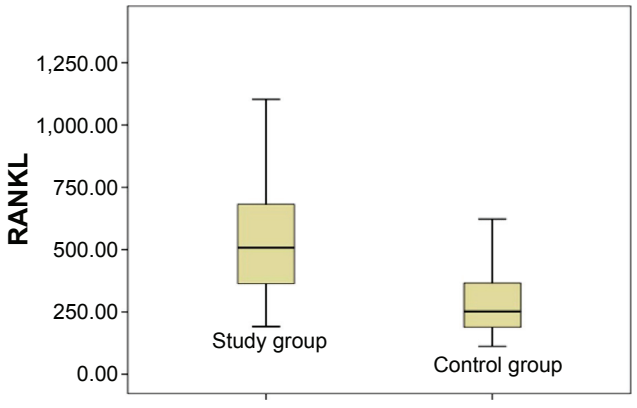

Figure 2 Distribution of RANKL values in the study and control groups.

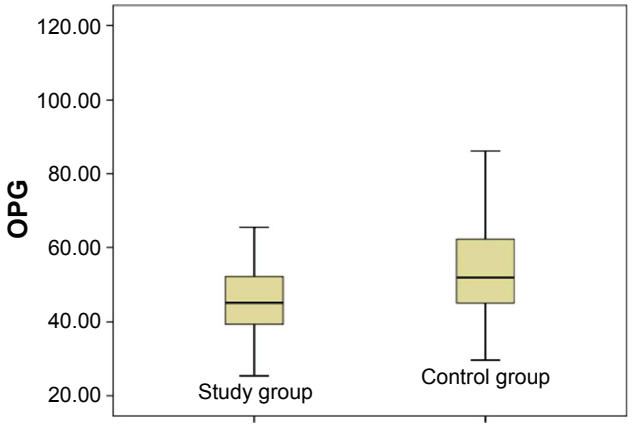

Figure 3 Distribution of OPG values in the study and control groups.
Abbreviation: OPG, osteoprotegerin.

in the present study, an increase in Ca, P, and oxidative stress levels and a decrease in antioxidant enzyme activities were detected. We believe that such effects which were observed on electrical workers who are exposed to high EMF even in breaks might have been caused by spending a significant part of their shift in substations and high-voltage transmission lines.

Important health problems of the present day include osteoporosis, fractures, and stress fractures. In bone DEXA scans, mean BMD measures of L1–L4 lumbar vertebrae and femur as well as ALP and P levels were observed significantly higher in the study group than the control group. Moreover, levels of RANK, RANKL, and OPG support the idea that a strong predisposition for osteoporosis may increase for those working around HVETL. In comparison between the experimental and control groups, bone loss was found to be resulted from the EMF exposure and not from age. These results indicate that bone damage may increase due to the EMF exposure.

Experiments on mice indicated that bone density and volume decrease, osteoporosis progressing with fractures and deformities appear in the absence of OPG,[27,28] and osteoporosis is reversed by intravenous OPG injection.[29] Osteopetrosis characterized with osteoclastogenesis was observed on the mice of which genetic structure of OPG was modified.[30] These data show that OPG is necessary to preserve the bone mass physiologically. RANKL, which is an agent stimulating the dendritic cells, acts as a life factor for mature T cells and regulates proliferations.[31,32] Such activities were observed to be dependent to the activation of RANKL by binding to membrane receptor RANK.[33] Similar approaches with OPG were tried to understand the role of RANKL in the bone metabolism. Despite OPG, severe osteoporosis was observed on the mice with genetically modified RANKL;[8] complete disappearance of osteoclasts and development of osteoporosis were observed in the mice without RANKL.[34,35] According to these data, OPG is a strong bone protective agent, whereas RANKL is a preresorptive factor. In vitro trials also seem to support the in vivo data.[34–37] Although there are studies indicating that low-frequency EMF provides an increase on recovery of bone fractures and BMD in the literature,[38–41] therapeutic doses of EMWs for osteoporosis were only observed when they were applied in pulses with low doses of 15–72 Hz.[42] Long-term occupational exposure to EMWs in higher doses has

Table 4 Comparison of thyroid function tests and thyroid's diameter measurements between groups

Measured parameters	Control group	Study group	*P*-value
FT3, mean ± SD	3.34±0.32	3.22±0.51	0.302*
FT4, mean ± SD	1.21 (0.92–2.67)	1 (0–3.19)	**<0.001****
TSH	1.66 (0.48–4.34)	1.41 (0.01–7.72)	0.180**
RapD	16.15 (12.5–24)	18 (8–37)	0.056**
LapD	15.6 (12.1–24.3)	17 (10–30)	**0.037****
Istmus D	3.35 (2.20–5.9)	3.3 (1–13)	0.647**

Notes: *Independent *t*-test and **Mann–Whitney *U*-test was applied. The data were presented as median (minimum–maximum) unless stated otherwise. Bold *P*-value shows the difference was statistically significant ($P<0.05$).
Abbreviations: RapD, right anteroposterior diameter; LapD, left anteroposterior diameter; Istmus D, tiroid istmus diameter; TSH, thyroid-stimulating hormone; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid-stimulating hormone; SD, standard deviation.

Table 5 Comparison L1–L4 and femoral BMD values with the DEXA results as per study group's ages

Bone type	Age (years)	N	T-score	*P*-value
L1–L4	20–29	4	−1.35±0.65	
	30–39	24	−0.97±0.53	0.504
	40–49	15	−1.28±0.57	0.904
	50 and older	4	−1.28±0.62	0.918
Femur	20–29	4	−1.02±0.51	
	30–39	24	−0.39±0.48	0.167
	40–49	15	−0.88±0.58	0.770
	50 and older	4	−0.78±0.34	0.674

Note: Independent *t*-test was applied. The data were given as mean ± standard deviation.
Abbreviations: BMD, bone mineral density; DEXA, dual-energy X-ray absorptiometry; *t*-test, independent samples *t*-test.

Table 6 Comparison L1–L4 and femoral BMD values with the DEXA results according to work experience

Bone type	Work experience (years)	N	T-score	*P*-value
L1–L4	10–19	32	−1.02±0.55	0.255*
	20 and older	15	−1.36±0.76	
Femur	10–19	32	−0.44±0.28	**0.021***
	20 and older	15	−0.94±0.51	

Notes: *Independent *t*-test was applied. Bold *P*-value defines the significant difference ($P<0.05$). The data were given as mean ± standard deviation.
Abbreviations: BMD, bone mineral density; DEXA, dual-energy X-ray absorptiometry.

Table 7 Comparison of the bone biochemistry parameters according to work experience

Biochemistry parameters	Work experience (years)	N	Mean	*P*-value
Ca	10–19	32	9.27±0.27	0.872*
	20 and older	15	9.29±0.50	
P (mg/dL)	10–19	32	2.85±0.44	0.281*
	20 and older	15	2.71±0.31	
ALP (U/L)	10–19	32	84.93±13.63	**0.044***
	20 and older	15	94.67±23.63	
Creatine (mg/dL)	10–19	32	0.90±0.11	0.69*
	20 and older	15	0.89±0.08	
RANK (pg/mL)	10–19	32	96.89±41.96	0.182*
	20 and older	15	113.56±82.20	
RANKL (pmol/L)	10–19	32	391.33±109.84	0.166*
	20 and older	15	443.78±168.88	

Notes: *Independent *t*-test was applied. Bold *P*-value defines the significant difference ($P<0.05$). The data were given as mean ± standard deviation.
Abbreviations: ALP, alkaline phosphatase; P, phosphor.

a reverse effect. Atay et al[42] detected a significant decrease in BMD levels in the iliac wing area where mobile phones with 900–1,800 MHz are carried when compared with the other side in their study. Similarly, Cidem et al reported a decrease in bone density of the forearm which are used by the mobile phone owners while holding the phone.[43] Kunt and Dayıoğlu and Kunt et al found in their study conducted on the radiology employee that the lowest densitometry level was in MRI employee.[44,45]

In the clinical trials reporting the preventive effect for osteoporosis and increase of BMD, treatment protocols applied to the study groups are dependent on the principle of application of a certain EMW dose for a certain period. In other words, a doze of exposure is certain and may be limited. However, a decrease in femoral and lumbar BMD levels of the electrical workers was met. This is contrary to the protective effect of low-frequency EMWs on bone metabolism. Possible factors include dose of the magnetic field exposed and duration of exposure. Although the effect of low-frequency EMWs to prevent osteoporosis was brought into the forefront in the literature, long-term exposure to the magnetic field around HVETL may cause a hazardous effect in the bone metabolism rather than a protective effect and creates an effect which is similar to those by devices creating high-frequency EMF such as cell phones. From this point of view, we believe that low-dose EMFs may have a therapeutic effect, whereas long-term and high-dose EMWs have a destructive effect on the BMD.

Effects of low-frequency EMWs of which electrical workers who are exposed to electromagnetic radiation most is not like the effects of a high-frequency EMWs. No temperature increase was detected in the temperature measurements performed on the electrical workers. Therefore, heat-dependent effects such as MRI devices creating high-EMWs are not observed in electrical workers. However, the exposure of these individuals to low-frequency EMWs intermittently for a long period, in other words, the effects of chronic exposure may appear after years. The reason for that is the inability of the organism to repair the damage until next exposure and accumulation of the damages for exposures to repetitive EM radiation, even in low frequencies.

Besides studies reporting that EMF activates the formation and growth of the bones, inhibits osteoblastic activity, provides contribution to the healing of the bone fractures, and affects the granulation of formation of fibrous tissues in the wound healing;[46,47] some studies demonstrated that biological effects of the low-frequency at the cellular level include creating change at the levels of proliferation and differentiation,[48,49] changes at the levels of messenger ions such as Ca^{2+},[50,51] and creating changes in the shape and format of the cells.[52,53] Studies conducted about the effects of EMFs on the bone formation and fracture healing report different mechanism of action. In these studies, the mechanisms of action have been explained as the osteogenesis-stimulating mechanism,[54–58] and physiological and physical effects on the bone metabolism and cellular processes. Furthermore, it has been reported that EMF has effects on the calcium channels, intracellular ionized calcium changes, receptor behavior and genes, and that EMF increases the synthesis and transcription of deoxyribonucleic acid (DNA), intercellular calcium and the synthesis of messenger ribonucleic acid of type-I collagen, stimulating the production of extracellular

Table 8 Comparison of serum oxidative stress index between groups

Oxidative stress parameters	Control group	Study group	*P*-value
TAS (mmol Trolox Equiv/L)	1.93 (0.40–3.73) 0.84	1.62 (0.16–3.96)	**0.017****
TOS (μmol H_2O_2 equiv/L)	7.63±3.10	9.39±3.68	**0.013***
OSI (AU)	487.82±462.29	957.32±1,201.97	**0.013***

Notes: *Independent *t*-test, **Mann–Whitney *U*-test. Data are median (minimum–maximum) unless otherwise indicated. Bold *P*-value defines the significant difference ($P<0.05$).
Abbreviations: TAS, total antioxidant status; TOS, total oxidant status; OSI, oxidative stress index.

matrix.[56,58] According to all of these results, further radiologic, biochemical, and histopathologic studies are needed to demonstrate the effects of the low- and high-frequency EMFs on the bone tissues and fracture healing as well as to clarify EMFs' mechanisms of action.

Many studies were carried out for the effect of EMF to thyroid hormone synthesis and different results were reported. In a large-scale study, Bergamaschi et al detected no significant difference on the workers exposed to EMF because of cell phone use in terms of the TSH level;[59] Selmaoui et al found that low-dose EMF exposure for every other night or continuously did not affect serum total-free thyroxin (T4) and triiodothyronine (T3) as well as TSH levels.[60] No significant effect of low-dose EMF exposure for a long period was found on TSH in human studies carried out in a similar manner with less participation,[61,62] whereas no difference was detected on individuals exposed to low-density EMF for a long period in terms of the frequency of thyroid cancer.[63] Koyu et al found a significant decrease in T3, T4, and TSH levels in the rats who were exposed to a low-dose EMF for 4 weeks when compared with the control group.[64] Another study carried out with rats detected a significant decrease in serum thyroid hormone levels as a result of low-dose EMF exposure for a long period in comparison with the control group.[65,66] De seze et al detected on volunteer males that cell phone use for 2 hours a day for one month reduced TSH levels by 21%.[67]

A positive correlation was shown between the effect of radiation on different endocrine organs and radiation dose and exposure duration.[68] Low TSH levels were shown more frequent in those with longer duration of exposure to EMF and duration of talking with cell phone,[46] whereas some studies showed an increase in thyroid hormone and TSH levels as a result of long-term exposure to EMF of rats.[69,70] In the present study, we found FT4 levels significantly lower in the workers who are exposed to EMF for a long period, and no significant difference in FT3 and TSH levels were detected. Although a low dose causes a decrease in T4, it may depend on long-term exposure to EMF. Moreover, more nodules were observed in the study group in percentage when compared to the normal population, but no statistically significant difference was detected. In the comparison for gland sizes, a significant increase was detected in the dimensions of the left lobe particularly in the study group than the control group. Rajkovic et al detected an increase in the volume density of thyroid follicles histologically on the rats exposed to a low-dose EMF for 3 months.[65] Exposure to ionizing radiation increases the risk of benign or malign nodule. Palpable thyroid nodules are detected in 20%–30% of the population affected by radiation.[71] However, there is not any study which investigates the effect of electromagnetic radiation on the thyroid gland in the literature. In the present study, occupational higher electromagnetic radiation is not confronted as a significant risk factor statistically in terms of thyroid nodule frequency and parenchyma echogenicity. Nevertheless, the increase in the gland sizes is statistically significant.

Conclusion

One of the occupational groups who are exposed to electromagnetic radiation most is electrical workers. The electrical workers who are exposed to EMF radiation caused by high-voltage transmission lines and transformers for a long period were observed to complain about general indisposition, exhaustion, apathy, anxiety, and headache. Furthermore, a decrease in BMD, serum ALP, Ca, P, RANK, RANKL, and antioxidant enzyme levels as well as an increase in oxidative stresses and OPGs were observed. Consequently, it was observed that the balance between construction and destruction in the bone metabolism of the electrical workers who are employed in HVETL replaced toward destruction and led to a decrease in OPG levels and an increase in RANK and RANKL levels. In line with the previous studies reporting that long-term exposure to an EMF causes disorders in many organs and systems, it is considered that long-term exposure to an EMF affects bone and thyroid metabolism and also increases OSI by increasing the TOS and decreasing the antioxidant status.

Periodical investigations, EMF measurements around the workplaces, and raising awareness of the electrical workers about these exposures should be done to detect possible negative impacts on the electrical workers who are exposed to electromagnetic radiation.

The present study has some limitations. The first limitation is that the majority of the employees had not any thyroid USS before and were not aware of the nodule during the study. The second limitation is the requirement of new studies including more electrical workers to obtain more reliable data.

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Disclosure

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Antenna Towers make it a Dog's Life…

Animals don't know anything about electromagnetic pollution. It just makes them sick. The effects of cellular and wireless phones on the health of dogs, cats, horses and cows.

Hiding is futile: Cellular radiation can find you everywhere.

In today's day and age, we're no longer taught how to understand nature. We're taught instead to analyze it, change it and exploit it. There are only a handful of people today that fully appreciate nature's inherent wisdom. Humans tend to primarily focus their attention on quick success and comfort. Viktor Schauberger's warning, however, that "if we hope to survive, we must first understand nature and then copy it," has never been more topical.

Nature is the expression of a vision, an elaborate, detailed and planned undertaking based on principles that are valid in both the visible and invisible world, in the macro and microcosm. Modern science attempts to solve the puzzle of life through analysis and detailed research. It constantly overlooks the fact, however, that things are often more than the sum of their parts.

Nature is the example. It shows us the principles of life, what's good for our health and what makes us sick. We're faced with these perfect examples on a daily basis, but modern science and today's economics forge their own "laws" that butt heads with nature and haughtily hope to win.

We disturb and destroy nature on a daily basis with our environmentally adverse technologies. Plants and animals suffer stoically and quietly from the effects of mobile radio and similar communications technologies. AC-produced microwaves don't occur naturally in nature, so we can't expect it to know how to react to them either. Dying forests have as much, if not more, to do with microwaves than with CO2 and acid rain.

A bird flock's or a whale's sense of orientation becomes scrambled. They become lost or end up beaching, thus meeting their end. Many bird species are breeding less often and are in danger of becoming extinct. Cats, dogs, birds, cattle, bees and horses are the focus of the rest of this article and the following cases highlight exactly what we're doing to our beloved companions every day.

Animals may not know the danger of microwaves, but they still suffer from their effects. Animals are neither hysterical nor hypochondriac and make the perfect test subjects for the allegedly “unproven” side effects of mobile phones and other communications radiation. Animals cannot lie and don’t make a show of their suffering. They simply become sick and die.

From Bees to People

“The information-processing and function systems of today’s humans, plants and animals are bombarded with artificial magnetic, electric and electromagnetic fields from numerous mobile and telecommunications sources in a concentration and intensity as never before. The consequences of these developments put forth by their critics cannot be overlooked any longer. Bees and other insects are disappearing. Birds avoid certain regions and are disoriented in others. Humans suffer functional problems and other sicknesses. And the evidence that suggests some of these problems may be inheritable means we’re passing them on to the next generation.”


Puzzling bee deaths: Cell phone radiation leads to deadly wrong turns.

This is the sobering testimony of Dr. Ulrich Warnke, an internationally renowned German scientist at the University of Saarland, given in his recently published report, *Bienen, Vögel und Menschen über die Zerstörung der Natur durch Elektrosmog (Bees, Birds and Humans – on Electrosmog’s Destructive Effects on Nature), following years of research.*

The bio-scientist is familiar with nature’s electromagnetic ways like few others. In his study, which marks the beginning of a series of newly published literature by independent scientists, doctors and technicians, he’s shown how intelligently and delicately nature has woven electrical and magnetic fields into the fabric of life. He’s just as convincing at showing how irresponsible we’ve been recently when it comes to dealing with these natural forces. By his approximations, modern humanity is posed to destroy in decades, with electromagnetic radiation what nature has built over the course of millions of years.

The introduction to Ulrich Warnke’s report explains: “The destruction of the necessities of life has already wiped out many species for good. Most people have remained uninterested, however, since these species have filled ecological niches, not affecting their personal lives in any way. Now, the endangerment of these animals is, however, threatening human existence in new and unexpected ways. The constantly

changing and increasingly stronger artificial energy fields emanating from technological sources confuse animals that rely on the electrical, magnetic and electromagnetic fields within the Earth's atmosphere for orientation and navigation and make it impossible for them to find their way back to their dwelling grounds. Most humans would assumedly take no note of this if it didn't affect one of the most important insect species: the honeybee. The honeybee is an irreplaceable link in the process of fructification. No bees means scarce fruit, vegetable and crop harvests."

"If the bee disappeared off the surface of the earth, then man would only have four years left to live. No more bees, no more pollination, no more plants, no more animals, no more people," wrote Albert Einstein.

Worker bees are no longer returning to their hives, whereby the queen and the entire brood perish. Science has already come up with a name for this occurrence: *Colony Collapse Disorder (CCD),* which accounts for a previously unexplained disruption in bee behavior.1 Unusual drops in bee populations have already been observed in Switzerland, the United States, Canada, New Zealand and, most recently, in Austria, Germany, South Tyrol, Spain and Poland. 25 to 50 percent of American beekeepers have reported losses due to CCD. Within half a year, 50 to 90 percent of their bees disappeared. Those that have remained are so weak that they hardly produce any honey. The great bee extinction is already under way in the USA. Lately, truckloads of beehives have been imported for large sums of money in order to pollinate the fields. This is how far removed from nature we've become. 2006 saw an 11% drop in US honey production. It's looking about the same in Switzerland.

Investigations have uncovered various sources for the recent phenomena, but none fully come to a conclusion: winters alone appear to not have been severe enough to account for the losses. There aren't any genetically modified plants in Switzerland, for instance, whose pollen can harm bees. Monoculture, the use of land for only one crop, doesn't exist in Switzerland to the degree it does in America. Poisonous insecticides have been used for decades.

The Austrian Ministry of Land Use, Forestry, Environment and Water Use reported the following to Dr. Andreas Kohl at the National Council in April 2006: "Scientific research has proven that low frequency electromagnetic fields can have a negative effect on bees. (…) Studies show that bees in an electrical field of over four kilovolts per meter, for example, in the direct vicinity of a 380 kv high-voltage power line, produce less honey and show an increased mortality rate."

Prof. Dr. Ferdinand Ruzicka, a beekeeper himself and published author in various beekeeping journals, compiled his own extensive findings from personal observations and surveys among fellow beekeepers. "The problems only surfaced once multiple transmitter towers went up next to my bee colonies." According to Ruzicka's observations, his bee populations were weakened by cellular communications radiation to the point that they were more susceptible to various diseases and entire populations ended up failing completely.

Bees, as well as butterflies, whose overall populations have shrunk dramatically in recent years, are considered to be very delicate life forms. According to Dr. Ruzicka, bee populations fifteen years ago, compared to bees today, were able to withstand a considerably more aggressive infestation of Varroa mites.

A Veterinarian Sounds the Alarm

The veterinarian Christian Métraux, from Wabern, Switzerland, gives an account of his experiences with cordless telephones and wireless Internet connections and their effects on house pets. Electromagnetic high frequencies are generated by cordless telephones (DECT) and wireless Internet and computer networks (WLAN). With few exceptions, the DECT-telephone ceaselessly produces electrosmog, spreading it day and night throughout the entire house, even when the telephone is not in use or when the receiver is in its cradle. WLAN Access Points send their electronic pulses as long as they are connected to a power source.

According to Métraux: “The problem is not so much the momentary contamination as it is the accumulation over a longer period of time. This explains why a person often does not make a connection between definitive, current disturbances and the original acquirement of this technology. Many disturbances appear subtly and are not immediately perceivable. If this unnoticed congestion is already quite advanced and deep, acute ailments can also emerge as if out of thin air.”

The long-term risks associated with high-frequency wireless technologies are still relatively unknown or are trivialized. Many think that “only” the cell phone is harmful. “In my practice, I handle animals with traditional medicine and acupuncture. For me, it is principally about making an exact diagnosis, searching for the causes of a sickness, so that the proper therapy can be exactly determined. A purely symptomatic treatment cannot eliminate the causes, but may help temporarily. Within the scope of the therapy, the rapid removal of the perturbing cause should be the highest priority.”

The following examples make this clear: electromagnetic high frequencies can be the cause of illness as well as an impediment to treatment.

E-smog Also Makes Animals Sick

Whether horses, dogs or cats – a wireless DECT-telephone in the home harms all.

The following examples derive from the everyday practice of Christian Métraux. The veterinarian reported that a dog was lame in the fore legs and the hind leg for six months. The acupuncture diagnosis identified acupuncture points that are typical for the strain from high-frequency electrosmog. As soon as the cordless telephone had been taken away, the lameness disappeared. The healing process was aided by an acupuncture treatment. Unfortunately, the dog suffered a relapse when he was taken for the holidays to a family that had a DECT-telephone in their house. Three days after his return to his interference-free home, the ailments disappeared once again.

The owner of the dog suffered from headaches and painful joints (pain in her elbows, shoulder joint and fingers) for seven years. Both the family doctor, who had treated her for osteoarthritis, as well as a naturopathic doctor, who had prescribed elixirs to her, had no success. Without the DECT-telephone, most of her ailments completely disappeared after two months. Suggestively, only the headaches would appear now and then.

Electromagnetic high frequencies as an impediment to treatment: A horse suffering from chronic lameness in the right ankle. After four treatments, classical acupuncture brought about decent but only temporary success and arthritis could not be identified in the X-ray photographs. During every session, however, the same, typical acupuncture points were consistently disturbed, which in my experience points to a

contamination of high frequency electrosmog. As soon as the DECT-telephone was removed from the house, the horse's ailments subsided within a few days without any kind of further treatment. The horse has not relapsed since then. The owner of the horse owned a DECT-telephone for two years and, a year after this acquisition, she started suffering from intense pains in her upper jaw below her right eye. Dentists and eye doctors, acupuncture and changing the lenses in her glasses did not bring any success or solution. After the removal of the DECT-telephone, however, the pains—which had become almost unbearable—began to progressively subside after two days and completely disappeared shortly thereafter.

Electromagnetic high frequencies obviously disturb gland functions as well: A young dog suffering from chronic diarrhea and dysfunction of the thyroid gland. Different treatments were unsuccessful. After the cordless telephone was experimentally removed from the home, the dog became healthy. After weaning the dog off of hormone treatment, two further blood tests, taken 14 months apart from each other, confirmed that the thyroid gland was working correctly once again. The DECT-telephone was never plugged in again and the diarrhea never appeared again.

Electromagnetic high frequencies also lead to acute, spontaneous ailments, as the following example demonstrates: a horse with an acute, painful swelling in the area of its right hip. After three weeks of unsuccessful treatment, the horse was to be taken to the slaughterhouse. Since the typical acupuncture symptoms were present, we asked the owner to remove his DECT-telephone as a last resort, thereby discharging the electrosmog from the acupuncture points. And lo and behold: a rapid and lasting recovery occurred. In the meantime, the horse is working quite normally again and taking part in exhibitions!

A guinea pig suffering from acute occurrences of paralysis in its hindquarters. It was no wonder that there was a DECT-transmitting station in the room where it lived. The use of acupuncture led to an immediate recovery in the practice and the animal did not suffer a relapse, because the owners replaced their DECT-telephone with a classic corded telephone that very day.

Electromagnetic high frequencies lead to incurable skin and eye diseases: A cat was in the care of a veterinarian for a year due to a skin disease on the outside of the ear. Many salves and treatments were unsuccessful. A few days after the removal of the DECT-telephone, the skin lesion began to heal and then to fully convalesce. A second cat in the household is, furthermore, considerably less aggressive since then.

End of extract „Antenna Towers make it a Dog's Life…"

Vet Christian Métraux further outlines more examples about the negative effects of electro-smog from his professional experience, and gives advice as to what affected pet owners can do about it. This article also explores studies about the (not so) mysterious cattle deaths on farms due to mobile phone antenna, as well as the new incidence of crippled chicks. We also look at the sobering conclusions that renowned researchers are drawing from all this. Find the entire article in our Facts are Facts print edition no.3.

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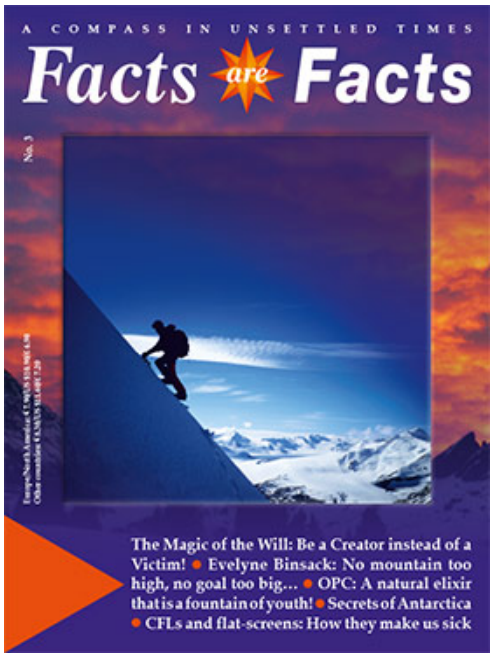

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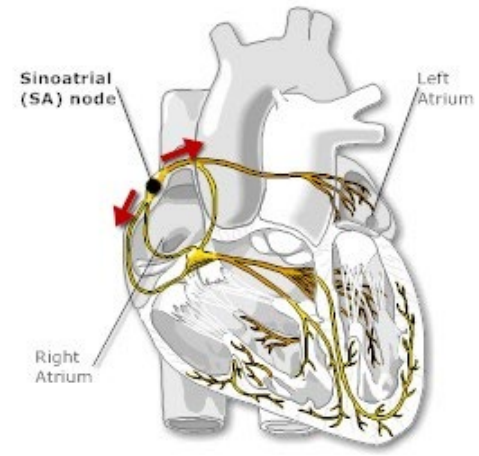
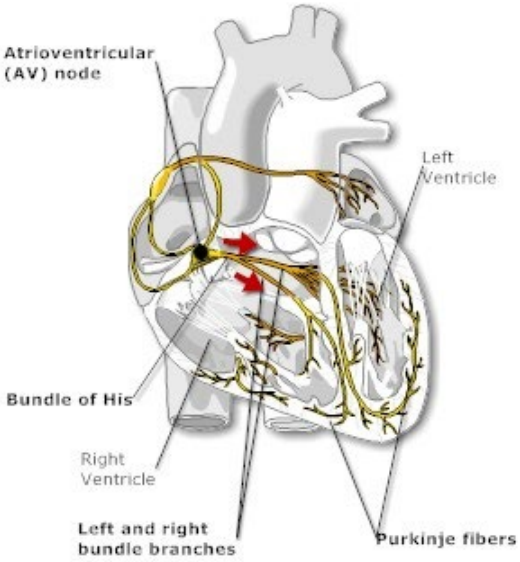


The heart's electrical system controls all the events that occur when your heart pumps blood.
Each beat of your heart begins with an electrical signal from the sinoatrial node, called SA node.

The signal is generated as the two vena cavae fill your heart's right atrium with blood from other parts of your body. The signal spreads across the cells of your heart's right and left atria. This signal causes the atria to contract. This action pushes blood through the open valves from the atria into both ventricles.

The signal arrives at the AV node near the ventricles, where it slows for an instant to allow your heart's right and left ventricles to fill with blood. The signal is released and moves to the His bundle located in the walls of your heart's ventricles.



The signal is released and moves next to the bundle of His located in your heart's ventricles. From the bundle of His, the signal fibers divide into left and right bundle branches which run through your heart's septum.

The signal leaves the left and right bundle branches through the Purkinje fibers that connect directly to the cells in the walls of your heart's left and right ventricles.
As the signal spreads across the cells of your heart's ventricle walls, both ventricles contract, but not at exactly the same moment. The left ventricle contracts an instant before the right ventricle. This pushes blood through the pulmonary valve (for the right ventricle) to your lungs, and through the aortic valve (for the left ventricle) to the rest of your body.

As the signal passes, the walls of the ventricles relax and await the next signal.

Source: National Heart Lung and Blood Institute, National Institutes of Health. nhlbi.nih.gov

http://www.whale.to/b/persinger.html

ON THE POSSIBILITY OF DIRECTLY ACCESSING EVERY HUMAN BRAIN BY ELECTROMAGNETIC INDUCTION OF FUNDAMENTAL ALGORITHMS

By M.A. Persinger

Laurentian University

June 1995

Perceptual and Motor Skills, June 1995, 80, 791-799.

Summary.-- Contemporary neuroscience suggests the existence of fundamental algorithms by which all sensory transduction is translated into the intrinsic, brain-specific code. Direct stimulation of these codes within the human temporal or limbic cortices by applied electromagnetic patterns may require energy levels which are within the range of both geomagnetic activity and contemporary communication networks. A process which is coupled to the narrow band of brain temperature could allow all normal human brains to be affected by a subharmonic whose frequency range at about 10 Hz would only vary by 0.1 Hz.

The pursuit of the basic algorithms by which all human brains operate can be considered a central theme of modern neuroscience. Although individual differences are expected to accommodate most of the variance in any specific neurobehavioral measure, there should exist basic patterns of information and structure within brain space. They would be determined by the human genome, i.e., be species-specific, and would contribute to or would serve as the substrate upon which all phenomena that affect neurobehavioral measures are superimposed.

One logical extrapolation to a neurophysical basis of consciousness is that all experiences must exist as correlates of complex but determined sequences of electromagnetic matrices. They would control the theme for the format of cognition and affect while the myriad of possible serial collections of random variations of "noise" within the matrices could potentially differentiate between individual brains. Identification of these

sequences could also allow direct access to the most complex neurocognitive processes associated with the sense of self, human consciousness and the aggregate of experiential representations (episodic memory) that define the individual within the brain (Squire, 1987).

The existence of fundamental commonalities between all human brains by which a similar physical stimulus can affect them is not a new concept. It is demonstrated daily by the similar shifts in qualitative functions that are evoked by psychotropic drugs. Classes of chemical structures, crudely classified as antidepressant, antipsychotic, or anxiolytic compounds, produce general attenuations of lowered mood, extreme eccentric thinking, or extreme vigilance. The characteristics of these changes are very similar within millions of different human brains regardless of their cultural or genetic history. The idiosyncratic experiences such as the specific thoughts and images which reflect each person's continuing process of adaptation are superimposed upon these general functions. When translated into the language of neuroelectrical domains, the unique components of individual consciousness would be both embedded within and interacting with the species-invariant patterns.

We have been studying the phenomenological consequences of exposure to complex electromagnetic fields whose temporal structures have been derived from the most recently observed neuroelectrical profiles such as burst-firing or long-term potentiating sequences (Brown, Chapman, Kairiss, & Keenan, 1988) which can be considered the prototypical basis of a major domain of brain activity. These temporal patterns of potential codes for accessing and influencing neuronal aggregates have been applied across the two cerebral hemispheres (through the regions of the temporoparietal lobes or within the region of the hippocampal-amygdaloid complex) of the brain as weak electromagnetic fields whose intensities are usually less than 10 milligauss (1 microT). The purpose of this research, as suggested by both E.R. John (1967) and Sommerhoff (1974), is to identify the basic codes for the language of the representational systems within the human brain.

In the tradition of Johannes Mueller, we have assumed that the normal transduction of stimuli by sensors into afferent, graded potentials and the subsequent translation into digital patterns of action potentials (which are more likely to behave functionally as a composite of pixels within a neural field) can be circumvented by _direct_ introduction of this information within the brain. Induction of complex information would require simulation of the resonance patterns which would normally be transiently created by sensory afferents. The basic premise is

that synthetic duplication of the neuroelectrical correlates generated by sensors to an actual stimulus should produce identical experiences without the presence of that stimulus.

We have focused upon the polymodal and most labile portions of the parahippocampal (Van Hoesen, 1982) and entorhinal cortices (Vinagradova, 1975) and the anterior superior gyrus of the temporal cortices (Bancaud, Brunet-Bourgin, Chauvel, & Halgren, 1994) as the region within which circumvention would be most probable. Extraction and translation of neural patterns from different sensory inputs into common codes occur within these regions before they are consciously perceived (Edelman, 1989). That central codes are present was shown by E.R. John (1967, pp. 348-349) who reported an immediate transference of the operant control of a response from a pulsatile auditory stimulus to a pulsatile visual stimulus if its _temporal_pattern_ was identical to the previous (acoustic) stimulus.

We (Fleming, Persinger, & Koren, 1994) reported that whole brain exposure of rats to a 5-microT burst-firing magnetic field for 1 sec. every 4 sec. evoked an analgesic response that was similar to that elicited by the application of more noxious, tactile simulation for 1 sec. every 4 sec. directly to the footpads. Direct electrical stimulation of the limbic structures which simulate episodic, systemic application of muscarinic (cholinergic) agents can evoke electrical kindling (Cain, 1989). More recently, direct induction of chaotic electrical sequences within the labile CA1 region of the hippocampus has been shown either to promote and attenuate paroxysmal discharges (Schiff, Jerger, Duong, Chang, Spano, & Ditto, 1994).

These results strongly indicate that imitation of the temporal pattern of sensory transmission directly within the brain by any nonbiogenic stimuli can evoke changes which are just as effective as (and perhaps require less energy than) classical transduction. As stated more recently and succinctly by E.R. John (1990), the fundamental operation of brain electrical activity suggests that some form of frequency encoding may play a significant role in informational transactions within and between brain structures. Consciousness would be associated with an electromagnetic pattern generated by a neural aggregate with invariant statistical features which are independent of the cells contributing to each feature (John 1990, p. 53).

The effects of applied time-varying magnetic fields upon brain activity have been considered minimal or within the range of normal biological limits unless the intensity of the field exceeded natural endogenous or exogenous (ambient) levels by several orders of magnitude. Until very recently, almost all of the studies from which this conclusion was derived involved

highly redundant stimuli such as 60 Hz fields or repetitive pulses. A simple illustration presents the problem: only 1 min. of a 60-Hz sine-wave field exposes a neural net to 3,600 presentations (60 sec. x 60 cycles per sec.) of the _same_ redundant information. Even general estimates of habituation (Persinger, 1979) such as the equation H=IRT2/Rt (IRT=interresponse time, Rt=duration of response) indicate that habituation to the stimulus would have occurred long before its termination after 1 min. Although the burst-firing frequencies (100 to 200 Hz) of the hippocampal neurons, for example, exceed this pattern, they are not temporally symmetrical and exhibit a variability of interstimulus intervals that would contain different information and would attenuate habituation.

The apparent dependence of organismic responses upon the intensity of the applied electromagnetic field, the "intensity-dependent response curve," could simply be an artifact of the absence of biorelevant information within the wave pattern. If the temporal structure of the applied electromagnetic field contained detailed and biorelevant information (Richards, Persinger, & Koren, 1993), then the intensity of the field required to elicit a response could be several orders of magnitude below the values which have been previously found to elicit changes. For example, Sandyk (1992) and Jacobson (1994) have found that complex magnetic fields with variable interstimulus pulse durations could evoke unprecedented changes in melatonin levels even with intensities within the nanoT range.

The classical counterargument that "very strong" magnetic fields must be present "to exceed or to compensate for the electromagnetic noise associated with intrinsic (Boltzmann) thermal energies" is based upon equations and calculations for the quantitative indices of aggregates of molecular activity and not upon the _pattern_ of their interaction. There are other possibilities. For example, Weaver and Astumian (1990) have shown mathematically that detection of very weak (microV/cm) fields can occur if the response is exhibited within a narrow band of frequencies; the detection is a function of both thermally induced fluctuations in membrane potential and the maximum increment of change in the membrane potential which is evoked by the applied magnetic field. The ion-cyclotron-resonance model which was initiated by the research of Blackman, Bename, Rabinowitz, House, and Joines (1985) and supported by Lerchl, Reiter, Howes, Honaka, and Stokkan (1991) indicates that, when an alternating magnetic field at a distance (resonance) frequency is superimposed upon a steady-state magnetic field, the movement of calcium and other ions can be facilitated with very small

energies. More than 25 years ago, Ludwig (1968) developed a compelling (but hereto ignored) mathematical argument which described the absorption of atmospherics within the brain.

Above these minimal thresholds, the information content of the wave structure becomes essential. The simplest analogy would be the response of a complex neural network such as a human being to sonic energy. If only a 1000-Hz (sine wave) tone were presented, the intensity required to evoke a response could well exceed 90 db; in this instance the avoidant response would be overt and crude. However, if the structure of the sonic field was modified to exhibit the complex pattern which was equivalent to biorelevant information such as "help me, I am dying," field strengths several orders of magnitude weaker, e.g., 30 db, could be sufficient. This single, brief but information-rich stimulus would evoke a response which could recruit every major cognitive domain.

If the information within the structure of the applied magnetic field is a major source of its neurobehavioral effect, then the "intensity-dependent" responses which are interpreted as support for experimental hypotheses of biomagnetic interaction could be both epiphenomenal and artifactual. Such amplification of electromagnetic-field strengths would also increase the intensity of the extremely subtle and almost always ignored subharmonics, ripples, and other temporal anomalies which are superimposed upon or within the primary frequency. These subtle anomalies would be due to the artifacts within the different electronic circuits and components whose similarities are based upon the fidelity of the endpoint (the primary frequency) despite the different geometries employed to produce the endpoint.

If information rather than intensity is important for interaction with the neural network (Jahn & Dunne, 1987), then _these_ unspecified "background" patterns may be the source of both the experimental effects and the failures of interlaboratory replications. A concrete example of this problem exists within the putative association between exposure to power (60 Hz) frequency magnetic fields and certain types of cancer. The existence of these transients, often superimposed upon the fundamental 60-Hz frequency, is still the least considered factor in the attempts to specify the characteristics of the fields which promote aberrant mitosis (Wilson, Stevens, & Anderson, 1990).

Within the last five years, several researchers have reported that direct and significant effects upon specific neuropatterns can be evoked by extremely weak magnetic fields whose intensities are within the range of normal geomagnetic variations. Sandyk (1992) has discerned significant changes in vulnerable subjects

such as patients who were diagnosed with neurological disorders following exposure of short durations to magnetic fields whose strengths are within the pT to nT range but whose spatial applications are multifocal (a fasces-type structure) and designed to introduce heterogeneous patterns within a very localized brain space. The effective components of the field (which are assumed to be discrete temporal patterns due to the modulation of the frequency and intensity of the electromagnetic fields) are not always obvious; however, the power levels for these amplitudes are similar to those associated with the signals (generated globally by radio and communication systems) within which most human beings are exposed constantly.

The most parsimonious process by which all human brains could be affected would require (1) the immersion of all the approximately 6 billion brains of the human species within the same medium or (2) a coercive interaction because there was facilitation of a very narrow-band window of vulnerability within each brain. For the first option, the steady-state or "permanent" component of the earth's magnetic field meets the criterion. The possibility that masses of susceptible people could be influenced during critical conditions by extremely small variations (less than 1%) of the steady-state amplitude (50,000 nT) of the earth's magnetic field such as during geomagnetic storms (50 to 500 nT) has been discussed elsewhere (Persinger, 1983). Recent experimental evidence which has shown a threshold in geomagnetic activity of about 20 nT to 30 nT for the report of vestibular experiences in human beings and the facilitation of limbic seizures in rodents is consistent with this hypothesis.

The potential for the creation of an aggregate process with gestalt-like properties which reflect the average characteristics of the brains that are maintained with this field and that generate the aggregate has also been developed (Persinger & Lafreniere, 1977) and has been labelled the "geopsyche." This phenomenon would be analogous to the vectorial characteristics of an electromagnetic field which is induced by current moving through billions of elements such as wires contained within a relative small volume compared to the source. Such gestalts, like fields in general, also affect the elements which contribute to the matrix (Freeman, 1990).

The second option would require access to a very narrow limit of physical properties within which all brains are maintained to generate consciousness and the experience of self-awareness. This factor would be primarily loaded by the variable of brain temperature. Although the relationship between absolute temperature and wavelength is generally clear [an example which can be described by Wien's law and is well documented in

astrophysics (Wyatt, 1965)], the implications for access to brain activity have not been explored. The fragile neurocognitive processes that maintain consciousness and the sense of self normally exist between 308[degrees]K and 312[degrees]K (35[degrees]C and 39[degrees]C). The fundamental wavelength associated with this emission is about 10 micrometers which is well within the long infrared wavelength.

However, the ratio of this normal range divided by the absolute temperature for normal brain activity which maintains neurocognitive processes is only about 0.013 (4[degrees]K/312[degrees]K) or 1.3%. If there were a subharmonic pattern in naturally occurring or technically generated magnetic fields which also reflected this ratio, then all brains which were operative within this temperature range could be affected by the harmonic. For example, if 11.3 Hz were one of these subharmonic electromagnetic frequencies, variations of only 1.3% of this mean, i.e., 11.3 Hz +/- [plus or minus] 0.1 Hz, would hypothetically be sufficient to affect the operations of all normal brains. If this "major carrier frequency" contained biorelevant information by being modulated in a meaningful way, then the effective intensities could well be within the natural range for background radiation (microwatts/cm2) and could be hidden as chaotic components within the electromagnetic noise associated with power generation and use.

One of the major direct prophylactics to the effects of these fields would require alterations in core (brain) temperature such as deep but reversible hypothermia. However, this condition would disrupt the biochemical process upon which neuronal activity and hence consciousness depends. Treatments which precipitate alterations in neural activity, similar to those which are associated with crude hypothermia, would be less disruptive. Specific candidates which affect multiple receptor systems such as clozepine (Clozaril) and acepromazine could be possible pharmacological interventions.

The characteristics of the algorithm for euthermic individuals are likely to be conspicuous (once isolated) but should now be hidden within the synchronous activity which is (1) modified and filtered by aggregates of neurons and (2) modulated by sensory inputs and intrinsic oscillations (Kepler, Marder, & Abbott, 1990) before they are crudely measured by electrodes. Because the fundamental algorithm would be essentially a stable parameter of body temperature, most electrode montages (including monopolar to a nonbrain reference, e.g., ear) would cancel or attenuate this index. Effectively, the algorithm would be expressed in a manner similar to descriptors for other aggregate phenomena as a physical constant

or as a limited set of these constants. This suggestion is commensurate with the observation that the underlying neuronal networks which coordinate millions of neurons manifest the properties of a (mathematical) strange attractor with a very limited number of degrees of freedom (Lopes, Da Silva, Kamphuis, Van Neerven, & Pijn, 1990).

The physical chemical evidence for a fundamental process, driven by a narrow limit of biological temperature, has been accumulating. Fixed, oscillatory electromagnetic variations have been shown _in_vitro_ for enzymes of the glycolytic pathway (Higgins, Frenkel, Hulme, Lucas, & Rangazas, 1973) whose narrow band of temperature sensitivity (around 37[degrees]C) is well known. Although these oscillations are often measured as periods (2.5-min. cycles), Ruegg (1973) reported a clear temperature dependence of these oscillations within a range of 1 to 20 Hz between 20[degrees]C and 35[degrees]C in invertebrate muscle.

The most probable brain source which might serve as the primary modulatory of these biochemical oscillators would involve structures within the thalamus (Steriade & Deschenes, 1984). Neuronal aggregates with surprisingly fixed (within 0.1-Hz) oscillations are found within this structure and depend primarily upon neurons that require gamma amino butyric acid or GABA (von Krosigk, Bal, & McCormick, 1993). This inhibitory amino acid is specially derived from the normal, temperature-sensitive degradation of glucose by the GABA shunt (Delorey & Olsen, 1994).

Within the last two decades (Persinger, Ludwig, & Ossenkopp, 1973) a potential has emerged which was improbable but which is now marginally feasible. This potential is the technical capability to influence directly the major portion of the approximately six billion brains of the human species without mediation through classical sensory modalities by generating neural information within a physical medium within which all members of the species are immersed. The historical emergence of such possibilities, which have ranged from gunpowder to atomic fission, have resulted in major changes in the social evolution that occurred inordinately quickly after the implementation. Reduction of the risk of the inappropriate application of these technologies requires the continued and open discussion of their _realistic_ feasibility and implications within the scientific and public domain.

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US Electromagnetic Weapons and Human Rights

By Peter Phillips, Lew Brown and Bridget Thornton

As Study of the History of US Intelligence Community Human Rights Violations and Continuing Research in Electromagnetic Weapons

Completed December 2006

Sonoma State University
Project Censored
Media Freedom Foundation

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US Electromagnetic Weapons and Human Rights

By Peter Phillips, Lew Brown and Bridget Thornton

This research explores the current capabilities of the US military to use electromagnetic (EMF) devices to harass, intimidate, and kill individuals and the continuing possibilities of violations of human rights by the testing and deployment of these weapons. To establish historical precedent in the US for such acts, we document long-term human rights and freedom of thought violations by US military/intelligence organizations. Additionally, we explore contemporary evidence of on-going government research in EMF weapons technologies and examine the potentialities of continuing human rights abuses.

In the 1950s and 60s the CIA began work to find means for influencing human cognition, emotion and behavior. Through the use of the psychological understanding of the human being as a social animal and the ability to manipulate a subject's environment through isolation, drugs and hypnosis, US funded scientists have long searched for better means of controlling human behavior. This research has included the use of wireless directed electromagnetic energy under the heading of "Information Warfare" and "Non Lethal Weapons." New technological capabilities have been developed in black budget projects[1] over the last few decades— including the ability to influence human emotion, disrupt thought, and present excruciating pain through the manipulation of magnetic fields. The US military and intelligence agencies have at their disposal frightful new weapons, weapons that have likely already been covertly used and/or tested on humans, both here and abroad, and which could be directed against the public in the event of mass protests or civil disturbance.

Human Rights belong to people collectively. To believe in rights for some and not others is a denial of the humanness of people worldwide. Yet, denial is exactly what Congress and George W. Bush did with the signing of the Military Commission Act of 2006. The new official US policy is that torture and suspension of due process are acceptable for anyone the president deems to be a terrorist or supporter. This act is the overt denial of the inalienable rights of human beings propagated in our Declaration of Independence and the Universal Declaration of Human Rights. More so, US actions declared to the world that the US suspends human rights for those it believes are evil.

The precious words, "We hold these truths to be self-evident, that all men are created equal, that they are endowed by their Creator with certain unalienable Rights, that among these are Life, Liberty and the pursuit of Happiness," did not declare that only some men (and women) possess unalienable rights. Our independence was founded on the understanding that all men and women are recognized by this nation as having innate rights derived by their humanity.

Likewise, the Universal Declaration of Human Rights, created by the United Nations in 1948, signed and ratified by the US Congress, specifies in its preamble that "recognition of the inherent dignity and of the equal and inalienable rights of all members of the human family is the foundation of

[1] Black budgets are government funded projects that are classified/secret to Congress and the American people. For an in-depth analysis on the topic, see Weiner, Tim , *Blank Check: The Pentagon's Black Budget,* Warner: 1990.

freedom, justice and peace in the world."

The Universal Declaration of Human Rights has been a guide for international law for most of six decades, and as such binds the United States to its general principles. Article 10 states that "everyone is entitled to full equality, to a fair and public hearing by an independent and impartial tribunal, in the determination of his rights and obligations and of any criminal charge against him," and Article 5 specifically prohibits torture or cruel, inhuman or degrading treatment or punishment. Both of these basic human rights have been superceded by the passage the of Military Commissions Act of 2006.

Additionally, the Universal Declaration of Human rights declares that everyone has the right to freedom of thought and freedom of expression and opinion. This means that humans have the inalienable right to be able to freely think their own thoughts and discover their own truths. This paper addresses this most fundamental human right and explores the pending threats to individual freedom of thought posed by new EMF weapons technologies.

Freedom of thought or cognitive liberty is the natural human right of each person to be secure in their ability to perceive the world to the best of their ability. To have true cognitive liberty in a world as complex as ours would mean that first we must have access to truthful and unbiased information about the actions of others and the general state of the world. The Center for Cognitive Liberties defines this as "the right of each individual to think independently and autonomously, to use the full spectrum of his or her mind, and to engage in multiple modes of thought."[2] Without accurate representations we cannot make independently informed choices. It is imperative that the human body and mind be considered sacrosanct. To invade a person's body without their consent is an egregious human rights crime.

The circumstance may soon arrive in which anti-war or human rights protesters suddenly feel a burning sensation akin to touching a hot skillet over their entire body. Simultaneously they may hear terrifying nauseating screaming, which while not produced externally, fills their brains with overwhelming disruption. Not only are both phenomena currently possible, but designs for more powerful EMF technologies receive continuous funding from the US Government.

We are in a time of extremism, permanent war, and the unilateral manifestation of ethnocentrism and power by a cabal of people in the US government. These power elites have been in operation for decades and are set on nothing less than the total US military domination of the world. They defy the foundational values of the American people to achieve their ends. This is not a new phenomenon. The repression of human rights has been present within the US Government throughout our history. [3]

A long thread of sociological research documents the existence of a dominant ruling class in the US that sets policy and determines national political priorities. The American ruling class is complex and inter-competitive, maintaining itself through interacting families of high social standing with

[2] See the Center for Cognitive Liberty at http://www.cognitiveliberty.org/

[3] For a full discussion on the Global Dominance Group currently operating in the US see: http://www.projectcensored.org/downloads/Global_Dominance_Group.pdf

similar life styles, corporate affiliations, and memberships in elite social clubs and private schools.[4]

This American ruling class is self-perpetuating, [5] maintaining its influence through policy-making institutions such as the National Manufacturing Association, National Chamber of Commerce, Business Council, Business Roundtable, Conference Board, American Enterprise Institute, Council on Foreign Relations and other business-centered policy groups.[6] C. Wright Mills, in his 1956 book *The Power Elite*, documents how World War II solidified a trinity of power in the US, comprised of corporate, military and government elites in a centralized power structure motivated by class interests and working in unison through "higher circles" of contact and agreement. Mills described how the power elite were those "who decide whatever is decided" of major consequence.[7]

With the advent of the military-industrial complex after World War II, President Eisenhower observed that an internal military industrial power faction was consolidating their long-term plans for the domination of America and, eventually, the world. Eisenhower was in no position to fight these men, and history records his feelings on the subject with the text of his short farewell address:

> "….But threats, new in kind or degree, constantly arise. Of these, I mention two only…
>
> …This conjunction of an immense military establishment and a large arms industry is new in the American experience. The total influence – economic, political, even spiritual – is felt in every city, every Statehouse, every office of the Federal government. We recognize the imperative need for this development. Yet we must not fail to comprehend its grave implications. Our toil, resources and livelihood are all involved; so is the very structure of our society.
>
> In the councils of government, we must guard against the acquisition of unwarranted influence, whether sought or unsought, by the military-industrial complex. The potential for the disastrous rise of misplaced power exists and will persist.
>
> We must never let the weight of this combination endanger our liberties or democratic processes. We should take nothing for granted. Only an alert and

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[4] G. William Domhoff, Who *Rules America? (New York:* McGraw Hill, 2006 [5th ed.] and Peter Phillips, *A Relative Advantage: Sociology of the San Francisco Bohemian Club*, 1994, (http://library.sonoma.edu/regional/faculty/phillips/bohemianindex.html)

[5] Early studies by Charles Beard in the *Economic Interpretations of the Constitution of the United States* (1929), established that economic elites formulated the US Constitution to serve their own special interests. Henry Klien (1933) in his book *Dynastic America* claimed that wealth in America has power never before known in the world and was centered in the top 2% of the population owning some 60% of the country. Ferdinard Lundberg (1937) wrote Am*erican's Sixty Families* documenting inter-marring self-perpetuating families where wealth is the "indispensable handmaiden of government. C.Wright Mills determined in 1945 (American Business Elites, *Journal of Economic History*, Dec. 1945) that nine out of ten business elites from1750 to 1879 came from well to do families.

[6] See R. Brady, *Business as a System of Power*, (New York: Columbia University Press, 1943) and Val Burris, Elite Policy Planning Networks in the United State, American Sociological Association paper 1991.

[7] C. Wright Mills, *The Power Elite*, (New York: Oxford University Press, 1956).

> knowledgeable citizenry can compel the proper meshing of the huge industrial and military machinery of defense with our peaceful methods and goals, so that security and liberty may prosper together.
>
> Akin to, and largely responsible for the sweeping changes in our industrial-military posture, has been the technological revolution during recent decades.
>
> In this revolution, research has become central, it also becomes more formalized, complex, and costly. A steadily increasing share is conducted for, by, or at the direction of, the Federal government."[8]

We now understand that Eisenhower was referring to the conjunction of redirected tax monies to research secret new technology aimed at nothing less than increasing the controlling power of the military industrial elite to a global scale.

One particular faction of ambitious men, the former cold warriors and emerging neo-conservatives, were close followers of philosopher Leo Strauss. This elite group included not just generals and industrialists but philosophers, scientists, academics, and politicians have now become the most powerful public-private war organization ever known.

Strauss espoused an elitist philosophy that fawned over the characteristics of those who inherited wealth and lived lives of leisure to pursue whatever their interests may be. His ideas have been transformed into a cogent ideology in which the media, religion, and government are used to subdue the masses while the real "nobles" follow their own will without regard to the laws designed to control lesser men. Strauss was likewise fond of secrecy, as a necessity for control, because if the lesser men found out what was being done to them they would no doubt be upset.

"The people will not be happy to learn that there is only one natural right – the right of the superior to rule over the inferior, the master over the slave, the husband over the wife, and the wise few over the vulgar many." In *On Tyranny*, Strauss refers to this natural right as the "tyrannical teaching" of his beloved ancients..[9]

Leo Strauss, Albert Wohlstetter, and others at the University of Chicago's Committee on Social Thought receive wide credit for promoting the neo-conservative agenda through their students, Paul Wolfowitz, Allan Bloom, and Bloom's student Richard Perle.

Canadian cultural review magazine *Adbusters*, defines neo-conservatism as, "The belief that Democracy, however flawed, was best defended by an ignorant public pumped on nationalism and religion. Only a militantly nationalist state could deter human aggression …such nationalism requires an external threat and if one cannot be found it must be manufactured."[10]

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[8] Public Papers of the Presidents, Dwight D. Eisenhower, 1960, p. 1035- 1040
[9] Leo Strauss, "On Tyranny", Edited by Victor Gourevitch and Michael S. Roth, University Of Chicago Press, 2000.
[10] Guy Caron, "Anatomy of a Neo-Conservative White House," *Canadian Dimension*, May 1, 2005.

The neo-conservative philosophy emerged as a reaction to the 1960s era of social revolutions. Numerous officials and associates in the Reagan and George H.W. Bush presidencies were strongly influenced by the neo-conservative philosophy including: John Ashcroft, Charles Fairbanks, Richard Cheney, Kenneth Adelman, Elliot Abrams, William Kristol and Douglas Feith.[11]

Within the Ford administration there was a split between Cold War traditionalists seeking to minimize confrontations through diplomacy and detente and neo-conservatives advocating stronger confrontations with the Soviet's "Evil Empire." The latter group became more entrenched when George H.W. Bush became CIA Director. Bush allowed the formation of "Team B" headed by Richard Pipes along with Paul Wolfowitz, Lewis Libby, Paul Nitze and others, who formed the second Committee on the Present Danger to raise awareness of the Soviet threat and the continuing need for a strong aggressive defense policy. Their efforts led to strong anti-Soviet positioning during the Reagan administration. [12]

The Committees on the Present Danger (CPD) extend from the 1950s Russian threat to the present. The current CPD proudly boasts on their website;

> "In times of great challenge to the security of the United States, Republicans, Democrats, and Independents have traditionally joined to make an assertive defense of American interests.
>
> Twice before in American history, The Committee on the Present Danger has risen to this challenge. It emerged in 1950 as a bipartisan education and advocacy organization dedicated to building a national consensus for a strong defense against Soviet expansionism. In 1976, the Committee on the Present Danger reemerged, with leadership from the labor movement, bipartisan representatives of the foreign policy community and academia, all of whom were concerned about strategic drift in US security policy. With victory in the Cold War, the mission of the Committee on the Present Danger was considered complete and consequently was deactivated.
>
> Today, the current CPD promotes radical Islamists as the primary threat to the American people and millions of others who prize liberty. They claim that the threat is global. They also claim that they operate from cells in a number of countries. Rogue regimes seek power by making common cause with terrorist groups. The prospect that this deadly collusion may include weapons of mass murder was the justification for the invasion of Iraq."[13]

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[11] Alain Frachon and Daniel Vernet, "The Strategist and the Philosopher: Leo Strauss and Albert Wlhlestetter," *Le Monde*, April 16, 2003, English translation: *Counterpunch* 6/2/03.

[12] Anne Hessing Cahn, Team B; The Trillion-dollar Experiment, *Bulletin of the Atomic Scientists,* April 1993, Volume 49, No. 03

[13] The Committee on the Present Danger mission statement can be accessed at http://www.fightingterror.org/whoweare/index.cfm

Journalist John Pilger recalls his interview with neo-conservative Richard Perle during the Reagan administration: “I interviewed Perle when he was advising Reagan; and when he spoke about 'total war,' I mistakenly dismissed him as mad. He recently used the term again in describing America's 'war on terror', “No stages, This is total war. We are fighting a variety of enemies. There are lots of them out there. All this talk about first we are going to do Afghanistan, then we will do Iraq . . . this is entirely the wrong way to go about it. If we just let our vision of the world go forth, and we embrace it entirely and we don't try to piece together clever diplomacy, but just wage a total war . . . our children will sing great songs about us years from now.”[14]

There is ample evidence available to show that some individuals within government and industry have little problem with violating the public trust and using their positions to kill, maim, torture and destroy. It is of the utmost importance to our traditional American values of human rights and cognitive liberty that we recognize this threat from within. We must move to identify those who show these proclivities and ensure that their activities have adequate oversight.

Stanley Milgram's famous experiment involving obedience to authority proved that individuals are fairly easily cowed into submitting to anyone who has a claim of authority, and that on average 61 percent of people will administer pain to another person if instructed to do so.[15] Both test groups in these experiments rationalized their behavior by appealing to “the greater good.” Because it was for the “advancement of science” they were able to be convinced they should ignore personal judgment and obey the instructions given to them by the experimenters.[16]

Martin Orne, who was one of those paid by the CIA to conduct experiments on obedience, showed in 1962 that people would go to tremendous lengths to please a person in authority. Orne conducted research that involved presenting subjects with a stack of 2,000 pages of random numbers and instructing them to add each two adjacent numbers until he returned. Over 90 percent of the test subjects continued in this meaningless task for up to five hours.[17]

Today the combination of political climate and technological capability presents a condition in which widespread manipulation of, not only the flow of information through the media, but also the manipulation of the emotional states and cognitive ability in large populations could be achieved. If policy elites are unaccountable to the public for their actions, and the public has been emotionally manipulated to support them, we can assume that they will certainly abuse their positions in the pursuit of their agendas.

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[14] John Pilger, “The World Will Know The Truth,” *New Statesman* (London) (December 16 2002).
[15] Stanley Milgram “Obedience to Authority: An Experimental View”, New York: HarperCollins, 2004.
[16] “Obedience as a determinant of behavior is of particular relevance to our time,” Behavioral Study of Obedience, Stanley Milgram, Yale University, *Journal of Abnormal and Social Psychology*, Vol. 67, No. 4, p. 371
[17] See Martin Orne-Orne, Martin T., “On The Social Psychology of the Psychological Experiment: With Particular Reference to Demand Characteristics and Their Implications,”*Am. Psychol*. 17 (1962): 776-783, Orne, M.T. The potential uses of hypnosis in interrogation. In A.D. Biderman (Ed.), *The Manipulation of Human Behavior* (pp. 169-215). New York: John Wiley & Sons, 1961

Previous human rights and cognitive liberty violations are evidenced in CIA and FBI records pertaining to the infamous MK-ULTRA project and the grim record of harassment and subversion uncovered in the COINTELPRO program in force through the 1950s and into the 1970s. We also examined some of the cases of illegal experimentation on the public dating back to the 1930s. We consider, in depth, the forms of electromagnetic weapons entering the battlefield today that trace their origins back through the secret projects of the Defense Department in the 1950s and 1960s.

Psychological Warfare, Information War, and mind control may seem to be exotic topics, but the impact of these technologies and techniques is profound. Our minds are being impacted through a longstanding series of programs aimed at manipulating public opinion through intelligence agencies, think tanks, corporate media and a host of non-governmental organizations designed to engender fear, division and uncertainty in the public.[18] Media manipulation involving the artificial framing of our collective reality is often a hit or miss proposition, but psychological operations have been carried out in the past, and are being carried out even today, through the practices of "Information Warfare," directed at enemies abroad and at the American people.[19]

According to Mary C. FitzGerald of the Hudson Institute, New-concept weapons, such as laser, electromagnetic, plasma, climatic, genetic and biotechnological are the central principle driving the modernization of national defense. The potential for these weapons to be used for both good and bad deserves a great deal of attention, but there is little to be found in the media or discussed by our administration.[20]

The US is a system of many institutions including those whose sole function is to provide government oversight. When problems arise that threaten the stability of the country or the safety of the people, the US government is designed to have checks and balances that allow the people to challenge misconduct either directly or through congressional representatives. Increasingly, oversight is disintegrating. According to a 2006 report in the *Boston Globe*, the intelligence committee does not read most intelligence reports in their entirety.[21]

The media is complicit in omitting information necessary to make democratic decisions.[22] A global dominance agenda includes penetration into the boardrooms of the corporate media in the US. A research team at Sonoma State University recently finished conducting a network analysis of the

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[18] For an analysis on the interlocking of the corporate media, think tanks and government organizations, see Peter Phillips, Bridget Thornton and Lew Brown " The Global Dominance Group and the US Corporate Media" in *Censored 2007*, Seven Stories Press.

[19] See: Snow, Nancy, *Information War American Propaganda, Free Speech, and Opinion Control Since 9/11*, 2004 Seven Stories Press and Chomsky, Noam *Media Control: The Spectacular Achievements of Propaganda*, 2002 Seven Stories Press

[20] In researching this article, there are no instances of remarks by senior White House, Pentagon, or Congressional officials that specifically address the human effects of non-lethal EMF weapons. A search in Lexis Nexis from 2001-2006 returned no results in American mainstream media.

[21] Classified Intelligence Bills Often Are Unread: Secret Process Can Discourage House Debate, Susan Milligan, *Boston Globe* August 6, 2006.

[22] The Global Dominance Group and the US Corporate media, by Peter Phillips, Bridget Thornton and Lew Brown, published in *Censored 2007*, Seven Stories Press, 2006, Chapter 10,

boards of directors of the ten big media organizations in the US. The team determined that only 118 people comprise the membership on the boards of director of the ten big media giants. These 118 individuals in turn sit on the corporate boards of 288 national and international corporations. Four of the top 10 media corporations in the US have DOD contractors on their boards of directors including:

William Kennard: New York Times, Carlyle Group
Douglas Warner III, GE (NBC), Bechtel
John Bryson: Disney (ABC), Boeing
Alwyn Lewis: Disney (ABC), Halliburton
Douglas McCorkindale: Gannett, Lockheed-Martin

Given an interlocked media network, big media in the US effectively represent corporate America's interests. The media elite, a key component of policy elites in the US, are the watchdogs of acceptable ideological messages, the controllers of news and information content, and the decision makers regarding media resources

It is not suggested that everyone in the government believes in global domination, nor that it is the intent of every government official to 'cover up' misconduct.[23] Scientists involved in potentially harmful technology are not 'mad scientists.' In fact, there are many reports in the public sphere addressing government and military misconduct that are put forth by people within these very institutions. The problem is when the government threatens whistleblowers, intimidates officials with job loss, infiltrates activist organizations, and increases surveillance[24].

PSYCHOLOGICAL WAR

Modern Psychological Operations (Psy-Ops) were significantly advanced in the Second World War [25]and were brought to bear on the American public during the 1950s with the formation of a widespread network of social scientists, journalists, politicians, military specialists and intelligence operatives. Psy-Ops were used to promote a variety of programs in cooperation with the Industrial Military Complex. Their key piece of information warfare was the Communist Red Menace.[26]

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[23] Remarks on Classification, The Hon. Lee Hamilton, Information Security Oversight Office, October 18, 2005. "At a time when the US intelligence community is under intense scrutiny in the aftermath of 9/11 and the failure to find weapons of mass destruction in Iraq, we only increase public skepticism about our government by denying the public information."

[24] See: Valerie Plame, the Richard Leiby, Spy Who Got Shoved Out Into the Cold, *Washington Post,* October 29, 2005; Page C01; Amended 2006 surveillance bill by Bush; The FBI and the Engineering of Consent, Noam Chomsky, From *Public Eye Magazine*, Volume One, Number Two; and Demian Bulwa, Oakland: Police spies chosen to lead war protest, *San Francisco Chronicle*, Friday, July 28, 2006.

[25] See William E. Daugherty and Morris Janowitz, *A Psychological Warfare Casebook,* Baltimore, MD: Johns Hopkins University Press, 1958. In particular, see Daugherty's article on "US Psychological Warfare Organizations in World War II," pp. 126-136.

[26] For a current view of these kinds of operations and how they are outsourced see James Bamford's article in the *Rolling Stone,* The Man Who Sold the War Meet John Rendon, Bush's General In The Propaganda War, November 17, 2005. For more information on CIA control of the media refer to Carl Bernstein, "The CIA and the Media -- How America's

One of the opening salvos in this war of deception was fired by George Kennan, the American ambassador to Moscow, describing the Soviet threat in a "long cable" sent to Washington in 1946. Kennan spent decades studying the Russian political scene. He became convinced that there would be little chance of cooperation with the Soviets and recommended a number of actions, most notably the institution of "political war" through the newly formed CIA - a decision he later regretted, even arguing for the elimination of the CIA in 1997.[27]

In the late 1950s, a right-wing cadre of men within the new CIA was busy building secret armies, planning assassinations, and generally devising plans for world domination that still play out today. Operation Gladio was one example, well documented and international in scope, in which right-wing members of the US intelligence community created "stay-behind" armies in many of the nations of Europe. Those armies managed to infiltrate the highest levels of politics (most notably in Italy where the term "Gladio" refers to a double edged sword) and have been held responsible for numerous false-flag terrorist acts through the 1980s and 1990s. Terror and propaganda often go hand-in-hand in the extremist elements within our military and intelligence communities.[28]

To counter the divisions within the intelligence community, a greater voice was given to organizations formal and informal. In the 1950s, one such group, the first Committee on the Present Danger (CPD), promulgated a series of "gap crises." The Bomber Gap, the Missile Gap, the Space Gap, and the Brainwashing and Psychotronic Gap were used to justify increased military technology spending. Congress was led to believe that the Soviets were a much greater threat than they actually were, and that a terrifying new weapon was being developed that threatened America. They were thus convinced to vote for virtually any black budget proposal that came their way. The CPD ran a series of broadcasts to the public through the Mutual Broadcasting Network that spread fear in the minds of the public.

Under the first civilian CIA Director, Allen Welsh Dulles, the Company began to push forward with its agenda of manufacturing consent from the American people for a new state of perpetual war industrialization. Dulles was a well-connected individual, a successful spy for the OSS in Switzerland during the war, related to three secretaries of state, and the chief advisor to Dewey when he ran for President in 1948. Dulles had access to the highest echelons of policy making and his

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Most Powerful News Media Worked Hand in Glove with the Central IntelligenceAgency and Why the Church Committee Covered It Up", *Rolling Stone,* October 20, 1977, p.63.-the title of the original operation was "Mockingbird"

[27] George F. Kennan. "Spy and Counterspy." *The New York Times,* May 18, 1997. For a sympathetic biography see George F. Kennan and *The Making of American Foreign Policy, 1947-1950*, Wilson D. Miscamble, C.S.C, 1993 Princeton University Press. George F. Kennan. "Policy Planning Staff memorandum on the inauguration of organized political warfare", May 4, 1948. Published in Foreign Relations of the United States, 1945-1950: Emergence of the Intelligence Establishment. Discusses the need for political warfare: that is, measures short of war, such as propaganda and covert operations.

[28] History News Network, USA 13 June 2005, Terrorism in Western Europe: An Approach to NATO's Secret Stay-Behind Armies, by Daniele Ganser, *The Whitehead Journal of Diplomacy and International Relations* 1 June 2005, Kennan published his analysis anonymously in *Foreign Affairs*, the official magazine of the Council for Foreign Relations (CFR). [Mr. X (Alias 'George C. Kennan): "The Sources of Soviet Conduct", in *Foreign Affairs*, July 1947.] (http://www.isn.ethz.ch/php/documents/collection_gladio/Terrorism_Western_Europe.pdf.)

influence was global in scope, counting among his close friends Henry Luce, publisher of *Newsweek*. Relying heavily upon established circles of contacts within the nation's media elites, Dulles recruited key members of the media to work directly for the CIA under Operation Mockingbird. Mockingbird was a psychological information campaign against the American people. In a campaign that would lead to acceptance of blanket secrecy for "national security", "the Red Scare" became the excuse for spending vast sums of money on weapon systems and an increase in covert operations both in foreign countries and within the United States. In the 1950s and 1960s, movies, news articles, books, radio and television programs were carefully laced with anti-communist messages and images designed to produce an acceptance of the policies being promoted by the defense elite's propaganda machine.[29]

> "Among the executives who lent their cooperation to the Agency were William Paley of the Columbia Broadcasting System, Henry Luce of Time Inc., Arthur Hays Sulzberger of the *New York Times,* Barry Bingham Sr. of the *Louisville Courier-Journal* and James Copley of the Copley News Service. Other organizations which cooperated with the CIA include the American Broadcasting Company, the National Broadcasting Company, the Associated Press, United Press International, Reuters, Hearst Newspapers, Scripps-Howard, *Newsweek* magazine, the Mutual Broadcasting System, The *Miami Herald,* and the old *Saturday Evening Post* and *New York Herald-Tribune.* By far the most valuable of these associations, according to CIA officials, have been with *The New York Times,* CBS, and Time Inc."[30]

One of the engineers of this deception was a former head of the stay-behind network, Edward W. Barrett, director of the Interdepartmental Psychological Strategy Board (IPSB) and, not coincidentally an editor at *Newsweek.* Barrett was seen as being very effective in his efforts to manipulate public opinion. At the same time, CPD was a "non-political group of citizens of the western coast" and launched a media campaign in favor of the urgent reinforcement of the national defense. Among the organizers of the Committee were Frank Altschul (Director of the Council for Foreign Relations), William Donovan (former head of the OSS during WWII) and General Dwight D. Eisenhower.[31]

All of this activity was more than enough to stoke the fears of the public and encourage policy makers to accept the Cold War view of the world. This allowed Truman to convince Congress to approve a tripled military budget that provided funding for secret research and development and turn a blind eye (in the name of National Security) to "black operations" programs authorized under the new Cold War rubric of "containment" and aimed at undermining otherwise peaceful nations and

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[29] Victor Marchetti and John D. Marks, *The CIA and The Cult of Intelligence,* Dell Books,1975 (as a matter of general interest this is reportedly the first book the Government went to court to have censored. There are 168 missing pages as a result of the courts ruling but the spaces were retained in the first edition.)

[30] "The CIA and the Media", Carl Bernstein *Rolling Stone,* Oct. 20, 1977

[31] David F. Krugler, Will It Play in Peoria? The 1950 Campaign of Truth and the Reconstruction of Cold War Propaganda, British Association of American Studies Annual Conference April 1997 University of Birmingham, Birmingham, England

fomenting war, torture and assassination in countries as diverse as Iran, Guatemala and Indochina.[32]

Post-war developments in Europe, especially the British withdrawal from Greece, led Truman to decide it was necessary to have a permanent American presence in the old continent to counteract the Communist influence.[33] General George C. Marshall, Secretary of State, designed a vast plan that mixed economic assistance and secret actions aimed at establishing democracies and making sure that voters in foreign countries made "the right choice." National Security Council directive NSC 10/2, essentially written by Kennan, made official the creation of an anti-Communist interference network.[34]

The US intelligence community had an ace in the hole, Reinhardt Gehlen, a Nazi spymaster with an existing network of agents became the front man in Eastern Europe for American intelligence. General Reinhardt Gehlen proved to be troublesome for the CIA over the years. Communist counter-spies infiltrated his network, his information was often incorrect, and he had downplayed his eagerness to serve the Reich. But Gehlen was only one of thousands of Nazis recruited to assist in the new "Cold War" through Operation Paperclip.[35] In fact, the intelligence assets acquired by bringing the Gestapo onto the US public payroll was overshadowed by the acquisition of dozens of brilliant Nazi scientists and researchers.

At this juncture, Truman, through the application of the 1947 National Security Act and the newly formed National Security Council[36], authorized a vast number of secret projects involving chemical, biological, nuclear and electromagnetic experiments. Former Nazis were put in charge of many of the most sensitive programs and facilities. The Army Ballistic Missile Agency (ABMA) was entrusted to the former SS officer Wernher von Braun.[37] Kurt Debus, another ex-SS officer, directed Cape Canaveral. At this time scientists began working on "black" projects in earnest, including attempts at finally developing the "lost" theories of Nicola Tesla, the Serbian-born American physicist, into military and intelligence applications.[38]

TESLA AND EMF

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[32] William Blum, *Killing Hope: US Military and CIA Interventions Since World War II,* Monroe, Maine: Common Courage Press, 1995; Ralph McGehee, *Deadly Deceits: My 25 years in the CIA,* New York: Sheridan Square Publications, 1983. http://www.sourcewatch.org/index.php?title=CIA Footnote on Ops)

[33] Daniele Ganser, *NATO's Secret Armies. Operation Gladio and Terrorism in Western Europe,* Frank Cass Publishers, 2004.

[34] See the Federation of American Scientists Intelligence resource program, National Security Council [NSC] Truman Administration [1947-1953] at http://www.fas.org/irp/offdocs/nsc-hst/index.html.

[35] Linda Hunt, *Secret Agenda: The United States Government, Nazi Scientists and Project Paperclip, 1945-1990,* St. Martin's Press, 1991.

[36] The National Security Act of 1947 can be accessed at http://www.state.gov/r/pa/ho/time/cwr/17603.htm

[37] Biography of Werner VonBraun produced by NASA: ww.hq.nasa.gov/office/pao/History/sputnik/braun.html and at the Marshall Space Flight Center located at http://history.msfc.nasa.gov/vonbraun/index.html

[38] Hunt, L. *Secret Agenda. The United States Government, Nazi Scientists, and Project Paperclip, 1945 to 1990*. New York: St. Martin's Press, 1991. Simpson, C. "Blowback. The First Full Account of America's Recruitment of Nazis, and the Disastrous Effect on Our Domestic and Foreign Policy". New York: Weidenfeld and Nicolson, 1988

Military interest into the weaponization of the electromagnetic spectrum has a long history, based on the theoretical work of Nikola Tesla. Radar, in its early inception, was seen not only as a means of tracking the position and speed of enemy targets, but as a potential weapon in its own right. There are very real problems however with overcoming the normal decrease in effect of an electromagnetic field over distance. This effect is a natural function of the laws of physics and applies to both electrical and magnetic fields[39]. In short, the strength of a field drops off in inverse proportion to the distance of the target from the source. Without a means of concentrating and directing a beam of energy across long distances, any effect that an EMF weapon may have would be limited to its immediate vicinity. From 1900 until his death in 1943, Nikola Tesla worked to develop just such a weapon.

In a letter to the *New York Times* editor in 1908 Telsa wrote,

> "When I spoke of future warfare I meant that it should be conducted by direct application of electrical waves without the use of aerial engines or other implements of destruction...What I said in regard to the greatest achievement of the man of science whose mind is bent upon the mastery of the physical universe, was nothing more than what I stated in one of my unpublished addresses, from which I quote: "According to an adopted theory, every ponderable atom is differentiated from a tenuous fluid, filling all space merely by spinning motion, as a whirl of water in a calm lake. By being set in movement this fluid, the ether, becomes gross matter. Its movement arrested, the primary substance reverts to its normal state. It appears, then, possible for man through harnessed energy of the medium and suitable agencies for starting and stopping ether whirls to cause matter to form and disappear. At his command, almost without effort on his part, old worlds would vanish and new ones would spring into being. He could alter the size of this planet, control its seasons, adjust its distance from the sun, guide it on its eternal journey along any path he might choose, through the depths of the universe. He could make planets collide and produce his suns and stars, his heat and light; he could originate life in all its infinite forms. To cause at will the birth and death of matter would be man's grandest deed, which would give him the mastery of physical creation, make him fulfill his ultimate destiny."[40]

Tesla made several claims during the latter years of his life, published by the *New York Times* in what became an annual event. His theory of the hidden nature of our universe supplants those of many of his contemporaries in that he was able to infer a multidimensional model of the universe that is only now being investigated through the theoretical mathematics of our leading physicists.[41]

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[39] There are two laws of note here: the inverse square law, which relates to forces such as gravity, and the inverse cube law, which relates to electromagnetic forces. Both equations describe the relationship between the power of the force and the decrease in that forces effect over distance. In regards to magnetism we refer to the work of Maxwell. One easily accessible online source for his equations is: http://www.rialian.com/rnboyd/maxwell.htm A good place to start for understanding the man and his work is the James Clerk Maxwell Foundation at: http://www.clerkmaxwellfoundation.org/html/links.html

[40] *New York Times,* April 21st, 1908 (p.5 column 6) Tesla Letter to the Editor :.

[41] "The Cosmic Triangle: Revealing the State of the Universe," in the May 28, 1999 issue of the journal *Science*

Tesla also developed means of remotely controlling aircraft as early as 1915, foreshadowing the Unmanned Ariel Vehicles (UAVs) of today's battlefields. In 1934 Tesla offers to build a "Death Ray" that would make the power of an opponents air force obsolete. This was one of the earliest recorded statements regarding directed energy weapons.[42] Tesla's offer to build this device for the US government for a bargain price, but with many caveats, was refused by officials who, preferred instead to pump money into the new Army Air Corp, which in turn gave rise to the military aviation complex that we have today.[43]

Before the war the airline industry was not a major part of the economic life of the nation.[44] With huge wartime contracts, however, corporations such as Hughes, McDonnell Douglas, Lockheed, and Northrop quickly grew in power commensurate with the financial bonanza that was unearthed in the battlefields of Europe and the Pacific.[45] These companies formed the core of the "military-industrial complex." Their investors and managers began to consolidate their clout in political circles to keep the nation on a wartime economic footing, a simple and vastly powerful weapon that would make aircraft, bombs, missiles and attendant industries irrelevant would certainly be seen as a direct threat to the growing power of military arsenal. Instead, a "black budget" program was put into motion, which exploited the work of Robert Oppenheimer, Albert Einstein and others. The Manhattan Project, developed by the DOD in 1942, generated a vastly destructive weapon that required a well-established and unbelievably expensive aerospace industry, along with unprecedented levels of secrecy and autonomy from Congress and the public.[46]

The US government also ignored Tesla's offer to produce a "city killing machine," which was composed of an electromagnetic shield and a wireless torpedo. Tesla made several proposals during the 1930s, none of which received funding. Among Tesla's claims, published annually on his birthday in the *New York Times,* were methods of harnessing the power of the sun to electrify the earth and provide free electrical power to anybody, anywhere.

Tesla did, however, conceive of at least one device that became a major part of our nation's arsenal -

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discusses Dark Energy and Margaret Cheney, *Tesla: A Man Out of Time*, Dell Publishing, 1983.

[42] Front page *New York Times,* July 11 1934 was entitled, "TESLA, AT 78, BARES NEW 'DEATH BEAM'" and told of the inventor's proposal that would "send concentrated beams of particles through the free air, of such tremendous energy that they will bring down a fleet of 10,000 enemy airplanes at a distance of 250 miles..."

[43] To illustrate the control of science for corporate profit, Tesla's practical applications all shared one thing in common, the were devoid of any profitable application. As a result, Tesla's development of wireless electricity has never borne fruit, leaving us still in the 21st century surrounded by a landscape of transmission wires, faulty electrical grids, destructive (though profitable) electrical generation systems, wars for oil, and a suffering environment. See Marc J. Seifer, *The Life and Times of Nikola Tesla,* Citadel Press, 1998.

[44] John B. Rae, *Climb to Greatness: The American Aircraft Industry, 1920-1960*, Cambridge: MIT Press, 1968. Roger E. Bilstein, *The American Aerospace Industry: From Workshop to Global Enterprise*, New York: Twayne Publishers, 1996.

[45] Carol L. Cook, *The Aerospace Industry: Its History and How it Affects the US Economy*, Yale-New Haven Teachers Institute, 2005.

[46] See the National Atomic Museum's archives concerning the Manhattan Project at http://www.atomicmuseum.com/tour/manhattanproject.cfm and the Brookings Institute's archives at http://www.brook.edu/FP/PROJECTS/NUCWCOST/MANHATTN.HTM

radar. As early as 1917 he published his theory and developed the first prototype in 1934. It is from the basis of this technology that future research into weaponizing the electromagnetic spectrum proceeded. At the same time Tesla was working on methods of transmitting and receiving communication signals through interplanetary space and reading the images on a sleeping person's retina (by extension mind reading). His prediction that future wars would be fought with electromagnetic means foreshadowed the rise of electronic warfare and the non-lethal weapons technology being deployed today. [47]

At first glance, it would seem probable that the military had taken over the management of Tesla's material. In fact, a number of projects related to his life's work were in development. For instance, the building of beam weapons at Wright Patterson Air Force Base under the code name "Project Nick"[48] headed by Brigadier General L.C. Craigie. This project was however, cancelled due to an apparent lack of understanding of Tesla's means of transmitting high-energy waves without a loss of power over great distances. Defense Advanced Research Projects Agency (DARPA) began another project in 1958 codenamed "Seesaw" at Lawrence Livermore Labs[49] aimed at combating reported Soviet advances in electromagnetic weapons and defenses, advances that many believe came about after 1952 when the bulk of Tesla's research and personal effects were turned over to his nephew, Sava Kosanovic, who promptly whisked them away to Yugoslavia. Eight years later Soviet Premier Nikita Khrushchev would state that, "A new and fantastic weapon is in the hatching stage,"[50] horrifying many and prompting calls for more effective means of using EMF, espionage and counter-espionage.

On February 9, 1981, the office of the Undersecretary of Defense Research and Engineering department sent a letter to the FBI that requested the papers of Tesla, stating, "We believe that certain of Tesla's papers may contain basic principles which would be of considerable value to certain ongoing research within the DOD. It would be very helpful to have access to these papers. The letter was signed by Lt. Col. Allan J. Mclaren, an R.O.T.C. graduate from M.I.T. in 1960, who later went on to become a project director with Lockheed Martin Space Systems from which he retired in 2003.[51]

This section of his memo to the FBI was not declassified until 1993. In response, the FBI issued the same response as to all of the other inquiries with one exception, this time they identified who it was that examined the stored effects; it was the Office of Scientific Research and Development from

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[47] *New York Times,* 1937 "…will send concentrated beams of particles through the free air, of such tremendous energy that they will bring down a fleet of 10,000 enemy airplanes at a distance of 250 miles from the defending nation's border and will cause armies of millions to drop dead in their tracks When put into operation, Dr. Tesla said, this latest invention of his would make war impossible. This death-beam, he asserted, would surround each country like an invisible Chinese wall, only a million times more impenetrable. It would make every nation impregnable against attack by airplanes or by large invading armies." For an interesting article about Tesla's "Death Ray" and the relationship to Tunguska see: http://www.viewzone.com/tesla.ray.html)

[48] Tesla: Master of Lightning, archived at PBS: www.pbs.org/tesla/ll/ll_mispapers.html

[49] Tesla: Life and Legacy, Missing Papers, archived at PBS: http://www.pbs.org/tesla/ll/ll_mispapers.html.

[50] Max Frankel, "Khrushchev Says Soviets Will Cut Forces a Third; Sees 'Fantastic Weapon', *New York Times*, January 15,1960.

[51] See Tesla's FBI files at the FBI FOIA site located at http://foia.fbi.gov/foiaindex/tesla.htm.

MIT, a breeding ground of CIA. technical types the Office of Naval Intelligence and agents from US Naval Research.[52] What they may have been looking for had likely already been taken, according to a recent PBS special entitled *Tesla: Life and Legacy*, Tesla's nephew reported that Tesla's most recent journal was missing from the bulk of material stored by the OAP.[53] In recent years high profile projects such as the High Altitude Auroral Project ("HAARP"), the Strategic Defense Initiative ("Star Wars"), and many of the devices promoted by proponents of "Non-Lethal Weapons" have Tesla's intellectual fingerprints all over them.[54]

MK-ULTRA

In terms of mind-control and the breaking down of prisoners for military interrogations, the events at Abu-Ghraib, Guantanamo, and in the CIA network of secret prisons dotting the globe, all have their intellectual origin in the work carried out by a network of scientists under the behest of the intelligence community beginning in the World War II period. Mind-control, per se, refers to a well-funded, broad based series of programs designed to explore the furthest reaches of human cognitive ability. The Nazis, as well as the Japanese, had been experimenting on prisoners throughout the war. Recovery of the records of these experiments led the US to proceed with investigations into new means of interrogations and the building of resistance to interrogations of US personnel..[55]

The CIA, in association with various other agencies, undertook a long series of experiments on unsuspecting prisoners, students, military personnel and others recruited into one of the at least 162 subprojects of what became known as MKULTRA.[56] Interest was certainly piqued by the case of Cardinal Mindseztny and the reports of brainwashing techniques used on American soldiers in prisoner of war camps in Korea[57]. But even prior to the Korean War the resiliency of the human mind was being tested by researchers on the black budget. These projects reportedly at times violated every conceivable notion of human rights and dignity.[58]

Frank Olson, a mid-level CIA operative, worked on the development of aerosol delivery of drugs and poisons at Ft. Detrick, Maryland. His work, which is still classified, was. funded through MKULTRA. Olson took a trip to England where MI6 and the CIA were working together on ways to

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[52] Tesla: Life and Legacy, Missing Papers, archived at PBS: http://www.pbs.org/tesla/ll/ll_mispapers.html.
[53] Tesla: Master of Lightning PBS documentary Dec. 12th, 2000.
[54] Box#8 of Declassified CIA documents pertaining to MKULTRA contains the following fragment: The Application of Tesla's Technology in Today's World. Obtain, online, through the National Security Archives at http://www.gwu.edu/~nsarchiv/
[55] Harris, S. (1994) *Factories Of Death: Japanese Biological Warfare, 1932-45, And The American Cover-Up*. London: Routledge.Tanaka, Y. 1998. *Hidden Horrors: Japanese War Crimes in World War II. Boulder,* Colorado: Westview Press, Michalczyk, J. J. 1994. *Medicine, ethics, and the Third Reich: Historical and Contemporary Issues* (METR). Kansas City, Missouri: Sheed & Ward
[56] This site provides a selection of memorandum from within the CIA, in which funding is discussed. http://cryptome.org/mkultra-0003.htm Digital MK-Ultra files can be found at: http://www.intellnet.org/mkultra/general note about MK-ULTRA funding)
[57] Stephen Budiansky, Erica E. Goode and Ted Gest, "The Cold War Experiments", *U.S News and World Report* January 24, 1994.
[58] Patricia Greenfield, CIA's Behavior Caper, *APA Monitor,* December 1977, pp. 1, 10-11

prevent allied spies and servicemen from yielding to interrogation. Olson also traveled to Frankfurt, where the two agencies conducted fatal experiments on prisoners of war and others considered to be "expendable." Olson had an ethical dilemma with the research and, after voicing his concerns, returned to the United States. On November 28, 1953, Olson was in room 1018A of the Hotel Statler in New York. At 2 a.m., Olson fell from the 10th floor window of his room to his death on the sidewalk below. The headline reported his death as an accident or suicide. This report was discredited when, in 1975, another official lie was issued to ease his family's suffering and deflect public scrutiny. This time Olson was called the victim of an LSD experiment.[59] Media reports cited in the *New York Times* focused on the sensational aspects of LSD use and psychic warfare, but did not dwell on the more egregious violations of human rights and dignity inherent in the programs overseen by the CIA.[60]

The truth was not revealed until 1994 when his son finally had his body exhumed and examined. The autopsy showed that Olson's left temple had been fractured before he fell. According to the *New York Times Magazine* CIA tradecraft books from 1953, that have since been released teach that "one of the surest methods of killing somebody without a trace involves impairing their reflexes with alcohol (or drugs) and then stepping up behind them and stunning them with a blow to the temple. After that you quickly grab their ankles and in a single motion flip them over a bridge, balcony or out of a window more than 70 feet off of the ground."[61] What Olson saw, and what cost him his life and his family their peace of mind for 30 years, was the beginning of a long term strategy to develop means of making individual both resistant to "brainwashing" and to control the actions of individuals.[62] The cover story that was used to justify the beginning of the project was that there was a "brainwashing gap" with the Koreans.[63]

Experimenters used college students, servicemen, mental patients, the poor and, in several instances, children as young as four years old, in attempts to create untraceable assassins, couriers and other operatives. MKULTRA sub-projects involved the services of many notable universities and used a number of false front corporations such as the Foundation for the Study of Human Ecology and think tanks such as RAND, to shield the source of funding from those with ethical "problems."[64] We would still know nothing of these activities had it not been for the release of 16,000 pages of documents in 1977 through the FOIA request filed by the surviving family of Frank Olson. Unfortunately CIA Director Richard Helms ordered the destruction of any MKULTRA records

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[59] Thomas O'Toole, "CIA Infiltrated 17 Area Groups, Gave out LSD Suicide Revealed", front-page story *Washington Post,* June 11, 1975.

[60] Carl Bernstein, "The CIA and the Media: How Americas Most Powerful News Media Worked Hand in Glove with the Central Intelligence Agency and Why the Church Committee Covered It Up", *Rolling Stone*, October 20, 1977.

[61] Michael Ignatieff, "What did the C.I.A. Do to Eric Olson's Father?" *New York Times Magazine*, April 1, 2001.

[62] ibid. and The Frank Olson Project at http://www.frankolsonproject.org/Contents.htmlhttp://www.frankolsonproject.org/Statements/FamilyStatement2002.html. Dr. Eric Olson continues to do what he can to bring to light the truth of his father's death. At the above website there are memorandum written by Dick Cheney to Donald Rumsfeld in regards to the families lawsuit during the Ford administration in 1975

[63] Reported in the *New York Times* as "Mind Control Studies had Origin in Trial of Mindszenty", Aug. 2, 1977, p.16.

[64] See Athan G. Theoharis, "Researching the Intelligence Agencies: The Problem of Covert Activities", *The Public Historian*, 1984 National Council on Public History, University of California Press.

shortly before the order came in to his office[65], leaving an incomplete picture of a concerted effort by various agencies to create new and better means of controlling the thoughts, emotions and thus behavior, of unsuspecting individuals.

ILLEGAL EXPERIMENTATION

MKULTRA was, however, neither the first nor the last project funded by government or industry to experiment on people in the name of some greater good. A quick review of the history of secret experimentation and medical atrocities reveals a pattern of deadly behavior

The Tuskegee Experiments in 1932 cruelly condemned scores of black men to death from syphilis.[66]

The Pellagra Incident, in which millions died over two decades, in spite of the fact that the US Public Health Service knew at the time that these deaths were caused by little more than a niacin deficiency.[67]

In 1940 scientists exposed four-hundred prisoners in Chicago with malaria (a US experiment Nazis cited at the Nuremberg trials to defend their own experimentation).[68]

During WWII, Seventh Day Adventist conscientious objectors were enlisted into Operation Whitecoat by the US Army and the Adventist Church. They were told that they were being tested for defensive research purposes while the government was in fact testing offensive chemical and biological weapons.[69]

After WWII, matters became far worse for those who were caught up in the web of illegal scientific testing. In 1947 Colonel E.E. Kirkpatrick of the US Atomic Energy Commission issued a secret document stating that the agency would begin administering intravenous doses of radioactive substances to human subjects. At the same time atomic tests in which the residents of Utah and Nevada were purposely exposed to radioactive fallout. There were also a series of operations during the 1940s and 1950s in which US cities were attacked secretly by the military through the spread of biological agents in order to track their propagation through a real population.[70]

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[65] Project MKULTRA, The CIA's Program of Research in Behavioral Modification, August 3, 1977, US Senate, Select Committee on Intelligence, and Subcommittee on Health and Scientific Research of the Committee on Human Resources.

[66] Jean Heller (Associated Press), "Syphilis Victims in the US Study Went Untreated for 40 Years" *New York Times*, July 26, 1972: and VN Gamble, "Under the Shadow of Tuskegee: African Americans and Health Care." *American Journal of Public Health* 7(1997):1773-1778.

[67] Jon M. Harkness, "Prisoners and Pellagra", *Public Health Reports,* Sep/Oct96, Vol. 111 Issue 5, p 463.

[68] "They Were Cheap and Available: Prisoners as Research Subjects in Twentieth Century America." *British Medical Journal* 315:1437.

[69] Krista Thompson Smith, "Adventists and Biological Warfare", *Spectrum Magazine*, Vol 25, no. 3, March 1996 and David R. Franz, DVM, PhD, Cheryl D. Parrott, Ernest T. Takafuji, MD, MPH, "The US Biological Warfare and Biological Defense Programs" in Medical Aspects of Chemical and Biological Warfare, Part 1; *The Textbook of Military Medicine, Office of Surgeon General*, Borden Institute 1997; p. 425-436.

[70] Atomic Energy Commission Secret Memo by Kirkpatrick, E. E. Col. A January 8, 1947, This was a draft memo from

THE SCIENTISTS

Dr. Ewen Cameron[71]

Once the details of MKULTRA came to light, the focus in the media and in the Senate, was on the use of drugs, especially LSD. While the researchers within the project did indeed concentrate on developing a variety of hallucinogenic concoctions, they did so with an end in mind. The goal was to devise means and methods of enabling undercover operatives, soldiers, contractors or anyone who was involved in secret projects, to be able to keep those secrets if they were captured or interrogated. Hypnosis, combined with drugs, sensory deprivation and systematic abuse were seen as a means to that end. The leader in this pharmaceutical and psychological research was Dr. Ewen Cameron. Cameron was at the time, one of the most esteemed psychiatrists in the world. As president of the American Psychiatric Association, Canadian Psychiatric Association, and one of the founders of the World Psychiatric Association, Dr. Cameron began experimenting on brainwashing techniques as early as the 1930s with schizophrenic patients. At this time lobotomies were not yet in common use, though the procedure would begin to be implemented in 1936 on a wide scale. Electroshock therapy was some years from being accepted as a primary means of changing behavior.[72]

Cameron relied on torturous and highly stressful techniques for breaking down the personality of his patients. Schizophrenics would be stripped down naked beneath red lights for eight hours a day, sometimes for up to eight months with repeated messages inundating their senses. In other experiments Cameron would attempt to induce the delirium associated with a high fever by cooking his patients in an electric cage until their body temperature reached 102 degrees.

From January of 1957 until September of 1960 Cameron became one of the promising researchers the CIA turned to in order to develop means and methods of "brainwashing" and programming

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Colonel Kirkpatrick, Acting Manager, Field Operations of AEC, to the AEC Berkeley Area Engineer, puts the AEC stamp on termination of human testing, while simultaneously revealing it was going on under the Manhattan Project-at the request of Oppenhiemer: "Until the Atomic Energy Commission is able to consider sponsoring this type of experimentation, authorization cannot be given for the use of radioactive materials in human subjects under this contract." A more current report from the National Security Archives that clearly lays out the timeline and the assault by researchers on "subjects" can be found at http://www.gwu.edu/~nsarchiv/radiation/dir/mstreet/commeet/meet12/brief12/tab_f/br12f1d.txt----" Personal Statement from Elizabeth Zitrin, Attorney at Law Public Member of the Ad Hoc Committee on Radiation Experiments". For information on biological warfare experiments a good starting place is : *Biological Warfare: A Historical Perspective,* by LTC George W. Christopher, USAF, MC; LTC Theodore J. Cieslak, MC, USA, MAJ Julie A. Pavlin, MC, USA, and LTC (P) Edward M. Eitzen Jr., MC, USA. -- Operational Medicine Division, United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, Maryland, as posted at http://www.fas.org/nuke/guide/usa/cbw/bw.htm

[71] This section about Dr. Cameron is based on Orlikow Vs. United States, CIA Settlement of Some Complaints. Ewen Cameron and the Allan Memorial Institute - Subproject 68 funded by CIA from March 18, 1957 to June 30, 1960 Without conceding liability, in 1988 the CIA agreed to pay $750,000 to settle a case brought on behalf of nine plaintiffs who were subjected to federally funded mind control experiments sponsored by the CIA and conducted by prominent psychiatrist Ewen Cameron, M.D. The experiments included heavy does of LSD, electroshock and psychic driving.

[72] See "CIA Brainwashing Experiments", *MacLean's*; January 28, 1985, Vol. 98 Issue 6, p46, 1/3p and "A cold-war horror show's last act", *US News & World Report;* October 17, 88, Vol. 105 Issue 15, p13, 1/3p.

human beings to do the will of the agency. Cameron received $64,242.44[73] from the CIA. to develop a combination of techniques that would destroy an individual's memory of an event and enable the programmer to control their behavior through post-hypnotic commands. Cameron used a variety of drug combinations coupled with prolonged sleep deprivation, isolation, hypnosis, and electro convulsive therapy in order to "wipe" an individual's memory. His techniques worked, to a certain extent, but ethical considerations led the CIA to cut Cameron's funding in the US, prompting Cameron to move to Canada to continue his work with funding channeled through the Canadian Government.

He continued his work, officially, from 1961 until 1964 in Montreal where he received an additional $57,750.[74] During this time Cameron combined his techniques (in a "therapy" he called de-patterning) with electroconvulsive therapy in which the voltage introduced into one subjects brain, Linda Macdonald, exceeded the APA's guidelines by 76.5 times. He succeeded in wiping her memory and to this day, she cannot remember anything prior to 1963. In a January 17, 1984 broadcast of the Canadian Broadcasting System, a program called "The Fifth Estate" detailed the experiments of Cameron, prompting a burst of investigative journalism culminating in a class-action suit brought against the CIA by former subjects**.** In 1988, the case was settled out of court for $750,000, divided between 8 plaintiffs. Linda Macdonald received $100,000 and legal fees from the Canadian government, but Cameron himself, faced no punishment.[75]

Dr. Jose Delgado

Whereas Cameron focused on creating traumatized individuals through intense psychological pressure, Dr. Jose Delgado was investigating the direct route to control of "human subjects." Delgado physically invaded the brains of subjects with electrodes in order to create emotions and control actions with the push of a button. As he stated himself,

> "We need a program of psychosurgery for political control of our society. The purpose is physical control of the mind. Everyone who deviates from the given norm can be surgically mutilated. The individual may think that the most important reality is his own existence, but this is only his personal point of view. This lacks historical perspective. Man does not have the right to develop his own mind. This kind of liberal orientation has great appeal. We must electrically control the brain. Some day armies and generals will be controlled by electric stimulation of the brain." [76]

In his paper "Intracerebral Radio Stimulation and Recording in Completely Free Patients," Delgado observed that:

> "Radio Stimulation on different points in the amygdala and hippocampus in the four

[73] CIA MORI ID 17468: www.wanttoknow.info/mindcontrol
[74] Collins, Anne. *In the Sleep Room. The Story of CIA Brainwashing in Canada*. Ken Porter Books, 1988
[75] Tyner, Arlene. Mind-Control Part 1: Canadian and US Survivors Seek Justice, *PROBE Magazine*, March-April, 2000
[76] Dr. Jose M.R. Delgado Director of Neuropsychiatry, Yale University Medical School. Congressional Record, No. 26, Vol. 118 February 24, 1974.

> patients produced a variety of effect, including pleasant sensations, elation, deep thoughtful concentration, odd feelings, super relaxation (an essential precursor for deep hypnosis) colored visions, and other responses."[77]

Delgado, to his credit, did make great strides toward a better understanding the physiology of brain structures and their attendant behavioral and emotional correlates, strides that did not go unnoticed by the intelligence community and the military.

While Delgado worked in an area of specific interest, the direct stimulation of brain structures through implanted electronics, other researchers explored means of creating multiple personalities and programming the alternate personalities that emerged to do a variety of intelligence related work as operatives, still others explored the effects of various drug combinations and other "programming" and interrogation techniques aimed at creating super spies and breaking down enemy agents.

THE EXPOSURE OF WATERGATE/MKULTRA/COINTELPRO

According to testimony by Senator Edward Kennedy in 1977,

> "Some 2 years ago, the Senate Health Subcommittee heard chilling testimony about the human experimentation activities of the Central Intelligence Agency. The Deputy Director of the CIA revealed that over 30 universities and institutions were involved in an 'extensive testing and experimentation' program which included covert drug tests on unwitting citizens 'at all social levels, [high and low], native Americans and foreign.' Several of these [tests involved] the administration of LSD to 'unwitting subjects in [social] situations.' ... The Central Intelligence Agency drugged American citizens without their knowledge or consent. It used university facilities and personnel without their knowledge." [78]

As an example of the hubris wrought by institutions veiled in secrecy, given unlimited funds and staffed with amoral people we can only refer to the statement made by George White in a letter to MKUltra director Sidney Gottlieb: "I toiled wholeheartedly in the vineyards because it was fun, fun, fun! Where else could an *American* boy lie, cheat, rape and pillage with the sanction and blessing of the All Highest?" [79]

After Watergate, more information hit the papers, COINTELPRO was uncovered by a group of people who have never been apprehended, in spite of a six-year FBI investigation. The COINTELPRO program was secret until 1971, when an FBI field office was burglarized by a group

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[77] "Intracerebral Radio Stimulation and Recording in Completely Free Patients,", *The Journal of Nervous and Mental Disease,* Lippincott Williams & Wilkins, October, 1968.
[78] Testimony of US Senator Edward Kennedy, Joint Hearing before the Select Committee on Intelligence, US Senate, 95th Congress, 1977.
[79] (letter to Sidney Gottlieb) See also *Sex, drugs and the CIA*, by Douglas Valentine posted at http://www.counterpunch.org/valentine0621.html

calling themselves the Citizens' Commission to Investigate the FBI. These people broke into an FBI office in Pennsylvania, rifled through the filing cabinets and leaked to the press documents detailing the abuses suffered by a wide variety of activists, including a long-term plan to destroy Martin Luther King Jr.:

> "Agents tapped his phone, bugged his rooms, trumpeted his supposed commie connections, and his sexual proclivities, and sicced the Internal Revenue Service on him. When it was announced in 1964 that King would receive a Nobel Peace Prize, the FBI grew desperate. Hoping to prevent King from accepting the award, the Bureau mailed him a package containing a tape of phone calls documenting King's extramarital affairs and an anonymous, threatening letter (shown here in censored form). In barely concealed language, King was told to commit suicide before the award ceremony or risk seeing his "filthy, abnormal fraudulent self" exposed to the nation. Fortunately, King ignored the FBI's advice. He accepted the award and lived four more years until his assassination." [80]

Some of the largest COINTELPRO campaigns targeted the Socialist Worker's Party, the Ku Klux Klan, the "New Left" (including several anti-war groups such as the Students for a Democratic Society and the Student Nonviolent Coordinating Committee), Black Liberation groups (such as the Black Panthers and the Republic of New Africa), Puerto Rican independence groups, the American Indian Movement, and the Weather Underground. Later, Director Hoover declared that the centralized COINTELPRO was over, and that all future counterintelligence operations would be handled on a case-by-case basis.[81]

In addition, the MKULTRA documents hit the press and a number of books were written about the subject, most notable were' "The Search for the Manchurian Candidate" by John Marks, "Bluebird" by Colin A. Ross MD, and "A Nation Betrayed" by Carol Rutz. At this point victims began to come forward with claims of being horribly abused in these programs, one of the most famous is a woman named Candy Jones who described in stunning detail a tale of corruption and abuse.[82]

When Jimmy Carter became President in 1976 he promptly moved to introduce a modicum of control, he instituted the Foreign Intelligence Surveillance Act establishing an 11 member secret court to oversee the *s*urveillance activities of our covert agencies. As an example of the limited reporting requirements for the court we have the first report issued to Vice President

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[80] Martin Luther King, Jr., "Statement on Joseph Alsop and J. Edgar Hoover's charge of alleged Communist infiltration of the Civil Rights Movement," 23 April 1964 and Select Committee to Study Governmental Operations with Respect to Intelligence Activities, United States Senate, *Supplementary Detailed Staff Reports on Intelligence Activities and the Rights of Americans, Book III*, Final Report. 14 April 1976

[81] "Me and My Shadow": A History of the FBI's Covert Operations and COINTELPRO - Part 1. Produced by Adi Gevins, Pacifica Radio. 1976. Rebroadcast by Democracy Now! Wednesday, June 5, 2002. See also Paul Wolf's website for a detailed archive of official COINTELPRO documents and transcripts of the Church Committee hearings:http://www.icdc.com/~paulwolf/cointelpro/cointel.htm

[82] Donald Bain, . The Control of Candy Jones. Chicago, *Playboy Press*, 1976. (Reissued in 2002 by Barricade books as The CIA's Control of Candy Jones with a new introduction by Bain)

Mondale from Attorney General Benjamin R. Civiletti in 1979:

> This report is submitted pursuant to Section 107 of the Foreign Intelligence Surveillance Act of 1978, Title 50, United States Code Section 1807.
>
> During calendar year 1979, 199 applications were made for orders and extensions of orders approving electronic surveillance under the Act. The United States Foreign Intelligence Surveillance Court issued 207 orders granting authority for the requested electronic surveillances. No orders were entered which modified or denied the requested authority.[83]

Pointedly Carter's reform measure did not do anything to insure that the American public would be protected in the future from abuse and testing at the hands of the intelligence arm of the military-industrial complex. Carter's move to reform the CIA was to appoint an outsider as head of the agency, Admiral Stansfield Turner. After Turner took over as Director of the CIA 800 "rogue" agents were let go, though most all of them found work in various false front companies that had been set up in the previous years. [84]

Both the Rockefeller Commission and the Church Committee revealed a long standing pattern of both developing new psychological, pharmaceutical and radiological technologies, to influence individuals and groups and long standing pattern of behavior whereby politically disruptive citizens were systematically targeted, harassed and destroyed. Yet there have, to date, been no provisions instituted which would stop this behavior, nor is there any guarantee that these kinds of covert programs ever actually ceased. The only practical change engendered by the disclosures of the 1970s was to drive these kinds of operations further into the shadows. That such research and experimentation may still be occurring is evidenced by a DOD directive, issued by the Secretary of the Navy on November 6, 2006 that specifically requires prior approval of the Under Secretary of the Navy before conducting "severe or unusual intrusions, either physical or psychological, on human subjects (such as consciousness altering drugs, or mind-control techniques)."[85]

Non-Lethal Weapons Research Today

There is a long history that illustrates US Intelligence operations had tragic results for many involved. There was, however, no public debate surrounding these black operations because they were classified under the guise of national security. MKULTRA, Project PANDORA, plutonium testing, and many more projects conducted by the DOD and the CIA were exposed by committees

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[83] 1979 FISA report can be obtained at the Federation of American Scientists website: http://www.fas.org/irp/agency/doj/fisa/1979rept.html.

[84] William Blum, *The CIA: A Forgotten History,* Atlantic Highlands, New Jersey, Zed Books Ltd. 1986; Alan Moore Bill Sienkewitz, *Shadowplay-The Secret Team,* Forestville CA, Eclipse Books, 1987 and Leslie Cockburn, *Out of Control,* New York, Atlantic Monthly Press 1987.

[85] SECNAV Instruction 3900.39D, Subj: "Human Research Protection Program", November 6, 2006. www.fas.org/irp/DODdir/navy/**secnav**inst/3900_39d.pdf

led by Senators Rockefeller and Church in the 1970s.[86] However, tighter restrictions on human experiment including accountability and transparency did not occur until 1997, when President Clinton instituted revised protocols on human experiments.[87]

Official reports insist that the research involving experiments during the 1950s through the 1970s was destroyed. Yet, the scientists involved went without punishment, free to continue their careers.[88] Given the levels of ongoing EMF technology research today, and the recent retroactive approval of torture approved by the Military Commissions Act, it may be that human testing is occurring under post-9/11 national security protocols. Can we accept that all the psychological research conducted with government funding up to the 1970s was simply destroyed? At this time, the American public has no way to answer this question. The current administration classifies more information than any previous US administration.[89] Unclassified documents have even been recalled and re-classified.[90]

In the 1980s nuclear radiation experiments on humans became public knowledge and Russian tests making use of the electromagnetic spectrum were exposed.[91] Countries around the world passed laws and signed treaties in response to the danger of weapons that could adversely effect human behavior or manipulate human cognition. The Russians banned all EMF weapons in 2001.
These treaties have roots in the human radiation experiments of the 1950s, 1960s and 1970s. In effect, these treaties declared a basic tenant of human rights and cognitive liberties.[92]

In the quest for global military superiority, the US stepped up funding for the concept of the "Future Warrior" beginning in the late 1990s with the use of advanced nano-technology.[93] The idea was to streamline the military, improve soldier performance, control the fighting in real-time and avoid soldier mortality. Toward this end, the concept was to enhance the ability of soldiers in the field to interface with computer systems by using their own brain waves.[94] The US began to fund research

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[86] The Church and Rockefeller Committee reports can be accessed through the Assassination Archives and Research Center: http://www.aarclibrary.org/publib/church/contents.htm

[87] Memorandum of March 27, 1997--Strengthened Protections for Human Subjects of Classified Research. [Federal Register: May 13, 1997 (Volume 62, Number 92)] [Page 26367-26372].

[88] *Scientific American* talks about the work of Jose Delgado and states that Dr. Delgado stopped doing research as late as the 1990's, see: John Horgan, "The Forgotten Era of the Brain", *Scientific American,* September 26, 2005.

[89] Declassification in Reverse: The US Intelligence Community's Secret Historical Document Reclassification Program, Matthew M. Aid. Located at the George Washington University National Security Archive, http://www.gwu.edu/~nsarchiv/NSAEBB/NSAEBB179/#report.

[90] Executive Order 12958, originally signed by Clinton after Wen Ho Lee, a Los Alamos scientist was accused of giving the Chinese information, was amended by George W. Bush pm March 25, 2003. The amendment can be accessed at the White House website, http://www.whitehouse.gov/news/releases/2003/03/20030325-11.html.

[91] *The United Nations and Disarmament: 1945-1985* by the UN Department for Disarmament Affairs. (1985) New York, UN Publication Sales

[92] For a comprehensive listing of treaties and international conferences surrounding these concerns, see the Sunshine Project at http://www.sunshine-project.org/, See Also: *Human Rights: Beyond the Liberal Vision*, Judith Blau and Alberto Moncada, Rowman and Littlefield Publishers, 2005

[93] Amy Kruse, Program Manager at Defense Sciences Office, DARPA "Defense and Biology: Fundamentals for the Future". MIT also has The Institute for Soldier Nanotechnologies established in 2002 with a five-year, $50 million contract from the US Army, http://web.mit.edu/isn/index.html.

[94] See DARPA, "Neurotechnology for Intelligence Analysts", http://www.darpa.mil/dso/thrust/biosci/nia.htm.

into decoding the brain as well as other neurological research. President George H.W. Bush declared the 1990s "The Decade of the Brain".[95] At the same time, funding for computer to human interface poured into universities and Defense Advanced Research Projects Agency (DARPA) stepped up their research and development. In the universities, the field became "cognitive science" and within DARPA, the term "augmented cognition" was born.[96] While developments in brain research are touted for their amazing therapeutic advances in the medical field, they primarily serve the purposes of the US military.[97]

Americans have little idea about the research concerning the capabilities of electromagnetism, directed acoustics, or computer-human interfacing. The majority of Americans do not know that we are currently using these new-concept weapons in Iraq and Afghanistan. Indiana University law professor David Fidler stated to the *Economist*, "because these weapons are most likely to be used on civilians, it is not clear that using them is legal under the international rules governing armed conflict…if they are used in conjunction with conventional weapons, they could end up making war more deadly, rather than less."[98]

A peek into the US arsenal of weapons is like a look into a science fiction film. DARPA and various military research labs provide a view of the current technology available to enhance US soldiers in the field and manipulate the emotions and behaviors of the perceived enemy. As American sentiment toward the Iraq war spirals downward, along with the approval ratings of the US president, domestic civil disobedience is likely to rise, as it has in many countries in response to US foreign policy.

Are new electromagnetic weapons in the possession of the government be used on American citizens? The issue at hand is whether the research and technology currently being developed will benefit or harm us and how much liberty we are willing to sacrifice for a possibly skewed sense of national security and protection.

In September 2006, Air Force Secretary Michael Wynne announced that crowd control weapons should be tested on Americans first. "If we're not willing to use it here against our fellow citizens, then we should not be willing to use it in a wartime situation," said Wynne. "(Because) if I hit somebody with a non-lethal weapon and they claim that it injured them in a way that was not intended, I think that I would be vilified in the world press."[99]

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[95] The proclamation declaring the 1990's the "Decade of the Brain" was signed by President George H.W. Bush on July 17, 1990, which can be accessed at the Library of Congress, http://www.loc.gov/loc/brain/proclaim.html.
[96] See the Augmented Cognition International Society, http://www.augmentedcognition.org/history.htm.
[97] Fronteirs in Neuroscience- Artificial Intelligence in the Pentagon and Beyond. http://www.neuropsychiatryreviews.com/mar06/android.html
[98] "Electromagnetic weapons: Come fry with me", *The Economist,* January 30, 2003.
[99] Lolita C. Baldor, Associated Press, 9/12/2006. In addition to this comment, the Air Force released a declassified document located at the website of the Federation of American Scientists, (http://www.fas.org/sgp/eprint/hamilton.pdf directing the acquisitions team from the media. The author is the USAF principal deputy assistant secretary for acquisition, management and logistics, Darlene Druyun: "Effective immediately, I do not want anyone within the Air Force acquisition community discussing any of our programs with the media (on or off the record). This includes presenting program briefings in any forums at which the media may be present."

Non-lethal weapons sound harmless in relation to guns and bombs. However, non-lethal weapons are not just tazers and annoying sounds. Nor are they harmless. In fact, NLWs are such a concern that many countries have treaties demanding transparency. Beginning in the 1990s, groups have formed to provide oversight of NLW research, including international committees, concerned scientists, and citizens' groups including the Federation of American Scientists and the Center for Cognitive Liberty and Ethics.[100] The proliferation of NLWs have raised concern within the EU, Russia, and other countries, as records of Cold War abuses come to light and people come forward with complaints of illegal testing.[101]

The concern is more than a political issue and stretches beyond civil liberties into human rights as they relate to a person's cognitive liberties. The following section highlights technologies with the capability to control and manipulate individuals or large groups of people.

Crowd Control using the Electromagnetic Spectrum

The electromagnetic spectrum has provided the military with an expanse of weapons, which are operational and in military and private use today in the form of millimeter waves,[102] pulsed energy projectiles, and high power magnetic weapons.

Project Sheriff

The US has deployed the Project Sheriff active denial weapon in Iraq. Raytheon outfitted Humvees with their Silent Guardian Protection System, a device capable of heating the skin to 1/64 of an inch, causing instant pain similar to intense sunburn, [103] with the goal to facilitate dispersing a crowd. According to a report released by the Air Force on the human effects of this weapon, people with contact lenses and those wearing metal suffered greater effects. An imprint of a coin was discovered on the skin of a test subject and death or severe heart problems may occur.[104]

Pulsed Energy Projectiles

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[100] For a list of these groups see, Non Lethal Weapons, July 2005, compiled by Terry Kiss, Bibliographer, Air University Library, Maxwell AFB, AL accessed at the Maxwell Internet site, http://www.au.af.mil/au/aul/bibs/soft/nonlethal.htm and Appendix A of this paper.

[101] For further reading on these treaties, see *The Bulletin of Atomic Scientists* , September/October 1994 pp. 40-45 (vol. 50, no. 05), "The Soft Kill Fallacy" by Steven Aftergood and Barbara Hatch Rosenberg's in the same issue, "Sidebar: A non-lethal laundry list". Rosenberg cites the Conference on Disarmament, *Report of the Ad Hoc Committee on Chemical Weapons to the Conference on Disarmament*, Aug. 26, 1992, Nos. 22, 25, 34 (CD/1170) as well as the treaty, "Convention on Prohibition or Restriction of the Use of Certain Conventional Weapons Which May Be Deemed to Be Excessively Injurious or to Have Indiscriminate Effects."

[102] A detailed study conducted by Andrei G. Pakhomov, Yahya Akyel, Olga N. Pakhomova, Bruce E. Stuck, and Michael R. Murphy with the Brooks Air Force Base, Human Effectiveness Directorate, offers a scientific analysis of the effects of millimeter waves, "Current State and Implications of Research on Biological Effects of Millimeter Waves: A Literature Review", McKesson BioServices (A.G.P., Y.A., O.N.P.), U. S. Army Medical Research Detachment of the Walter Reed Army Institute of Research (B.E.S.), and Directed Energy Bioeffects Division, Human Effectiveness Directorate, Air Force Research Laboratory (M.R.M.), Brooks Air Force Base, San Antonio, TX.

[103] US Non Lethal Weapons for Iraq http://www.oft.osd.mil/library/library_files/article_461_Boston%20Globe.doc

[104] "Rumsfeld's Ray Gun," By Kelly Hearn, *AlterNet.* Posted August 19, 2005, http://www.alternet.org/story/24044/

Pulsed Energy Projectiles (PEPs) are another form of weaponry that is used to paralyze a victim with pain. According to *New Scientist* magazine, the expanding plasma effects nerve cells, but the long-term effects remain a public mystery.[105] The Joint Non-Lethal Weapons Program reports that, PEPs create a flash bang effect that startles and distracts.[106] However, the effects are much greater than just startling an individual. A 2001 *Time* magazine article states that the PEP "superheats the surface moisture around a target so rapidly that it literally explodes, producing a bright flash of light and a loud bang. The effect is like a stun grenade, but unlike a grenade the pep travels at nearly the speed of light and can take out a target with pinpoint accuracy…as far away as 2 km."[107]

While the effects of these weapons appear to be short-term and topical in nature, there is evidence that electromagnetic weapons have effects on the brain, including sleep disruption and behavior changes.[108] They can produce anxiety and fear or compliance in humans. It is possible to use these weapons as a means of torture, yet without knowing exactly when, where, and how the weapons are used, we are left to speculate.[109] An article by David Hambling in *New Scientist* magazine, March 2005, was titled, "Maximum pain is aim of new US weapons." In 2006, Dr. Brian Martin, associate professor in Science, Technology and Society, University of Wollongong, Australia, co-authored a paper entitled "Looming struggles over technology for border control," which describes the potential catastrophes that would lead to an extreme border protection plan. In the event of a natural disaster, or the rapid reduction of resources, or a major climactic change such as drought, rich countries will have a need to reinforce their borders against a massive influx of refugees. This scenario is often described in the nation-state context but it is possible to imagine such a perceived need in the event of internal civil unrest.

Directed Acoustics

In Maoist China, cities were equipped with megaphones, bombarding the people with on-going propaganda. The megaphones were in full vision of the people, yet there was no way to escape the sound. Today technology exists that fills a similar purpose. Voice to Skull directed acoustic devices are neuro-electromagnetic non-lethal weapons that can produce sounds within the skull of a human.[110]

A similar technology, known as Hypersonic Sound, is used in a similar fashion. According to its inventor, Elwood Norris of American Technology Corporation (ATC), the handheld speaker can

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[105] See government contract M67854-04-C-5074, University of Florida, Division of Sponsored Research, July 1, 2004. Also located at http://www.defensetech.org/peoplezapping.pdf

[106] According to a 2002 Joint Non Lethal Weapons Program document: www.dtic.mil/ndia/2002infantry/swenson.pdf

[107] Lev Grossman, "Beyond the Rubber Bullet", *Time Magazine,* July 21, 2002.

[108] David S. Walonick, "Effects of 6-10 Hz ELF on Brain Waves, www.borderlands.com/archives/arch/**elf**.htm

[109] David Hambling, Maximum Pain is Aim Of New US Weapons, *New Scientist*, March 2005.

[110] Definition from the Center for Army Lessons Learned, Fort Leavenworth, KS: "Nonlethal weapon which includes (1) a neuro-electromagnetic device which uses microwave transmission of sound into the skull of persons or animals by way of pulse-modulated microwave radiation; and (2) a silent sound device which can transmit sound into the skull of person or animals. NOTE: The sound modulation may be voice or audio subliminal messages. One application of V2K is use as an electronic scarecrow to frighten birds in the vicinity of airports."http://call.army.mil/products/thesaur/00016275.htm

focus sound waves directly at a person without anyone else hearing the sound. The technology is being tested by corporations such as McDonald's and Wal Mart to direct advertisements into a consumer's head.

The Long Rage Acoustical Device (LRAD),[111] is used by the military in situations such as crowd control, mass notification, and perimeter enforcement. For instance, an unruly mob may not hear a warning to disperse with traditional acoustic technology, or border enforcement agents may need to warn an approaching intruder to turn away or face bodily harm. The technology has advantages over lethal force, yet it also has the potential to inflict physical harm, emotional manipulation, and death. According to *Defense Update*, the LRAD can produce a 150-decibel acoustic beam from 300 meters away. The human threshold for pain is between 120 to 140 decibels.[112] In a 2003 *New York Times* article Mr. Norris demonstrates his technology to the reporter. At 1% of capacity, the reporter's eyes hurt, and hours later still experienced a headache.[113]

This technology can inflict permanent damage and death despite its classification as a non-lethal weapon. While the LRAD may be seen as a way to save lives in times of disaster or to avoid civilian casualties, the LRAD and similar directed acoustics may be cause for concern to those who exercise their right to assemble and conduct peaceful demonstrations and protests. The New York City police used the LRAD at the Republican National Convention and it was also used in Miami at a WTO Free Trade protests.[114] Covering one's ears will not protect a person and given, the long-range capabilities, fleeing from the beam may not help either (as evidenced in the use of directed acoustics against Jewish settlers in Gaza). The Associated Press (AP) reported that a device called "the scream" was used in a 2005 protest against Palestinians who "covered their ears and grabbed their heads, overcome by dizziness and nausea, after the vehicle-mounted device began sending out bursts of audible, but not loud, sound at intervals of about 10 seconds. An AP photographer at the scene said that even after he covered his ears, he continued to hear the sound ringing in his head."[115]

Neurological Technology

Neurobiology has many facets including therapeutic applications with Alzheimer's, epilepsy, depression, and stroke victims using Trancranial Magnetic Stimulation (TMS). Bush's Decade of the Brain produced outstanding advances for those with spinal cord injuries as well, which allows a paralyzed person to control a computer screen or a limb with a brain implant. There is also a new field in neurological research, Augmented Cognition. From universities to private business to the military, advances in neuro-technology can be used for amazing good. However, as we learned from the history of the Cold War, technology that has the capacity to heal also has the capacity to harm. Of great concern is the research being conducted at DARPA, which is trying to revolutionize the way soldiers receive information, respond to orders, adapt to stress, and perform while sleep

[111] The LRAD is another invention of Elwood Norris of American Technology Corporation.
[112] Jurgen Altmann, "Acoustic Weapons: A Prospective Assessment," *Science and Global Security*, Vol. 9, p. 13.
[113] Marshall Sella, "The Sound of Things to Come", *New York Times*, March 23, 2003.
[114] Amanda Onion, "RNC to Feature Unusual Forms of Sound", Aug. 25, 2004, ABC News
[115] Associated Press, "Israel May Use Sound Weapon On Settlers", 6/10/2005. Available at: http://www.huffingtonpost.com/2005/06/10/israel-may-use-sound-weap_n_2444.html

deprived.

TMS is being developed for military purposes using electrical impulses at close proximity to the skull to enhance mood, affect sleep patterns, and increase creativity.[116] This technology is beginning to replace electro-shock therapy. DARPA granted a contract to the Medical University of South Carolina to research now to improve a soldier's performance. A soldier's reaction to stress may be less intense, or a 40-hour flight will allow for the soldier to remain awake without the side effects of sleep deprivation.[117] Few, if any, understand the long-term effects of TMS, given its relative infancy in the overall field of Augmented Cognition. Does TMS produce unknown neurological effects ten, twenty, fifty years down the road? To what extent is TMS being researched? TMS is part of the overall field of Augmented Cognition. In essence, Augmented Cognition allows a human to interact with a computer through brain waves. The idea is to enhance a person's cognitive capabilities in the area of memory, learning, attention, visualization, and decision-making.

One application of augmented cognition allows a user to monitor a person's brain functions and send anticipatory commands to the person being monitored. For instance, a military command unit will be able to monitor a pilot in a cockpit, and based on the sensory output of the soldier, the base command can input messages directly into the pilot's brain to improve performance. DARPA describes this as a human computer symbiosis whereby, "This research will enable development of closed loop human-computer technologies, where the state of the user is measured, analyzed, and automatically adapted to by the computational system."[118] The increase in human-computer relations and the ability to manipulate and control a person's senses, memory, and neural output has wide implications.

The basic ability to enter a person's mind is not a futuristic fantasy. This is real and in prototype. DARPA began this research in 1983.[119] The Internet has become a focal point in our lives with reliance for information and communication. Our interaction and intimacy with computers is increasingly pervasive, as is our exposure to the field of augmented cognition. DARPA does not address the implications of such symbiosis, or the dilemma of he extent to which a person can or should be manipulated. The use of this technology is used for military purposes but it may not be long until it is used to "improve" the factory worker, prisoners, or the mentally ill.

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[116] "Transcranial Magnetic Stimulation: An Introduction", Grant Balfour, v1.0 - May 6, 2002 available at: www.cognitiveliberty.org/issues/TMS_index.html

[117] MUSC To Develop Brain Stimulation Device For Military, Charleston, SC, May 9, 2002, www.**musc**.edu/pr/darpa.htm, "The overall goal of the project is to use the unique resources at MUSC's Brain Stimulation Laboratory and Center for Advanced Imaging Research to determine if: 1. non-invasive stimulation of the brain can improve a soldier's performance, 2. and then design, manufacture and test a prototype of a system that would be capable of delivering this technology in the field."

[118] Improving Human Performance Through Advanced Cognitive System Technology, Dylan D Schmorrow and Amy A Kruse, LCDR MSC USN, Defense Advanced Research Projects Agency, Arlington, VA, Strategic Analysis Inc., Arlington, VA, Available at: http://ntsa.metapress.com/(2pq1al55mfylqgf0n3cvjc45)/app/home/contribution.asp?referrer=parent&backto=issue,91,167;journal,5,7;linkingpublicationresults,1:113340,1

[119] New Generation Technology: A strategic plan for its Development and Application to Critical Problems in Defense, DARPA, 1983.

The Implant

Another realm of brain research is the field of neural implants. Until recently, implants were a futuristic fantasy. Current advances in the private and military sectors have produced an implant that can allow a victim of a spinal cord injury to walk again or give an amputee the ability to control her leg with her mind. In the private sector, Cyberkinetics is leading the way to liberating some people from wheelchairs. This technology is a path to a more functional way of life, but it is also possible that the use of implants could be used for malevolence.

John Donohoe, founder, chief scientific officer, and director of Cyberkinetics, addressed the issue of mind control and neural implants. When asked if creating a brain-machine interface will open the door to mind control Donohoe responded, "We do that all the time already. Advertising is mind control. Even pharmaceutical agents are a form of mind control. When people have behaviors that deviate far from the norm, they are given medications that bring their mind back into the realm of behavior that we call normal. If a child were to have a seizure and became unconscious because of the seizure, and we controlled his mind so that he did not have seizures, that would be a wonderful thing. We want to do that."[120]

The Experts[121]

Many scientists, philosophers, psychologists, and military analysts have written on the possibilities of accumulating information directly from the human brain as well as controlling human beings for various governmental and militaristic purposes using the aforementioned technologies. What follows are excerpts from recent interviews conducted by the authors with notable experts focusing on the capabilities of US EMF technologies and concerns about human rights and cognitive liberty. We contacted twenty-two experts in the fields of EMF technologies, many would not comment. The following are quotes from four experts who were willing to publicly address the subject.

Vladimir Nikolaevich Lopatin

Director of The Republican Scientific Research Institute of Intellectual Property, Moscow, former Deputy of the State Duma of the Russian Federation on the Vologda from 1995 to 1999, and Senior Assistant to the General Public Prosecutor of the Russian Federation. During the 1990s Lopatin was active in the Russian Federation's banning of EMF technologies for military purposes.[122]

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[120] Neuroscience: John Donoghue By Aaron J. Sender, *Discover* Vol. 25 No. 11, November 2004, Mind & Brain

[121] Gaining interviews with DARPA scientists and officials at the Human Effectiveness Directorate at Brooks proved troublesome. For information about current projects, see DARPA Defense Science Program, specifically COL Geoffrey Ling, M.D., PhD's program "Human-Assisted Neural Devices" and Amy Kruse's Improving War fighter Information Intake Under Stress (AugCog) and Neurotechnology for Intelligence Analysts. At the Human Effectiveness Directorate see Andrei G. Pakhomov , Yahya Akyel , Olga N. Pakhomova , Bruce E. Stuck , Michael R. Murphy, "Current state and implications of research on biological effects of millimeter waves: A review of the literature", in *Bioelectromagnetics,* Volume 19, Issue 7 , Pages 393 - 413.

[122] The following are excerpts of an interview with Lopatin translated by U.C. Davis student, Tatiana Kanare.

The following are quotes from Lopatin:

"At the same time, the necessity of protection from information weapons, information terrorism and information war is being discussed more often during the last years."

"…according to the Security Department of the Russian Federation, directors of Russian Special Services and the Ministry of Defense of Russia. Based on the data of special services, by the beginning of the 21st century expenses for purchasing means of information war increased within the last 15 years in the USA in four times and are ahead of all armament programs. Information confrontation during the times of a regular war began to change to a new, higher level – information war."

"According to article 6 of the Federal Law "On weapons," as of July 30, 2001, on the territory of the Russian Federation it is forbidden to circulate as means of civil and service weapons: 'weapons and other objects, destructive ability of which is based on the use of electro-magnetic, light, heat, infrasound and ultrasound radiation and which have output parameters that exceed the amounts, set by state standards of the Russian Federation and norms of the federal body of executive power responsible for healthcare, and also mentioned above weapons and objects, manufactured outside of the territory of the Russian Federation'."

Carol Smith
British psychoanalyst, private practice in London, member of The College of Psychoanalysts and the Institute for Psychotherapy and Social Studies and member of their Ethics Committee.

Asked if there are human rights concerns associated with these particular non-lethal weapons, Smith answered, "Yes – it depends though by what is meant by 'the wrong hands'. For people who are targeted for experimentation – all such devices need testing – all hands are the wrong hands, be they government, private commercial, or sadistic/commercial. Ionatron, a large company based in Arizona, developed plasma channel directed energy weapons and state in their website: 'What are LIPC laser-guided directed-energy weapons? Laser-guided directed-energy weapons work like "man-made lightning" to disable people or things. LIPC technology is Ionatron's proprietary type of laser-guided directed-energy weapon. LIPC stands for laser-induced plasma channel; the plasma channel is how the energy is directed through the air at the target. Extremely fast femto-second lasers cause light to break into filaments, which form a plasma channel that conducts the energy like a virtual wire. This technology can be adjusted for non-lethal or lethal use'."

Discussing neurotechnology, Smith adds, "Brain mapping indicated to us the pleasure centers of the brain. TMS is the accessing these with rapidly changing magnetic fields to produce electrical fields.

If the right hand rule is operative, the effect of inducing electrical fields by changing magnetic fields improves mood.

(Lenz's law, however, gives the direction of the induced electromotive force (EMF) resulting from electromagnetic induction, thus: The EMF induced in an electric circuit always acts in such a

direction that the current it drives around a closed circuit produces a magnetic field which opposes the change in magnetic flux.) In other words, it would be possible to create depression and a feeling of overwhelming hopelessness by the induction of a current into the electrical circuit of the brain, which opposed the change in magnetic flux.[123]

"In 2004, The US Air Force Directorate: Controlled Effects gives a clear picture of objectives: "The Controlled Effects long-term challenge focuses technology developments in three primary areas Measured Global Force Projection looks at the exploitation of electromagnetic and other non-conventional force capabilities against facilities and equipment to achieve strategic, tactical, and lethal and non lethal force projection around the world. Controlled Personnel Effects investigates technologies to make selected adversaries think and act according to our needs. Dominant Remote Control seeks to control, at a distance, an enemy's vehicles, sensors, communications, and information systems and manipulate them for military purposes. The S&T Planning Review panel looked first at extending the applications of advanced military technologies currently under development and then at new, revolutionary technologies for their military significance."

"For the Controlled Personnel Effects capability, the S&T panel explored the potential for targeting individuals with non lethal force, from a militarily useful range, to make selected adversaries think or act according to our needs. Through the application of non-lethal force, it is possible to physically influence or incapacitate personnel. Advanced technologies could enable the war fighter to remotely create physical sensations such as pressure or temperature changes. A current example of this technology is Active Denial, a non-lethal counter-personnel millimeter wave system that creates a skin heating sensation to repel an individual or group of people without harm. By studying and modeling the human brain and nervous system, the ability to mentally influence or confuse personnel is also possible. Through sensory deception, it may be possible to create synthetic images, or holograms, to confuse an individual's visual sense or, in a similar manner, confuse his senses of sound, taste, touch, or smell. Through cognitive engineering, scientists can develop a better understanding of how an individual's cognitive processes (pattern recognition, visual conditioning, and difference detection) affect his decision-making processes. Once understood, scientists could use these cognitive models to predict a person's behavior under a variety of conditions with the potential to affect an adversary's mission accomplishment via a wide range of personnel effects."[124]

Dr. Dean Radin
Former positions at AT&T Bell Labs and GTE Labs on advanced telecommunications R&D, appointments at Princeton University, University of Edinburgh, University of Nevada, SRI International and Interval Research Corporation, co-founder of the Boundary Institute, Senior Scientist at the Institute of Noetic Sciences. Adjunct appointment at Sonoma State University, Distinguished Consulting Faculty for Saybrook Graduate School.

"I have spoken with experts in this area (extremely low frequency) about health effects in general

[123] To access Lenz's Law online, go to: http://www.launc.tased.edu.au/online/sciences/physics/ Lenz's.html
[124] For the complete briefing see the Air Force Research Lab website at http://www.afrlhorizons.com/Briefs/Jun04/DE0401.html.

and the consensus seems to be that non-ionizing EM radiation definitely does have effects on living systems, from individual cells to human behavior. The principle health concern is childhood leukemia associated with proximity to high-tension lines. There the epidemiological evidence is fairly clear. On other sources of EM, like cell phones and microwaves, the jury still seems to be out, although I strongly suspect that directed microwaves at non-ionizing strength can induce all sorts of behavioral changes through direct influence of the nervous system. This comes from my contacts in the non-lethal weapons arena, which is often lumped in with the hysteria over supposed psychic mind-control. All things being equal, I'd rather see development of non-lethal weapons than lethal ones. How such weapons are actually used is another matter, of course."

"The question is, were there *e*ver elements of the intel/military world engaged in experiments on human behavior (not mind) control? Yes, many decades ago, during the cold war. But is such work still taking place? I don't know, because if it is it would be a black project and then by definition only those involved would know of it. I hope no such projects are underway, because I do believe that EMF, used in nefarious ways, can destabilize the brain, and potentially generate feelings of violence or apathy. But I very strongly doubt that specific thoughts or intentions or actions can be induced"

Dr. Nick Begich
He is the editor of Earthpulse Flashpoints, a new-science book series and published articles in science, politics and education and is a well known lecturer, having presented throughout the United States and in nineteen countries. Begich has served as an expert witness and speaker before the European Parliament and has spoken on various issues for groups representing citizen concerns, statesmen and elected officials, scientists and others. He is the publisher and co-owner of Earthpulse Press and Executive Director of The Lay Institute of Technology, Inc. a Texas non-profit corporation.

"There are several ways that microwaves can affect humans. For instance, the Sheriff and weapons that can heat the skin for crowd control do what the military states but they are capable of much more. The thermal heating weapons act like a car radio; you can change the frequencies to get different effects. The electromagnetic weapons send an impulse through the nervous system. They can transfer sounds, like Woody Norris' directed acoustic weapons, which is contracted to the US government. It modulates a signal that is a radio frequency, which can be changed to affect certain organs. It can override an organ like the heart or the liver. So changing the perimeter is like changing the broadcast on the radio. These extremely low frequencies also have the capability to send messages directly into the head when only the receiver can hear it. (see the 1985 Radiofrequency Radiation Dosimetry Handbook)."

"The handbook talks about electromagnetics and about the rapid healing of bones. The frequencies can also be used to manipulate the brain and create a disequilibrium. These frequencies can also imbed signals on radio broadcasts to create a feeling of fear or anxiety. The US military would embed these signals on the Muslim prayer broadcasts during the first Gulf War. This was called Project Solo."

“During the 1990’s, in both presidential administrations, non-lethal weapons such as these and others received priority funding. The Secretary of Energy under Clinton, O’Leary, warned that over a 40 year period, 500,000 had been unwitting test subjects for military research on non-lethal weapons, including MKULTRA who claims among many victims, Ted Kaczinky, the Unabomber. There is no way to know who these people are or how to help them because there is paranoia in the military and no oversight in Congress. These black projects probably don’t even make it to the President.”

“The problem is that the military’s role is to be paranoid and think up scenarios where the worst can happen then prepare for this in order to protect the people from a hypothetical future event. But there is little to no oversight. The Senate Intelligence Committee is made up of people like Ted Stephens who thinks the internet is made up of pipes and tubes. These people do not have the required background knowledge to ask the right questions. According to the defense budget report, 40% of the budget is dedicated to black projects. There is no oversight and no public knowledge. In the European Union, things are much different.”

“In February 1998, I testified before the European Union parliament for an hour and a half and convinced them of the detrimental effects of non lethal weapons on humans, their behavior and their minds. The EU was convinced and passed a resolution banning the use of weapons that can manipulate a person (see Parliament Resolution A4-005/99 entitled "Resolution on the Environment, Security, and Foreign Policy" passed on January 29, 1999). During the hearings, the US representative and NATO representatives sat in the back and declined to participate when asked. In the US, there is no such resolution or anything remotely close to being considered by any member of Congress. There is no concern for it in the US because no one knows about them.”

“During the 1980’s and 1990’s, there were a lot of papers that came out of the Naval War College and from top military officials that advocated using weapons that would cut down on the carnage seen by the American public in order to maintain public support. There was another paper that discusses how people will give up their liberties if they lived in a climate of fear by an outside enemy. If the US public knew about these weapons and what they could potentially asked to give up, their minds, the public would resist. So now, these weapons are being developed by the companies that comprise the industrial military complex who are immune from FOIA requests.”

“Without oversight, these weapons will a government to have absolute control. These weapons are most certainly in the hands of most industrialized countries. China certainly has them as intelligence reports released by the CIA reveal claims about these new concept weapons. There needs to be a debate in the public sphere because while these weapons appear frightening, they have amazing therapeutic potentials. There is the possibility of quicker healing and curing disease and what is just as important about government transparency concerning weapons is the transparency of life saving science being kept from the public. If we have the ability to cure and the government or military hides this, we have just as big a problem.”

Summary Analysis of Expert Interviews

From the four interviews we were able to complete, there is a clear consensus of concern for the potentiality of human rights abuses with EMF weapons testing and use. They collectively agree that the US is the leading global researcher in this area and spends increasingly more money building this technology. It is also clear that we know very little about the actual levels of experimentation, research, and capabilities of EMF weapons technologies due to high levels of US government security.

Department of Defense Military Contractors

Military contractors run our wars in concert with power elites. The corporation also has the power to determine which studies will reach the public.[125] To be certain, the military, in the interest of budgets, will allow negative or alarming studies to remain unreported or lost in a sea of classified documents.

The power of the military and DOD contractors is staggering. In the interest of national security and lessons learned from an open democracy during the 1970s and the 1990s, operations have become more black. In essence, no one can know with certainty what our military, government, or corporations have in store for the world, though, we have some clues.

Michael Vickers, senior adviser to the Secretary of Defense for the 2005 Quadrennial Defense Review and principal strategist for the largest covert action program in the CIA's history, recently testified on the importance of black operations:

"US Special Operations Command's (SOCOM) emphasis after 9/11 has been to make white Special Operations Forces (SOF) more gray and black SOF more black. It is imperative, however, that white and black SOF be integrated fully from a strategic perspective."[126]

The money involved in the non-lethal weapons industry is growing and military contractors are reaping the profits. According to Defense Industry Daily, Aardvark Tactical, Inc. in Azusa, CA won a $50 million contract to develop non-lethal weapons, anti-terrorism capabilities, and riot gear.[127] Ionatron was awarded a $12 million contract to develop the Laser Induced Plasma Channel technology which produces man-made lightening bolts.[128] SAIC received a $49 million in November 2004 to develop High Power Microwave and other directed energy systems while Fiore Industries received a $16.35 million contract for similar technology and ITT received a $7.85 million contract

[125] From *Microwave News*, July 2006, "Radiation Research and The Cult of Negative Results:" "When we investigated who sponsored the microwave-DNA papers published in Radiation Research, we discovered that four out of five were paid for by the wireless industry —notably Motorola— and/or the US Air Force, both of which have a long history of trying to control or suppress EMF research. Indeed, industry and the USAF paid for more than 75% of all the negative genotox studies, that is those published in all the various journals."
[126] According to Michael Vickers biography at the Center for Strategic Defense Budget Studies' website, "The paramilitary operation that drove the Soviet army out of Afghanistan and played a major role in ending the Cold War." http://www.csbaonline.org/6About_Us/2Staff_Directory/Michael_Vickers.htm
[127] "$50M for USMC Riot Gear, Protection Items, and Non-Lethal Weapons", *Defense Industry Daily*, July 27, 2005.
[128] "Ionatron Facing Scrutiny Over Laser Projects", *Defense Industry Daily,* May 24, 2006.

for the same in 2000.[129] Fiore Industries received a $7.1 million for High Power Microwave Research and Experiment Program as early as 1994 and the same year Hughes Missile Systems Company received a $6.6 million contract for *High Power Microwave Suppression of Enemy Air Defense Technology*.[130] Lockheed Martin secured a deal with DARPA in 2005 to continue the development of the Space Based Radar Antenna Technology in a $19.5 million contract.[131] According to the Lockheed press release, the technology, "could significantly increase global persistent surveillance coverage".

In May of 2006, the Air Force issued $24 million in contracts for "Electro Magnetic Effects Research and Development" to Northrup Gruman, Voss Scientific, Lockheed Martin, Electro Magnetic Applications, and SAIC among others.[132] The DOD viewed electromagnetic research and development as a key component in future wars as early as the 1990s. Emmett Paige Jr., Assistant Secretary of Defense for Command, Control, Communications and Intelligence declared in 1996 that, "Well over a decade ago, a Soviet general reportedly said something like 'to prevail in the next conflict, one must control the electromagnetic spectrum.' That statement proved true in the Bacca Valley and on deserts in Iraq. The Department of Defense is committed to ensuring that "in the next conflict it is we who will control the spectrum. We know its value'.[133] Increasingly, the value of non lethal weapons continues to rise as they produce fewer images of death in the media than traditional weapons."

In addition to DOD contractors, the realm of non-lethal weapons extends into the universities with millions of dollars in scholarships and research fellowships. Pennsylvania State University, sponsors the Institute for Non-Lethal Defense Technologies (INLDT), the University of Medicine and Dentistry of New Jersey has the Stress and Motivated Behavior Institute, University of New Hampshire houses the Non-lethal Technology Innovation Center, and many US military schools have classes directly related to non-lethal weapons technology.[134] There are also numerous conferences each year hosted by the Department of Defense, contractors and universities.[135] The business of non-lethal weapons is expanding and will continue to grow. In 2006, the Joint Non-Lethal Weapons Directorate received $43.9 million compared to $25.8 million in 2000.[136]

Ionatron's website states that, "…the market for new directed-energy applications (will increase to $12.7 billion over the next ten years for the defense market alone."[137]

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[129] "USAF Detachment 8 Continues US Research Into EMP-Microwave Weapons", *Defense Industry Daily*, March 7, 2006.
[130] ibid.
[131] Lockheed Martin news release, May 23, 2005, "Lockheed Martin Selected for Continued Development of the Innovative Space Based Radar Antenna Technology (ISAT)".
[132] US Department of Defense Office of the Assistant Secretary of Defense (Public Affairs), No. 169-06 March 01, 2006.
[133] United States Department of Defense Speech, Volume 11, Number 83, "Electromagnetic Spectrum: Key to Success in Future Conflicts", http://www.defenselink.mil/speeches/index.html.
[134] See Industrial College of the Armed Forces, Naval War College, and the US Army War College course offerings on their websites.
[135] Bunker, Robert J., "Non-Lethal Weapons Conferences", *Military Review,* vol. 80, no. 2, Mar./Apr. 2000, pp. 103-109.
[136] Pappalardo, Joe, "Homeland Defense Plan Favors Non-Lethal Technology", *National Defense Magazine,* June 2005.
[137] Direct quote from the Ionatron website: http://www.ionatron.com/default.aspx?id=4, accessed August 2006.

Despite Clinton's reforms on human testing, the government, military and the corporation will undoubtedly want to test these weapons on humans whenever possible. Easiest to test would be prisoners in undisclosed CIA detention centers, civilians in war torn regions, and even US citizens in protest crowds or civilian jails. In addition to the rubber bullets and pepper spray, which are common in many police forces, new concept weapons are also in use. Perhaps soon Americans will learn first-hand, the effects of the new human control technologies.

However, hundreds of people continue to assert that a person or persons, whom they do not know, have been targeting them with electromagnetic weapons in a widespread campaign of either illegal experimentation or outright persecution.

These experiences involved a number of discrete phenomena:

Hearing voices when no one was present.

Feeling sensations of burning, itching, tickling, or pressure with no apparent physical cause.

Sleeplessness and anxiety as a result of "humming" or "buzzing".

Loss of bodily control, such as twitching or jerking of an arm or leg suddenly and without control.

Unexpected emotional states, such as a sudden overwhelming feeling of dread, rage, lust or sorrow that passes as quickly as it arises.[138]

The levels of research on directed energy is now large enough to support a Directed Energy (DE) Professional Society made up of private contractors and Department of Defense officials with security clearances. They have been holding high security symposiums since spring 2001 including a planned meeting set for March 2007. The following is from the Directed Energy Professional Society's website.

"The Directed Energy (DE) Systems Symposium (March 2007) will focus on systems aspects of DE in a limited-attendance environment. The Systems Symposium consists of co-located technical sessions organized by five separate conferences, with joint technical and plenary sessions to encourage discussion outside narrow technical limits. Attendance at all sessions is limited to US citizens with classified visit requests on file.

[138] This list of symptoms was compiled from material available on the website of Californians Against Human Rights Abuses (CAHRA) and can be found at www.mindjustice.org. In addition the authors conducted interviews with seven individuals who wish to have their identities protected and who presented anecdotal and physical evidence to support their assertions. There is, however, little in the public domain that conclusively states the existence of direct human manipulation by governments, militaries or private companies/researchers in the current day, MKULTRA and other historic programs notwithstanding. However, there are many organizations that seek to help these people including concerned scientists, Russian Duma members and EU parliamentarians, psychologists and academics. A list of organizations follows in Appendix A.

Symposium Highlights

Beam Control Conference
Directed Energy Modeling and Simulation Conference
Employment of Directed Energy Weapons Conference
High Energy Laser Lethality Conference
High Power Microwave Systems and Effects Conference"[139]

The following are three course descriptions from the October Directed Energy Conference:

Course 9.†Military Utility Analysis for DE (Direct Energy) Systems

Classification: Secret

Course Description: This course will provide an overview of military worth analysis for DE weapon systems. The course will include a description of four areas of systems engineering assessment that are brought together to form military worth analysis. These are: 1) weapon system concept performance trade studies, 2) target vulnerability assessment, 3) engagement-level system operational effectiveness assessment, and 4) war gaming and mission/campaign level analysis. Each of these areas will be covered during the short course, with emphasis on the elements that are drawn from each of these areas to support military worth analysis. The course will particularly emphasize methods for assessing system level effectiveness in the context of traditional weapon effectiveness tools such as the Joint Munitions Effectiveness Manuals (JMEMs) and for providing data on DE weapons effectiveness to mission and campaign level analysis tools and to models and simulations used to support war gaming.

Topics to be covered include:

Definition of military worth analysis
Elements of DE weapon system performance trade studies and how they feed military worth analysis
Target vulnerability assessment and its use to support weapon effectiveness
Adapting standard weapon "kill" criteria to measure benefit of DE effects
Joint Munitions Effectiveness Manuals (JMEMs) weapon effectiveness models
Military utility studies
Modeling and simulation to support war games and war fighter exercises
Mission and campaign level modeling

Course 10. Laser Lethality

Classification: Secret

[139] Directed Energy Professional Society, Monterey, CA, 19-23 March 2007, Directed Energy Modeling and Simulation Conference 2007, http://www.deps.org/DEPSpages/DEMSconf07.html

Course Description: This course reviews laser material interactions over parameter ranges of interest for weapons applications. Fundamental considerations of the optical coupling of the laser energy into the material will be presented. This will be followed by physics-based treatments of the response of metals, organic-based materials, and ceramics to the laser irradiation.

Metals: Simple cw, one-dimensional treatments will be utilized to illustrate the general principles of the response of metals to laser radiation, but two-dimensional cases, phase changes, and pulsed effects will be discussed as well.

Organic Based Materials: The effects of high-energy laser (HEL) radiation on organic based materials, including fiber reinforced composites, plastics and coatings will be reviewed. Materials will range from char formers and charring ablators to clean ablators. The relationship between the pyrolysis processes taking place in various materials during HEL radiation will be reviewed as a function of material composition, form and structure.

Ceramic Materials: Considerations of the response of ceramic shapes when laser loading is added to in-service stresses will be presented. An understanding of these responses from models, which are based on a combination of the thermo-mechanical stress calculations and statistically based fracture initiation, will be presented.

Course 11.†Directed Energy Bioeffects

Classification: Secret

Course Description and Topics: This course will introduce the basics of the biological effects of Directed Energy on cells, tissues, organisms, and humans, with particular emphasis on the influence of such effects on the development of use of Directed-Energy-Emitting technologies.

The student will learn about the mechanisms, resulting damage, and mission impact of laser-tissue interaction. The student will learn what tissues are most susceptible to laser damage based on wavelength, exposure duration, and irradiance. The potential mission-impact of sub0-threshold, threshold, and suprathreshold exposures will be discussed.

Student will understand the nature of RF bioeffects research, including human/animal studies, modeling and simulation, and biotechnology approaches. Students will become familiar with current state of knowledge on potential health effects RF, such as cancer, memory loss, and birth defects. Students will become familiar with basis and structure of current RF safety standards, comparison between competing standards, and how RF safety standards are applied. Students will be instructed on common RF measurement equipment and important factors for investigating potential RF overexposures.

Topics to be covered include:

Laser damage of the eye (retina and cornea)

Laser damage to the skin
Laser safety standards
Laser damage as a function of energy, pulse duration, wavelength, and spot size
RF bioeffects research and the current scientific consensus on RF hazards
RF safety standards
RF measurement basics
Investigating RF overexposures"[140]

The US Joint Non-Lethal Weapons Directorate released a paper in 2004 which presents "Crowd Control Modeling and Simulation." This report discusses behavioral changes human populations.[141] That the Department of Defense calls for new weapons systems designed to work on the psychological underpinnings of a population should give human rights activists great cause for alarm. The use of electromagnetic weapons to alter the emotional state, hamper the ability of an enemy or US citizens, to think clearly, and result in chaos and pain are morally problematic for a number of reasons:

1. Creating fear, anxiety confusion and irrational behavior within an individual or a population is counterproductive to the operations of a free society and to the execution of warfare. Chaos only breeds the need for greater and greater means of physical repression; irrational behavior is by definition unpredictable and as such provides significant difficulty when the task is to secure an area.

2. These weapons leave no tell tale clues. There are no bullet holes or gross damage (with the exception of those designed to maim, burn or explode targets).

3. They are operated from a great distance, meaning that the operator has no feedback as to the effects of his or her actions. This provides us with a very dangerous circumstance very similar to Millgram's experiment where we can predict with certainty gross abuses of power.

4. Any device that invades a persons mind, either through induction of "evoked potentials" through electromagnetic means or through the various "crazy-making" tactics employed in both information warfare and psychological operations is a violation of human rights and cognitive liberty.

In terms of authorizing and administering tests of radioactive substances and other tests on unsuspecting members of the public, history shows that people without ethical standards can rise to positions of great responsibility and once ensconced in such positions of trust, produce the most horrifying abuses without fear of reprisal. When layers of secrecy overlay the activities of otherwise rational and intelligent men, the failings of their hearts more readily show. In the case of actually attempting to control human behavior through both overt and covert means our departments of defense and intelligence agencies, both subordinate to the executive branch of government have historically proven incapable of protecting the public and undeserving of the trust given them to

[140] Directed Energy Professional Society, *2006 Directed Energy Symposium Short Courses,* 30 October 2006 Albuquerque, New Mexico: http://www.deps.org/DEPSpages/DEsymp06ShortCourse.html
[141] Louis Slesin, "Radiation Research and The Cult of Negative Results", *Microwave News,* July 31, 2006.

perform their functions for the public good.

Total Surveillance: Cognitive Liberties vs. National Security

Today the US and the U.K. are becoming total surveillance societies in the name of national security. London, like cities across the US, is equipped with cameras citywide. Daily human actions are recorded with video and voice recognition device, while our email and computer usage is monitored. Increased demand for resources, the erosion of middle classes, war, poverty, and environmental disasters are historically factors leading to social uprisings and infiltration of political borders. As governments reinforce the threat of terror, people increasingly turn to their governments for protection.

The US has a long history of human rights violations through harassment, telephone tapping, video surveillance, behavior manipulation, torture, drug-induced states of conscience and psychological control. Congress's passage of the Military Commission Act of 2006 put universal human rights outside the scope of US policy. Today, the US government is using the most technologically advanced forms of surveillance and control, along with the propaganda of fear and intimidation against its citizens. The US engages in covert torture, covert imprisonment, increased censorship and the massive secret classification of government documents.[142]

A prominent neuroscientist, Francis Crick stated in 1994, that "your joys and your sorrows, your memories and your ambitions, your sense of personal identity and free will, are in fact no more than the behavior of a vast assembly of nerve cells and their associated molecules."[143]

Is it possible that today's scientists in the employ of the US neo-conservative global-dominance policy elites believe the same? According to Steven Rose, there are, "bad hats" in neuroscience: "There are always opportunists. The current affairs of our country have produced many."[144] The abundance of neuro-research has led to the development of several products by private business in the name of national security, including brain fingerprinting.[145]
John Norseen, a neuroscientist interested in Biofusion, the relationship between humans and

[142] For verification of US torturing people to death see, "US Operatives Torture Detainees to Death in Afghanistan and Iraq", Project Censored Top 10 Uncensored Stories of 2006:
http://www.projectcensored.org/censored_2007/index.htm#7
[143] Michael Shermer, "*Astonishing Mind:* Francis Crick 1916–2004 recollections on the life of a scientist".
[144] Steven Rose, *The 21st Century Brain: Explaining, Mending and Manipulating the Mind*, Jonathan Cape Publishing, March 31, 2005.
[145] The official explanation of Brain Fingerprinting from Dr. Lawrence Farwell: "Brain Fingerprinting testing is a scientific technique to determine whether or not specific information is stored in an individual's brain. We do this by measuring brain-wave responses to words, phrases, sounds or pictures presented by a computer. We present details about a crime, training or other types of specific knowledge, mixed in a sequence with other, irrelevant items. We use details that the person being tested would have encountered in the course of committing a crime, but that an innocent person would have no way of knowing. We can tell by the brainwave response if a person recognizes the stimulus or not. If the suspect recognizes the details of the crime, this indicates that he has a record of the crime stored in his brain." For more research, see the Brain Wave Science site, the official internet identity of Brain Fingerprinting Laboratories at http://www.brainwavescience.com/Publications.php.

computers, says, “If this research pans out you can begin to manipulate what someone is thinking even before they know it.” Norseen says he is agnostic on the moral ramifications of this research. He feels that he is not a “mad” scientist - just a dedicated one. “The ethics don’t concern me,” he says, “but they should concern someone else.”[146]

We, the authors of this report, contend that human ethics should concern every person who believes in human rights and desires control over their own mind and body. Our brains control our bodies, actions, and thought processes. If the government and the scientists they employ perceive that the human mind as simply a collection of neurons, it then becomes possible to justify the surveillance of the human mind and body for national security purposes.

The control and manipulation of a human brain is a terrifying possibility. Lieutenant Colonel Timothy L. Thomas, US Army (ret), published an article in the military journal *Parameters* which likens the mind as a new battlefield. He quotes a Russian army major in relation to mind wars, “It is completely clear that the state which is first to create such weapons will achieve incomparable superiority." Thomas expresses concern about “information dominance” though he stops short on the moral implications.[147]

Under the cover of secrecy provided by claims of national security, researchers in service to higher circle policy elites have implanted electrodes into human subjects to control minds and tortured prisoners and the mentally ill in efforts to find better “brainwashing” techniques. They have poisoned thousands with atomic testing, experimented on young children using drugs, trauma and hypnosis, sprayed major cities with biological agents to prepare for a future attack, overthrown governments, instituted mass killings, and engaged in every form of information distortion.

The current “War on Terror” has revealed to the public some of the tools that the military has been developing for decades. High profile weapons systems flash across the nightly reports of the major news networks, including highflying Stealth bombers on grainy green tinted video from the noses of “smart” bombs. On occasion glimpses are given through the media of what one article dubbed “Wonder Weapons.”[148] Weapons that fall under the military category of “Non-Lethal Weapons.” In fact the general position of the agencies who do comment on weapons that exploit the lower end of the electromagnetic spectrum is that they have no biological effect at all, except for what are dubbed “thermal effects,” in essence heating of human cells.[149]

Research into this subject has shown that this position is inaccurate, and that the effects of electromagnetic radiation weapons on human beings are in fact both chilling and dramatic. As reported in 2001, the statement of Dr. Eldon Byrd should be considered with great weight:

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[146] Douglas Pasternak, “John Norseen Reading your mind - and injecting smart thoughts”, *US News and World Report*, January 3-10, 2000.
[147] Timothy L. Thomas, The Mind Has No Firewall, *Parameters*, Spring 1998, pp. 84-92.
[148] Douglas Pasternak, “Wonder Weapons”, *Newsweek* August 22, 1994 p. 57.
[149] H. Pollack, “Epidemiologic data on American personnel in the Moscow embassy”, Bull N Y Acad Med., 1979 Dec;55(11):1182-6.

> "A medical engineer, Eldon Byrd, reported a case that illustrates this point. After working on the Polaris submarine, which carried long-range nuclear weapons, Byrd developed non-lethal weapons with reversible effects. He regarded this as a humanitarian alternative to 'punching holes in people and having their blood leak out' in battle. His inventions used magnetic fields at biologically active wave frequencies to affect brain function. Byrd could put animals to sleep at a distance and influence their movements. When the success of his research became evident, suddenly he was pulled off the project and it went "black." His believes the electromagnetic resonance weapons he developed have been used for psychological control of civilians rather than for exigencies in battle. That is, to ensure his participation, he was uninformed about the true nature of the project. Byrd's case also illustrates how morally tolerable operations may transition to morally intolerable operations, or at least rise above the atrocity line"[150]

Power elites who fund and support efforts at supplanting the will of the people do so from on high. Their ability to redirect public attention to ward external threats and away from their own motivations in effect silences opposition to their programs. By controlling the flow of information in society, the power elites provide the public with a limited choice in all matters that pertain to machinations of government and corporate control. Given more advanced technologies for the control of information unscrupulous individuals who ascribe to a "might makes right" philosophy may will find the ways and means of employing these technologies against those who would oppose their plans. The dangers here are great, in that the individual who would direct the torture and killing of innocents is usually removed from the actual fact. It is left up to lesser authorities to administer the beatings, bullets, and mind/body bending technologies.

For the US Government to unilaterally declare that our country will not comply with international human rights laws, nor uphold the core values of our nation's foundation is an indication of extremism that supersedes the values and beliefs of the American people. When such extremism exists we need to take seriously the founders' declaration that, " to secure these rights, Governments are instituted among Men, deriving their just powers from the consent of the governed, — That whenever any Form of Government becomes destructive of these ends, it is the Right of the People to alter or to abolish it, and to institute new Government, laying its foundation on such principles and organizing its powers in such form, as to them shall seem most likely to effect their Safety and Happiness." (Declaration of Independence 1776)

Peter Phillips is a Professor of Sociology at Sonoma State University and Director of Project Censored. Principle researchers on this report were Lew Brown and Bridget Thornton. Lew Brown holds a degree in Psychology and was the main writer and researcher on the historical sections of

[150] Military and Civilian Perspectives on the Ethics of Intelligence— Report on a Workshop at the Department of Philosophy Claremont Graduate University, September 29, 2000, Jean Maria Arrigo, Ph.D. Virginia Foundation for the Humanities and Public Policy Paper presented to The Joint Services Conference on Professional Ethics Springfield, Virginia January 25-26, 2001

this paper. Bridget Thornton is a senior level History major at Sonoma State University and the primary researcher and writer for the new EMF technologies portion. Final editing was completed by Trish Boreta with Project Censored. Special thanks to Andy Roth Ph.D. for his editorial review.

Appendix A

ORGANIZATIONS CONCERNED WITH ILLEGAL EXPERIMENTATION AND INDIVIDUAL VICTIMS

Angelic Harp Foundation
2219 Lexford LN.
Houston, Texas 77080-5216
713-461-0623
Fax: 713-461-0091
http://angelicharpfoundation.org

Center for Cognitive Liberty and Ethics
P.O. Box 73481
Davis, CA 95617-3481 USA
Fax: 205. 449. 3119

COPUS
Committee on the Public Understanding of Science
The Royal Society
6-9 Carlton House Terrace
London
SW1Y 5AG
United Kingdom
Fax +44 (0)20 7839 5561
http://www.copus.org.uk

Federation of American Scientists
1717 K St., NW Suite 209
Washington, DC 20036
Voice: (202)546-3300
Fax: (202)675-1010
http://www.fas.org

The Lay Institute
Nick Begich, Executive Director
Dallas, Texas
info@layinstitute.org

Mind Justice

Cheryl Welsh, Executive Director
E-mail: welsh@mindjustice.org

The Stockholm International Peace Research Institute
Signalistgatan
9 SE-169 70
Solna Sweden
Phone: +46-8-655 97 00
Fax: +46-8-655 97 33
E-mail: sipri@sipri.org

Sunshine Project Germany
The Sunshine Project
Scheplerstrasse 78
22767 Hamburg
Germany
Phone: +49 40 431 88 001
Fax: +49 40 67 50 39 88

Sunshine Project USA
PO Box 41987
Austin TX 78704
USA
Phone/Fax: +1 512 494 0545
http://www.sunshine-project.org

World Transhumanist Association
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Willington CT 06279 USA
http://www.transhumanism.org

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Journal of Cognitive Liberties
Center for Cognitive Liberties and Ethics

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Parameters, spring 1998, pp. 84-92.
Timothy L. Thomas

The Politics and Costs of Postmodern War in the Age of Bush II
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http://www.gseis.ucla.edu/faculty/kellner/essays/politicscostspostmodernwar.pdf

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National War College, CDR Debra O'Maddrell

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Magnetic Stimulation: An Introduction"
by Grant Balfour
v1.0 - May 6, 2002

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Authors: Simon R. Goerger; Michael L. McGinnis; Rudolph P. Darken
Military Academy West Point, NY, Dept. of System Engineering
by Robert J. Bunker

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Sakurai T[1], Satake A, Sumi S, Inoue K, Miyakoshi J.

Author information

Abstract

In this study, we investigated the effects of exposure to an extremely low frequency magnetic field (ELFMF) on hormone secretion from an islet derived insulinoma cell line, RIN-m. We stimulated RIN-m cells to secrete insulin under exposure to an ELFMF, using our established system for the exposure of cultured cells to an ELFMF at 5 mT and 60 Hz, or under sham exposure conditions for 1 h and observed the effects. In the presence of a depolarizing concentration of potassium (45 mM KCl), exposure to ELFMF significantly attenuated insulin release from RIN-m cells, compared to sham exposed cells. Treatment with nifedipine reduced the difference in insulin secretion between cells exposed to an ELFMF and sham exposed cells. The expression of mRNA encoding synaptosomal associated protein of 25 kDa (SNAP-25) and synaptotagmin 1, which play a role in exocytosis in hormone secretion and influx of calcium ions, decreased with exposure to an ELFMF in the presence of 45 mM KCl. These results suggest that exposure to ELFMF attenuates insulin secretion from RIN-m cells by affecting calcium influx through calcium channels.

Exhibit G: Mitochondrial Dysfunction and Disruption of Electrophysiology

Mitochondria are broadly vulnerable, in part because the integrity of their membranes is vital to their optimal functioning – including channels and electrical gradients, and their membranes can be damaged by free radicals which can be generated in myriad ways. Moreover, just about every step in their metabolic pathways can be targeted by environmental agents, including toxicants and drugs, as well as mutations [1]. This supports a cumulative allostatic load model for conditions in which mitochondrial dysfunction is an issue, which includes autism as well as myriad other chronic conditions.

Mitochondria are commonly discussed in terms of the biochemical pathways and cascades of events by which they metabolize glucose and generate energy. But in parallel with this level of function there also appears to be a dimension of electromagnetic radiation that is part of the activity of these organelles. For example, electromagnetic radiation can be propagated through the mitochondrial reticulum, which along with the mitochondria has a higher refractive index than the surrounding cell and can serve to propagate electromagnetic radiation within the network [2]. [2]. It is also the case that *"The physiological domain is characterized by small-amplitude oscillations in mitochondrial membrane potential (delta psi(m)) showing correlated behavior over a wide range of frequencies…. Under metabolic stress, when the balance between ROS [reactive oxygen species, or free radicals] generation and ROS scavenging [as by antioxidants] is perturbed, the mitochondrial network throughout the cell locks to one main low-frequency, high-amplitude oscillatory mode. This behavior has major pathological implications because the energy dissipation and cellular redox changes that occur during delta psi(m) depolarization result in suppression of electrical excitability and Ca2+ handling…"* [3]. These electromagnetic aspects of mitochondrial physiology and pathophysiology could very well be impacted by EMF/RFR.

Other types of mitochondrial damage have been documented in at least some of the studies that have examined the impacts of EMF/RFR upon mitochondria. These include reduced or absent mitochondrial cristae [4-6], mitochondrial DNA damage [7], swelling and crystallization [5], alterations and decreases in various lipids suggesting an increase in their use in cellular energetics [8], damage to mitochondrial DNA [7], and altered mobility and lipid peroxidation after exposures [9]. Also noted has been enhancement of brain mitochondrial function in Alzheimer's transgenic mice and normal mice [10]. The existent of positive as well as negative effects gives an indication of the high context dependence of exposure impacts, including physical factors such as frequency, duration, and tissue characteristics [11].

Secondary mitochondrial dysfunction (i.e. environmentally triggered rather than rooted directly in genetic mutations) [15-18] could result among other things from the already discussed potential for EMF/RFR to damage channels, membranes and mitochondria themselves as well as from toxicant exposures and immune challenges. In a meta-analysis of studies of children with ASC and mitochondrial disorder, the spectrum of severity varied, and 79% of the cases were identified by laboratory findings without associated genetic abnormalities [16].

Electrophysiology

Nervous system electrophysiology when disrupted by ELF-EMF and RFR can produce alterations in molecular, cellular and systems physiological function. It occurs in the brain as well as in the body, and impacts the transduction into the electrical signaling activities of the brain and nervous system. If the cells responsible for generating synapses and oscillatory signaling are laboring

under cellular and oxidative stress, lipid peroxidation, impaired calcium and other signaling system abnormalities, then mitochondrial metabolism will fall short, all the more so because of the challenges from the immune system which in turn be triggered to a major extent by environment. How well will synaptic signals be generated? How well will immune-activated and thereby distracted glial cells be able to modulate synaptic and network activity? [19-22] Microglial activation can impact excitatory neurotransmission mediated by astrocytes [23]. Cortical innate immune response increases local neuronal excitability and can lead to seizures [24,25]. Inflammation can play an important role in epilepsy [26].

Seizures and epilepsy

Epileptic seizures can be both caused by and cause oxidative stress and mitochondrial dysfunction. Seizures can cause extravasation of plasma into brain parenchyma [27-31]. which can trigger a vicious circle of tissue damage from albumin and greater irritability, as discussed above. Evidence suggests that if a BBB is already disrupted, there will be greater sensitivity to EMF/RFR exposure than if the BBB were intact [32,33], suggesting that such exposures can further exacerbate vicious circles already underway. The combination of pathophysiological and electrophysiological vulnerabilities has been explored in relation to the impact of EMF/RFR on people with epilepsy EMF/RFR exposures from mobile phone emissions have been shown to modulate brain excitability and to increase interhemispheric functional coupling [34,35]. In a rat model the combination of picrotoxin and microwave exposure at mobile phone-like intensities led to a progressive increase in neuronal activation and glial reactivity, with regional variability in the fall-off of these responses three days after picrotoxin treatment [36], suggesting a potential for interaction between a hyperexcitable brain and EMF/RFR exposure.

One critical issue here is nonlinearity and context and parameter sensitivity of impact. In one study, rat brain slices exposed to EMF/RFR showed reduced synaptic activity and diminution of amplitude of evoked potentials, while whole body exposure to rats led to synaptic facilitation and increased seizure susceptibility in the subsequent analysis of neocortical slices [37]. Another study unexpectedly identified enhanced rat pup post-seizure mortality after perinatal exposure to a specific frequency and intensity of exposure, and concluded that apparently innocuous exposures during early development might lead to vulnerability to stimuli presented later in development [38].

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Dirty Electricity Elevates Blood Sugar Among Electrically Sensitive Diabetics and May Explain Brittle Diabetes

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Abstract

Transient electromagnetic fields (dirty electricity), in the kilohertz range on electrical wiring, may be contributing to elevated blood sugar levels among diabetics and prediabetics. By closely following plasma glucose levels in four Type 1 and Type 2 diabetics, we find that they responded directly to the amount of dirty electricity in their environment. In an electromagnetically clean environment, Type 1 diabetics require less insulin and Type 2 diabetics have lower levels of plasma glucose. Dirty electricity, generated by electronic equipment and wireless devices, is ubiquitous in the environment. Exercise on a treadmill, which produces dirty electricity, increases plasma glucose. These findings may explain why brittle diabetics have difficulty regulating blood sugar. Based on estimates of people who suffer from symptoms of electrical hypersensitivity (3–35%), as many as 5–60 million diabetics worldwide may be affected. Exposure to electromagnetic pollution in its various forms may account for higher plasma glucose levels and may contribute to the misdiagnosis of diabetes. Reducing exposure to electromagnetic pollution by avoidance or with specially designed GS filters may enable some diabetics to better regulate their blood sugar with less medication and borderline or pre-diabetics to remain non diabetic longer.

Keywords: Radio frequency, Transients, Dirty electricity, Power quality, Plasma glucose, Blood sugar, Insulin, GS filters, Electrohypersensitivity, Brittle diabetes, Type 3 diabetes, Type 2 diabetes, Type 1 diabetes
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Introduction

Diabetes mellitus is increasing globally. According to the World Health Organization, in 1985 the global population of diabetics was 30 million (0.6% of the world population). This increased to 171 million (2.8% of the global population) by 2000, and it is expected to more than double to 366 million (4.5% of the global population) by 2030 (Wild et al., 2004; U.S. Census Bureau, 2005). Doctors attribute this rise in diabetes to poor diet and limited exercise, resulting in obesity, and seldom look for causes other than lifestyle and genetics.

This article presents a paradigm shift in the way we think about diabetes. In addition to Type 1 diabetics, who produce insufficient insulin, and Type 2 diabetics, who are unable to effectively use the insulin they produce, a third type of diabetes may be environmentally exacerbated or induced by exposure to electromagnetic frequencies.

Our increasing reliance on electronic devices and wireless technology is contributing to an unprecedented increase in our exposure to a broad range of electromagnetic frequencies, in urban and rural environments and in both developed and developing countries. This energy is generated within the home by computers, plasma televisions, energy efficient lighting and appliances, dimmer switches, cordless phones, and wireless routers, and it can enter the home and work environment from nearby cell phone and broadcast antennas as well as through ground current.

Although the position of most international health authorities, including the World Health Organization, is that this form of energy is benign as long as levels remain below guidelines, an increasing number of scientific studies report biological and health effects associated with electromagnetic pollution well below these guidelines (Sage and Carpenter, 2007). Epidemiological studies have documented increased risks for childhood leukemia associated with residential magnetic fields exposure (Ahlbom et al., 2000), greater risk for various cancers with occupational exposure to low-frequency electric and magnetic fields (Havas, 2000), miscarriages (Li et al., 2002), Lou Gehrig's disease (Neutra et al., 2002), brain tumors associated with cell phone use (Kundi et al., 2004), as well as cancers and symptoms of electrical hypersensitivity (EHS) for people living near cell phone and broadcast antennas (Altpeter et al., 1995; Michelozzi et al., 2002). Laboratory studies report increased proliferation of human breast cancer cells (Liburdy et al., 1993), single- and double-strand DNA breaks (Lai and Singh, 2005), increased permeability of the blood brain barrier (Royal Society of Canada, 1999), changes in calcium flux (Blackman et al., 1985), and changes in ornithine decarboxylase activity (Salford et al., 1994).

In this article, changes in plasma glucose, in response to electromagnetic pollution, for numerous measurements on four subjects—two with Type 1 diabetes taking insulin and two non medicated with Type 2 diabetes—are described. They include men and women, ranging in age from 12–80, as well as individuals recently diagnosed and those living with the disease for decades.

Case 1: 51-Year Old Male with Type 2 Diabetes

A 51-year old male with Type 2 diabetes, taking no medication, monitored his plasma glucose levels from April 24 to May 30, 2003. He also monitored the dirty electricity in his home using a Protek 506 Digital Multimeter connected to a ubiquitous filter (Graham, 2000) to remove the 60-Hz signal and its harmonics. Measurements were taken in the morning and randomly throughout the day. Low or no readings of dirty electricity were taken in an electromagnetic clean environment far from power lines and cell phone antennas (Fig. 1 upper graph). Three years later, the microsurge meter became available and Case 1 monitored his blood sugar levels once more (Fig. 1 lower graph). This meter provides a digital readout of the absolute changing voltage as a function of time (|dv/dt|, expressed as GS units) for the frequency range 4–100 kHz and with an accuracy of ±5% (Graham, 2003).

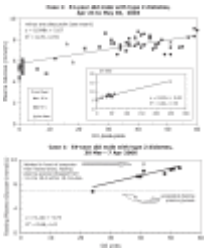

Figure 1

Case 1: *Upper chart*: Plasma glucose levels of a 51-year old male with Type 2 diabetes exposed to different levels of power quality. Insert shows the entire data set with one very high plasma glucose reading that was recorded during a period of high exposure **...**

Figure 1 shows a positive correlation between dirty electricity and plasma glucose levels taken randomly during the day (upper graph) and first thing in the morning (lower graph). His elevated plasma glucose is unrelated to eating. Working on a computer increases blood sugar, but these values decrease as much as 0.11 mmol/L[*] [2 mg/dL] per minute after moving away from the computer. Blood viscosity decreased as his plasma glucose levels dropped.

Case 1 also documented rapid changes in blood sugar as he moved from a medical clinic (environment with dirty electricity), to his parked vehicle (no dirty electricity), and back to the medical clinic. His blood sugar levels changed significantly within 20 min. His endocrinologist classified him as *pre-diabetic* when his blood sugar was tested immediately upon entering the medical clinic and as a *Type 2 diabetic* after a 20-min wait in the medical clinic. Measurement of blood sugar needs to be done in an electromagnetically clean environment to prevent misdiagnosis and to accurately determine the severity of the disease.

Case 2: 57-Year Old Female with Type 2 Diabetes

A 57-year old female with Type 2 diabetes takes no medication and controls her plasma glucose with exercise and a hypoglycemic diet. When she exercised by walking for 20–30 min at a mall after hours, her blood sugar levels dropped from a mean of 11.8 to 7.2 mmol/L [212 to 130 mg/dL] ($p = 0.045$). When she walked on a treadmill, her blood

sugar levels increased from 10 to 11.7 mmol/L [180 to 211 mg/dL] ($p = 0.058$) (Fig. 2). Treadmills have variable speed motors and produce dirty electricity.

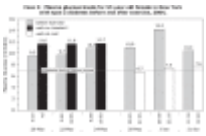

Figure 2
Case 2: Plasma glucose levels for a 57-year old female in New York with Type 2 diabetes, before and after walking for 20–30 min on a treadmill in her home and after hours at a mall.

Doctors recommend exercise for patients with diabetes. However, if that exercise is done in an electromagnetically dirty environment, and if the patient is sensitive to this form of energy, it may increase stress on the body and elevate levels of plasma glucose, as in Case 2.

This subject also measured her plasma glucose as she moved from an environment with dirty electricity to one that was clean, and back again. Her blood sugar in the dirty environment was 12.5 mmol/L [225 mg/dL] and within 20 min in the clean environment dropped to 10.6 mmol/L [191 mg/dL]. Within 5 min after returning to the dirty environment, her blood sugar rose to 10.8 mmol/L [194 mg/dL] and 15 min later to 12.6 mmol/L [227 mg/dL]. She did not eat or exercise during this period. Her elevated plasma glucose levels were associated with headaches, nausea, and joint pain in her home, where she was exposed to both dirty electricity and radio frequency radiation from nearby cell phone antennas. These exposures and symptoms were absent in the clean environment.

Case 3: 80-Year Old Female with Type 1 Diabetes

An 80-year old female with Type 1 diabetes, who takes insulin (Humlin® 70/30) twice daily, documented her blood sugar levels before breakfast and before dinner for one week. On June 12, 2004, the dirty electricity in her home was reduced from an average of 1,550 GS units (range: 600 to > 2,000) to 13 GS units (range 11 to 22) with Graham/Stetzer filters (GS filters). These filters provide a short to high frequency, and, thus, reduce transients on electrical wiring with an optimal filtering capacity between 4 and 100 kHz (Graham, 2000, 2002, 2003). They are similar to capacitors installed by industry to protect sensitive electronic equipment from power surges and to adjust the power factor. GS units measure the energy associated with dirty electricity (amplitude and frequency) and are a function of changing voltage with time (dv/dt). Dirty electricity can be measured using an oscilloscope or multi-meter set for peak-to-peak voltage or a Microsurge meter that provides a digital readout (GS units) and is easily used by non professionals.

Case 3 had mean fasting plasma glucose of 9.5 mmol/L [171 mg/dL] without the GS filters and 6.6 mmol/L [119 mg/dL] with the GS filters ($p = 0.02$) (Table 1). Her evening blood sugar did not change appreciable during this period, although it did differ on days

she was away from home. She was able to more than halve her insulin intake ($p = 0.03$) once the GS filters reduced the dirty electricity in her home (Table 1).

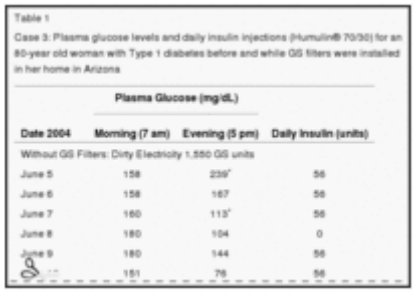

Table 1

Case 3: Plasma glucose levels and daily insulin injections (Humulin® 70/30) for an 80-year old woman with Type 1 diabetes before and while GS filters were installed in her home in Arizona

	Plasma Glucose (mg/dL)		
Date 2004	Morning (7 am)	Evening (5 pm)	Daily Insulin (units)
Without GS Filters: Dirty Electricity 1,550 GS units			
June 5	158	239*	56
June 6	158	167	56
June 7	160	113*	56
June 8	180	104	0
June 9	180	144	56
[illegible]	151	76	56

Case 4: 12-Year Old Male with Type 1 Diabetes

A mother and her 5 children, who were all home schooled, began to develop intermittent, excruciating headaches during the fall of 2002 in rural Wisconsin, shortly after they had a new septic system installed. The headaches continued and a power quality expert measured high levels of dirty electricity and ground current, possibly attributable to the septic system installation.

In December 2002, one child, a 12-year old male, was hospitalized and diagnosed with Type 1 diabetes. His younger sister had been living with diabetes since the age of 3 months and was one of the youngest children diagnosed with diabetes in the United States.

On January 14, 2003, the family installed GS filters to help alleviate their symptoms of electrical hypersensitivity. The headaches disappeared and the family's health began to improve. Shortly after the GS filters were installed, the mother had great difficulty controlling her son's blood sugar. She couldn't reduce the amount of insulin fast enough to keep it within an acceptable range and needed to give him sugar pills to prevent hypoglycemia (Fig. 3). He was taking a combination of Humalog® (H-insulin, a short-acting insulin) and Humulin® NRT (N-insulin, a long-lasting insulin).[1] During this period, her daughter's blood sugar levels began to drop as well.

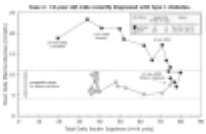

Figure 3

Case 4: Sequence of mean daily plasma glucose levels and total daily insulin injections for 12-year old male with Type 1 diabetes who was admitted to hospital in December 2002 and returned home on January 1, 2003. On January 14, 2003, GS filters were **...**

Doctors attribute the short-term improvement in blood sugar to the ‘‘honeymoon period’’, which is observed among some diabetics shortly after diagnosis and lasts from weeks to months and occasionally for years (Bernstein, 2003). The honeymoon period cannot explain the response of the subject’s sister, who had been living with Type 1 diabetes for years, and who also had lower plasma glucose levels and difficulty regulating her insulin within an acceptable range after the GS filters were installed and the dirty electricity was reduced.

Case 4 had higher levels of plasma glucose at 8 am (fasting) than at 2 am on some days before the GS filters were installed. This was not observed with the filters, except when sugar pills were taken at 2 am to deliberately increase blood sugar (Fig. 4). In Wisconsin, dirty electricity often increases in the middle of the night, beginning at 2–3 am and lasting from minutes to hours, as the electric utility makes changes in its system.

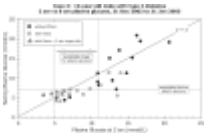

Figure 4
Case 4: Fasting (8 am) and 2 am plasma glucose levels for 12-year old male with Type 1 diabetes with and without GS filters. NOTE: Sugar pills were administered at 2 am for 5 d to prevent hypoglycemia while filters were installed.
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Discussion

These results show that plasma glucose levels, in the Type 1 and Type 2 diabetic cases reported, respond to electromagnetic pollution in the form of radio frequencies in the kHz range associated with indoor wiring (dirty electricity). Type 1 diabetics require less insulin in an electromagnetically clean environment and blood sugar levels for Type 2 diabetics increase with increasing exposure to dirty electricity.

In May 2006, a long-term health care facility in Ontario, Canada installed GS filters to reduce dirty electricity. Of the five diabetic residents, for whom data were available, two (aged 87 and 88) were insulin-dependent Type 1 diabetics. Both had significantly lower fasting plasma glucose levels ($p < 0.01$) after the GS filters were installed. Their insulin intake did not change during this period and nursing staff had to give them orange juice on several occasions to prevent hypoglycemia. The levels of plasma glucose of the remaining three, who were Type 2 diabetics, did not change during this period.

The GS filters, used in this study have been tested at the Yoyogi Natural Clinic in Japan (Sogabe, 2006). Three people participated in the study. Three hours after eating, their blood sugar was 6.3, 7.7, 17.9 mmol/L [113, 139, and 322 mg/dL] in an environment with more than 2,000 GS units of dirty electricity. GS filters reduced the dirty electricity to 30–35 GS units and, within 30 min, their plasma became less viscous and their blood sugar dropped to 5.6, 6.1, 16.1 mmol/L [101, 110, 290 mg/dL], respectively.

The person with the highest plasma glucose levels was a 28-year old male with Type 2 diabetes and fasting plasma glucose levels of 16.7 mmol/L [300 mg/dL]. Despite taking 250 mg of Glycoran®, 3 times a day, and 12 mg of Amaryl®, spread throughout the day, he still had difficultly regulating his blood sugar. Three days after installing 4 GS filters in his home, his blood sugar dropped to 6.9 mmol/L [124 mg/dL] and he was feeling well. He had been unable to achieve such low values with medication alone.

In this study, we classify diabetics whose blood sugar responds to electromagnetic pollution as Type 3 diabetics. In contrast to true Type 1 diabetics who produce insufficient insulin and true Type 2 diabetics who are unable to effectively use the insulin they produce, Type 3 diabetics are responding to environmental triggers that affect blood sugar readings and blood viscosity. These individuals may be better able to regulate plasma glucose by controlling their exposure to frequencies in the low RF range, and thus differ from true Type 1 and Type 2 diabetics whose blood sugar is not affected by this type of electromagnetic exposure.

The increase in blood viscosity with increasing exposure to dirty electricity is a critical observation. If this turns out to be the case among electrosensitive individuals, it may explain the symptoms of headaches, chest pain, higher blood pressure, blurred vision, and fatigue.

The percentage of diabetics who are likely to be affected by electromagnetic energy is unknown, but if the values are similar to those suffering from symptoms of electromagnetic hypersensitivity (EHS), 3–35% of the population (Philips and Philips, 2006), then globally between 5 and 60 million existing diabetics may have Type 3 diabetes as described in this study.

There is a growing body of *in vivo, in vitro,* and epidemiological evidence, which suggests a relationship between plasma glucose levels, insulin secretion, and exposure to electromagnetic energy at frequencies both lower and higher than the ones we tested in this study.

Altpeter et al. (1995) reported that for people living within a 2 km radius of a short-wave transmitter, in Schwarzenburg, Switzerland, the odds ratio (OR) for diabetes was 1.93 when compared with a population further away. There was a significant linear correlation ($R^2 = 0.99$) between daily median RF exposure and incidence of diabetes. The highest RF readings, recorded in the nearest zone (51 mA/m), were well below the International Radiation Protection Agency's 1988 guidelines of 73 mA/m. Those living near the transmitter also had difficulty falling and staying asleep, were restless, experienced weakness and fatigue, and had both limb and joint pain with statistically significant odds ratios between 2.5 and 3.5. These symptoms are typical of radio wave sickness or electrical hypersensitivity (Firstenberg, 2001). Failure of the transmitter for a 3-d period was associated with improved sleep and, hence, these reactions are biological not psychological.

Beale et al. (2001) reported that the prevalence of chronic illness, asthma, and Type 2 diabetes was linearly related to 50-Hz magnetic field exposure for adults living near transmission lines. For Type 2 diabetes, the crude OR was 8.3 (95% CI 1 to 177), but the OR adjusted for possible confounders (age and ethnicity) was reduced to 6.5 and was not statistically significant ($p > 0.05$). Epidemiological studies of power lines tend to focus on cancers, rather than diabetes, and, hence, limited information of this type is available.

Litovitz et al. (1994) exposed diabetic subjects to 60-Hz magnetic fields between 0.2–1 μT (2–10 mG) and noticed that blood glucose levels increased above 0.6 mT. No statistical tests were reported and no attempt was made to measure frequencies other than 60 Hz. Magnetic flux densities above 0.6 μT are realistic near transmission lines and overlap with the range documented in the Beale study (2001).

Jolley et al. (1982) exposed islets of Langerhans from rabbits to low-frequency pulsed magnetic fields and noted a reduction in insulin release during glucose stimulation compared with controls ($p < 0.002$). Similarly, Navakatikyan et al. (1994) exposed rats to 50-Hz magnetic fields for 23 h per day for 11 days at 10, 50, and 250 μT. Serum insulin levels decreased at the middle- and high-flux densities, which the authors associated with stress.

Sakurai et al. (2004) measured insulin secretion from an islet derived insulinoma cell line, RIN-m, exposed to low-frequency magnetic fields of 5 mT compared with sham exposure of less than 0.5 μT. Insulin secretion was reduced by approximately 30% when exposed to low-frequency magnetic fields compared to sham exposure. The authors conclude: “it might be desirable for diabetic patients who have insufficient insulin secretion from pancreatic islets to avoid exposure to ELFMF”. The magnetic flux density was exceptionally high in this experiment and is unlikely to be encountered in normal daily life. Studies of the incipient level of electromagnetic exposure, at which insulin secretion is reduced, would be useful.

Li et al. (2005) exposed hepatocytes *in vitro* to 50 Hz pulsed electric fields (0.7 V/m) and noted a conformation change in the insulin molecule and an 87% reduction in the binding capacity of insulin to its receptors compared with controls.

Stress often increases plasma glucose levels in diabetics (Hinkle and Wolf, 1950; Jolley et al., 1982). Studies with laboratory animals and *in vitro* studies with human cells show both low-frequency electromagnetic fields and non thermal RF radiation stimulates production of stress proteins, and that the biochemical reactions are the same over a range of frequencies and intensities (Blank and Goodman, 2004). Release of insulin is strongly inhibited by the stress hormone norepinephrine, which leads to increased blood glucose levels during stress. Rajendra et al. (2004) found elevated levels of norepinephrine in the brain of fertilized chick eggs on day 15 following exposure to 5, 50, and 100 μT. The “stress response” to electromagnetic energy may provide, yet, another mechanism that could explain Type 3 diabetes.

Reduced insulin secretion and reduced binding capacity of insulin to its receptors may explain the elevated levels of plasma glucose in Type 3 diabetics exposed to electromagnetic fields. More research on mechanisms is needed.

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Conclusions

In addition to lifestyle and genetics, the environment appears to be another factor contributing to high levels of blood sugar. This concept presents a possible paradigm shift in the way we think about diabetes and the consequences may be far reaching. As a result, we have labeled environmental diabetes as Type 3 diabetes.

We recognize that there is, as yet, no accepted definition of Type 3 diabetes and that our definition may be in conflict with others that have been suggested including a combination of Type 1 and Type 2, gestational diabetes, and that Alzheimer's Disease is a form of diabetes (Steen et al., 2005; de la Monte et al., 2006).

What we describe here is a totally different type in the sense it has an environmental trigger. Doctors have long suspected an environmental component but it has not been until now that one has been found.

The increasing exposure and ubiquitous nature of electromagnetic pollution may be contributing to the increasing incidence of this disease and the escalating cost of medical care. Diagnosis of diabetes needs to be done in an electromagnetically clean environment to prevent misdiagnosis, and to properly assess the severity of this disorder. Most medical centers have electronic equipment and use fluorescent lights that produce dirty electricity, which is likely to cause abnormally high blood sugar readings for those with a combination of diabetes and electrohypersensitivity (Type 3 diabetes). Dirty electricity may also explain why brittle diabetics have difficulty controlling their blood sugar levels.

Type 3 diabetes, as described in this study, is an emerging disease. Unlike true Type 1 and Type 2 diabetics whose blood sugar is not affected by dirty electricity, Type 3 diabetics may be better able to regulate their blood sugar with less medication, and those diagnosed as borderline or pre-diabetic may remain non diabetic longer by reducing their exposure to electromagnetic energy. The GS filters and the microsurge meter provide the tools needed for scientific investigation of dirty electricity and may help diabetics regulate their blood sugar by improving power quality in their home, school, and work environment. Minimizing exposure to radio frequencies (kHz to GHz), flowing along the ground or through the air, also needs to be addressed. Large-scale studies are needed in controlled settings to determine the percentage of the population with Type 3 diabetes.

These results are dramatic and warrant further investigation. If they are representative of what is happening worldwide, then electromagnetic pollution is adversely affecting the lives of millions of people.

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Acknowledgments

The author thanks the people who participated in this study; Dave Stetzer and Martin Graham for information about power quality; and reviewers for their critical comments and suggestions.

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Notes

Conflict of Interest

Please note that the author has no vested interest, financial or otherwise, in the commercial devices mentioned in this article.

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Footnotes

[*]Multiply by 18 to convert to mg/dL.

[1]Both the short-acting Humalog® (H-insulin) and the long-lasting Humulin[s] NPH (N-insulin) are produced by Eli Lilly.

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http://ehs.berkeley.edu/laser-safety/non-ionizing-radiation-safety-manual#policy

Non-Ionizing Radiation Safety Manual

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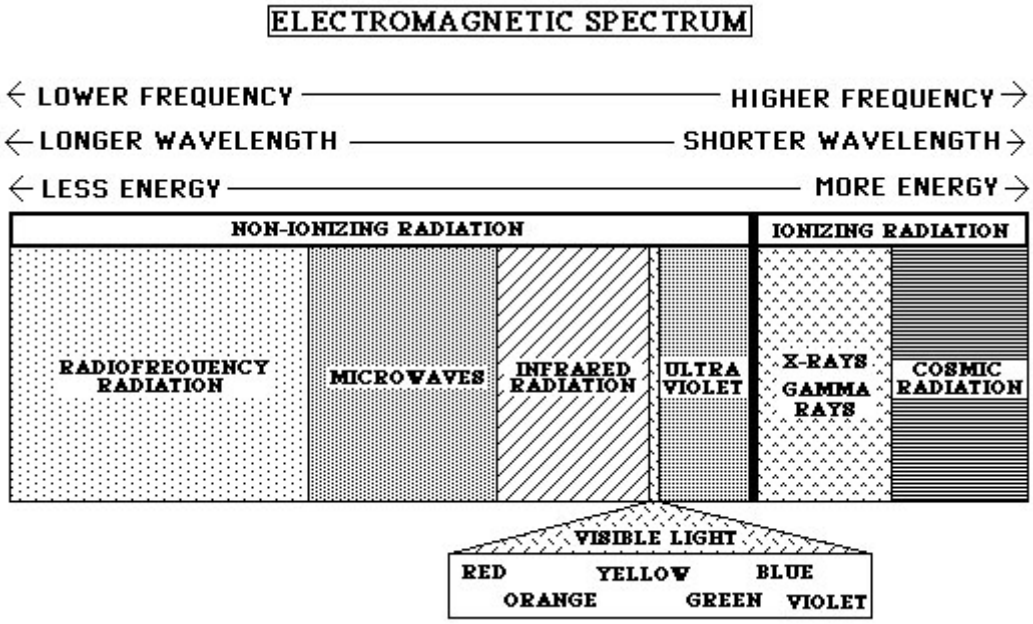
Introduction

The modern world is full of devices which, either directly or indirectly, act as sources of non-ionizing radiation (NIR). These sources produce NIR in the electromagnetic spectrum of wavelengths/frequencies ranging from 100 nm to static fields. Many NIR sources are present on the UC Berkeley campus, either in research applications or in ancillary equipment.

In general, NIR tends to be less hazardous to humans than ionizing radiation (ionizing radiation has a wavelength less than 100 nm or a photon energy greater than 12.4 electron Volts). However, depending on the wavelength/frequency and the irradiance (or power density) value, NIR sources may present a human health hazard. This manual is intended to provide guidance in maintaining a safe NIR work environment on the campus.



Non-Ionizing Radiation Safety Policy

It is the policy of the University of California at Berkeley to provide a workplace safe from the known hazards of NIR by assuring compliance with federal and state safety regulations. Presently, it is not clear if Extremely Low Frequency (ELF) Radiation poses any hazard to human health. However, the ICRP Interim Guidelines on Limits to 50/60 Hz Electric and Magnetic Fields are used by the campus as a precaution. The NIR safety program is upgraded as new regulations and standards become available.

This policy applies to all persons exposed to NIR hazards on UC Berkeley property. The UC Berkeley Office of Environment, Health & Safety (EH&S) has been assigned responsibility for implementing the NIR safety policies established by the campus Non-Ionizing Radiation Safety Committee (NIRSC).

NOTE: Ionizing radiation, lasers, and coherent light sources are not covered in this manual. For information on the hazards from these sources, see the campus Radiation Safety Manual, the Laser Safety Manual, and the Laser Safety Training Supplement. Please contact EH&S to obtain these documents or additional information.

Applicable Regulatory Standards & Guidelines

Non-coherent UV, Visible, Infrared Radiation Microwave/Radio Frequency Radiation	Title 8- CCR, ACGIH, ANSI Z136.2

	FCC OET 65, IEEE C95.1, Title 8-CCR, ACGIH
Extremely Low Frequency Radiation	IRPA/INIRC - NIR Protection Guidelines
Static Magnetic Fields	ACGIH

The California Code of Regulations (CCR, Title 8, Section 5085, Subchapter 7, Group 14, Article 104 – Nonionizing Radiation) establishes MPE (maximum permissible exposure) values for frequencies between 3 MHz and 300 GHz. At present, neither the state nor federal government regulates those frequencies below 3 MHz. The Institute of Electrical and Electronics Engineers (IEEE) C95.1 (1991) Standard recommends MPE values for frequencies between 3 MHz and 3 kHz. This standard is a revision of the American National Standard Institute (ANSI) C95.1 (1982) and is recognized by ANSI as the standard of safety practice.

The International Radiation Protection Association/International Non-Ionizing Radiation Committee (IRPA/INIRC) has published Interim Guidelines on Limits to 50/60 Hz Electric and Magnetic Fields. These guidelines are intended to limit the potential health effects of extremely low frequency (ELF is all frequencies below 3 kHz) radiation exposure. IRPA/INIRC recommends a continuous MPE of 1000 mG (0.1 mT) for exposure to uncontrolled environments over a lifetime. This standard agrees with the permissible magnetic flux exposure for persons wearing cardiac pacemakers recommended by the American Conference of Governmental Industrial Hygienists (ACGIH). NOTE: The ACGIH recommends the electrical field for persons wearing cardiac pacemakers not exceed 1.0 kV/m.

The Federal Communications Commission (FCC) publishes the OET 65 Standard which provides guidance on protection of workers and the public from microwave/RF radiation emissions from transmission towers and other broadcast facilities. The American National Standards Institute (ANSI) publishes the Z136.2 Standard for the Safe Use of Optical Fiber Communications Systems Utilizing Light Emitting Diodes.

Compliance with CCR Title 8 is required for all employers in the state of California. Enforcement of these regulations falls to Cal-OSHA, who inspects campus facilities to determine compliance with Title 8. Although the IEEE Standard is not a regulation, it does "...represent a consensus of the broad expertise on the subject within the institute..." and is commonly accepted within the United States as the safety guidance for frequencies between 3 MHz and 3 kHz. The IRPA Interim Guideline is the best guidance available on ELF safety that is based on international scientific consensus. The Swedish government has established a performance based emission standard for computer monitor manufacturers (the MPR-II Standard allows a MPE of 2.5 mG), but the safety need for this standard has not been accepted by the international scientific community.

Understanding and Evaluating Non-Ionizing Radiation Hazards

The properties and hazards of NIR can best be understood by considering the EM spectrum as three broad categories:

- Optical radiation (100 nm to 1 mm)
- Microwave radiation (300 GHz to 300 MHz)
- Radiofrequency and lower frequency radiation (300 MHz to Static Fields)

Basic characteristics of optical radiation (ultraviolet/visible light/infrared):

- Possess small wavelengths, large frequencies, and substantial energy (extreme UV approaches the photon energy of ionizing radiation).
- Optical theory can be applied to an analysis of the radiation field.
- Both thermal and photochemical (biological) effects are possible from exposures (depending on wavelength).
- Exposures normally occur in the far field where the E (electric) and H (magnetic) fields are strongly coupled.
- The inverse square law applies to any analysis of the radiation field.
- Only power density (S) measurements are normally considered in the hazard analysis.
- The radiation interacts readily with surfaces and can easily deposit energy in human tissues.

Basic characteristics of microwave radiation (300 GHz to 300 MHz):

- Possess intermediate wavelengths (1 mm to 1 m), frequencies, and moderate photon energy.
- Microwave theory can be applied to an analysis of the radiation field.
- Both thermal and induced current (biological) effects are possible from exposures.
- Exposures may occur in both the near and far fields.
- In hazard analysis, both E (electrical field) and H (magnetic field) measurements must be considered in addition to the power density (S) measurements.
- This type of radiation resonates (forms standing waves) in tissue dimensions with multiples of 1/2 wavelength (depending on the tissue orientation to the wave plane).

Basic characteristics of Radiofrequency and lower frequency (ELF, static) fields:

- Possess large wavelengths (>1 m), small frequencies, and very low energy.
- Circuit theory can be applied to an analysis of the radiation field.
- In general there is poor energy deposition in human tissue but thermal and induced current (biological) effects are possible.
- Exposures usually occur in the near field where the E and H fields are not coupled.
- The inverse square law may not apply.
- The E and H measurements must be considered separately for a hazard analysis (of RF).

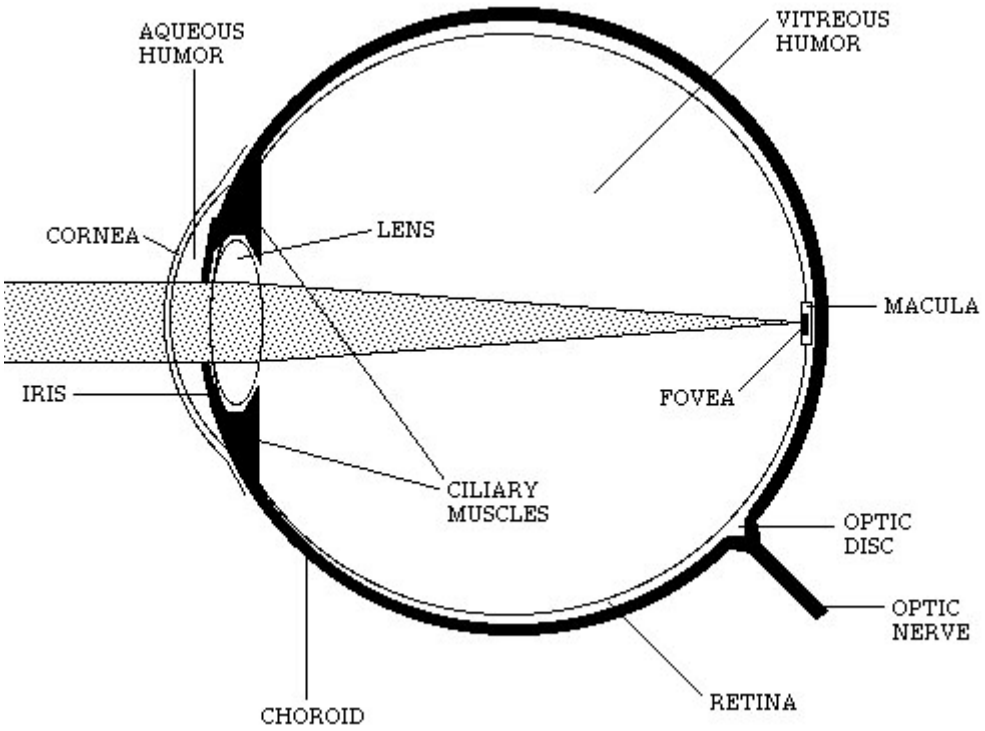
- At ELF and static fields, the magnetic field dominates the hazard analysis.
- This type of radiation can easily penetrate, but rarely deposit energy in tissue.

Module #1
Non-Coherent Light Source Safety

Many devices (or sources) produce either broadband or discrete wavelength radiation between 100 nm and 1 mm. Under certain conditions, these sources may present a health hazard. Factors affecting the potential hazard include: the specific wavelength(s) produced, the irradiance value, the source dimensions, and whether the radiation can access the eye or skin. Sources include (but are not limited to) the following:

- Lamps (filament, discharge, fluorescent, arc, solid state, etc.)
- Plasma sources (welding devices, surface deposition, etc.)
- Heat sources (furnaces, molten glass, open flames, etc.)

Whenever practical, sources of non-coherent light not intended for illumination purposes should be shielded to prevent exposure to the eye or skin. For sources intended to produce exposure (lamps), any unneeded wavelengths (example: ultraviolet emitted from mercury vapor lamps) should be removed with appropriate filtration.



Ultraviolet (UV) radiation is defined as having a wavelength between 10 nm and 400 nm. Specific wavelength "bands" are defined by the CIE (Commission International de l'Eclairage or International Commission on Illumination) as follows:

Physical Definition

- Extreme UV (10 nm to 100 nm)
- Vacuum UV (10 nm to 200 nm)
- Far UV (200 nm to 300 nm)
- Near UV (300 nm to 400 nm)

Photobiologic Definition

- UV-C (100 nm to 280 nm)
- UV-B (280 nm to 315 nm)
- UV-A (315 nm to 400 nm)

Ultraviolet Skin Hazards

Ultraviolet (UV) radiation is a known carcinogen for human skin. In addition to cancer induction, erythema (sunburn), and skin aging are also known products of ultraviolet skin exposure. Because the biological effects are dependent on the time of exposure, the specific UV wavelength, and the susceptibility of the individual exposed, it is considered prudent to prevent any unnecessary skin exposure to UV sources. Elimination of unnecessary skin exposure is reinforced by the fact that most individuals will receive substantial UV exposure from the sun during normal outdoor activities over a human lifetime.

UV radiation causes biological effects primarily through photochemical interactions. The UV wavelengths that produce the greatest biological effects fall in the UV-B, but other wavelengths can also be hazardous.

Skin protection is not difficult in theory, as most clothing tends to absorb some of the UV wavelengths. However, in practice, it is often difficult to properly motivate individuals to use appropriate skin protection unless they know they are receiving an erythema (sunburn) dose.

Protection of the skin from UV radiation hazards is best achieved though the use of clothing, gloves, and face shields. The use of UV skin blocks (creams or lotions) is

considered inadequate for protection against the high irradiance of man-made UV radiation sources.

Ultraviolet Eye Hazards

Various components of the human eye are susceptible to damage from extended exposure to direct/reflected UV exposure from photochemical effects. The UV wavelength is the determining factor as to which part(s) of the eye may absorb the radiation and suffer biological effects.

Absorption of UV wavelengths in the Human Eye

Wavelength	Cornea	Aqueous	Lens	Vitreous
100 nm - 280 nm	100%	0%	0%	0%
300 nm	92%	6%	2%	0%
320 nm	45%	16%	36%	1%
340 nm	37%	14%	48%	1%
360 nm	34%	12%	52%	2%

The cornea is like the skin in that it can be “sunburned” by exposure to too much UV radiation. This is called keratoconjunctivitis (snow blindness or welders flash), a condition where the corneal (epithelial) cells are damaged or destroyed. This condition usually does not present until 6 to 12 hours following the UV exposure. Although very painful (often described as having sand in the eyes) this condition is usually temporary (a few days) because the corneal cells will grow back. In very severe cases, the cornea may become clouded and corneal transplants may be needed to restore vision. Exposure to the UV-C and UV-B present the greatest risk to the cornea.

The lens of the eye is unique in that it is formed early in human development and is not regenerated should it become damaged. For normal vision, it is essential that the lens remains clear and transparent. Unfortunately, UV-A exposure is suspected as a cause of cataracts (clouding of the lens).

To protect the human eye from exposure to UV wavelengths, all that is usually needed is a pair of polycarbonate safety glasses or a polycarbonate face shield. This protective eyewear should be worn whenever there is a potential for ongoing UV radiation exposure. Contact the Office of Environment, Health & Safety (EH&S) for information and advice on appropriate UV protective eyewear.

Visible Light Hazards

All visible light (400 to 780 nm) entering the human eye is focused upon the sensitive cells of the retina where human vision occurs. The retina is the part of the eye normally considered at risk from visible light hazards.

Any very bright visible light source will cause a human aversion response (we either blink or turn our head away). Although we may see a retinal afterimage (which can last for several minutes), the aversion response time (about 0.25 seconds) will normally protect our vision. This aversion response should be trusted and obeyed. NEVER STARE AT ANY BRIGHT LIGHT SOURCE FOR AN EXTENDED PERIOD. Overriding the aversion response by forcing yourself to look at a bright light source may result in permanent injury to the retina. This type of injury can occur during a single prolonged exposure. Welders and other persons working with plasma sources are especially at risk for this type of injury.

NOTE: The aversion response cannot be relied upon to protect the eye from Class 3b or 4 laser exposure (see the Laser Safety Manual for more information).

Visible light sources that are not bright enough to cause retinal burns are not necessarily safe to view for an extended period. In fact, any sufficiently bright visible light source viewed for an extended period will eventually cause degradation of both night and color vision. Appropriate protective filters are needed for any light source that causes viewing discomfort when viewed for an extended period of time.

For these reasons, prolonged viewing of bright light sources (plasma arcs, flash lamps, etc.) should be limited by the use of appropriate filters. Traditionally, welding goggles or shields of the appropriate "shade number" will provide adequate protection for limited viewing of such sources. Please contact EH&S for advice on appropriate eye protection.

The blue light wavelengths (400 to 500 nm) present a unique hazard to the retina by causing photochemical effects similar to those found in UV radiation exposure. Visible light sources strongly weighted towards the blue should be evaluated by EH&S to determine if special protective eyewear is needed.

Infrared Radiation

Infrared (or heat) radiation is defined as having a wavelength between 780 nm and 1 mm. Specific biological effectiveness "bands" have been defined by the CIE (Commission International de l'Eclairage or International Commission on Illumination) as follows:

- IR-A (near IR) (780 nm to 1400 nm)
- IR-B (mid IR) (1400 nm to 3000 nm)
- IR-C (far IR) (3000 nm to 1 mm)

Infrared Radiation Hazards

Infrared radiation in the IR-A that enters the human eye will reach (and can be focused upon) the sensitive cells of the retina. For high irradiance sources in the IR-A, the retina is the part of the eye that is at risk. For sources in the IR-B and IR-C, both the skin and the cornea may be at risk from "flash burns." In addition, the heat deposited in the cornea may be conducted to the lens of the eye. This heating of the lens is believed to be the

cause of so called “glass blowers” cataracts because the heat transfer may cause clouding of the lens.

- Retinal IR Hazards (780 to 1400 nm) - possible retinal lesions from acute high irradiance exposures to small dimension sources.
- Lens IR Hazards (1400 to 1900 nm) - possible cataract induction from chronic lower irradiance exposures.
- Corneal IR Hazards (1900 nm to 1 mm) - possible flashburns from acute high irradiance exposures.
- Skin IR Hazards (1400 nm to 1 mm) - possible flashburns from acute high irradiance exposures.

The potential hazard is a function of the following:

- The exposure time (chronic or acute)
- The irradiance value (a function of both the image size and the source power)
- The environment (conditions of exposure)

Evaluation of IR hazards can be difficult, but reduction of eye exposure is relatively easy through the use of appropriate eye protection. As with visible light sources, the viewing of high irradiance IR sources (plasma arcs, flash lamps, etc.) should be limited by the use of appropriate filters. Traditionally, welding goggles or shields of the appropriate “shade number” will provide adequate protection for limited viewing of such sources. Specialized glassblowers goggles may be needed to protect against chronic exposures. Please contact the EH&S for advice on appropriate eye protection.

Module #2
Microwave and Radiofrequency Radiation Safety

Microwave/RF Radiation Sources

The campus contains many potential sources of microwave/RF radiation exposure. Some of these sources (primarily antennas) are designed to emit microwave/RF radiation into the environment. Other types of sources (co-axial cables, waveguides, transmission generators, heaters, and ovens) are designed to produce or safely contain the microwave/RF radiation, but may present a hazard should they leak for some reason. A third type of source (primarily power supplies) may create microwave/RF radiation as a byproduct of their operation.

Factors Affecting Exposure to Microwave/RF Radiation

The hazards from exposure to microwave/RF radiation are related to the following parameters:

- Frequency of the source
- Power density at the point of exposure
- Accessibility to the radiation field
- Does the exposure occur in the near or far field
- Orientation of the human body to the radiation field

This combination of factors is used in both evaluating and mitigating the hazard.

Potential Bioeffects of Exposure to Microwave/RF Radiation

In general, most biological effects of exposure to microwave/RF radiation are related to the direct heating of tissues (thermal effects) or the flow of current through tissue (induced current effects). Non-thermal effects resulting in carcinogenesis, teratogenesis, etc. have been demonstrated in animals but have not been proven by epidemiological studies on humans. The following biological effects have been demonstrated in humans:

- Cataract formation (from eye exposure).
- RF (induction) burns.
- Burns from contact with metal implants, spectacles, etc.

Standards for Microwave/RF Radiation Exposure Protection

A large number of standards have been developed for use in protecting individuals against overexposure to microwave/RF radiation. These standards often address only specific frequency bands or exposure conditions. In an effort to address the broad research potential for microwave/RF radiation exposure at UC Berkeley, the following table of exposure standards was developed. The table is a synthesis of several regulatory standards and guidelines (as indicated).

UCB Radio Frequency Exposure Standards
(Derived from ACGIH TLV, CCR Title 8, IRPA NIR, FCC OET 65,
and IEEE C95.1)

Occupational Exposure Limits
All exposures averaged over 0.1 hour (6 minutes)

Frequency Band	E field (V/m)	H Field (A/m)	S (mW/cm^2)
<3 kHz	5000	80 (1000 mG)	N/A
3 kHz - 100 kHz	614	1.63	100
100 kHz-1.34 MHz	614	1.63	100
1.34 MHz - 3 MHz	614	1.63	100
3 MHz - 30 MHz	1842/f	4.89/f	$900/f_2$

30 MHz - 100 MHz	61.4	0.163	1
100 MHz - 300 MHz	61.4	0.163	1
300 MHz - 3 GHz	N/A	N/A	f/300
3 GHz - 15 GHz	N/A	N/A	f/300
15 GHz - 30 GHz	137	0.36	5
30 GHz - 300 GHz	137	0.36	5

Where: f = frequency in MHz

Non-Occupational Exposure Limits
All exposures averaged over 0.5 hour (30 minutes)

Frequency Band	E field (V/m)	H Field (A/m)	S (mW/cm2)
<3 kHz	5000	80 (1000 mG)	N/A
3 kHz - 100 kHz	614	1.63	100
100 kHz-1.34 MHz	614	16.3/f	100
1.34 MHz - 3 MHz	823.8/f	16.3/f	$180/f_2$
3 MHz - 30 MHz	823.8/f	16.3/f	$180/f_2$
30 MHz - 100 MHz	27.5	$158.3/f_{1.688}$	0.2
100 MHz - 300 MHz	27.5	0.0729	0.2
300 MHz - 3 GHz	N/A	N/A	f/1500
3 GHz - 15 GHz	N/A	N/A	f/1500
15 GHz - 30 GHz	N/A	N/A	f/1500
30 GHz - 300 GHz	N/A	N/A	5

Key to Reference Standards

- International Non-ionizing Radiation Committee (INIRC) of the International Radiation Protection Association (IRPA) - Interim Guidelines on Limits of Exposure to 50/60 Hz Electric and Magnetic Fields (1989).
- Institute of Electrical and Electronics Engineers (IEEE) Publication C95.1 - Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 3 kHz to 300 GHz (1991).
- California Code of Regulations, Title 8 - Industrial Relations, Division 1 - Department of Industrial Relations, Chapter 4 - Division of Industrial Safety, Subchapter 7 - General Industry Safety Orders, Group 14 - Radiation and Radioactivity, Article 104 - Non-ionizing Radiation, Section 5085 - Radio frequency and Microwave Radiation.
- American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values for Chemical Substances and Physical Agents Physical Agents Section Sub-Frequency (30 kHz and below) Magnetic Fields & Sub-Frequency (30 kHz and below) and Static Electric Fields

- Federal Communications Commission Guidelines for Human Exposure to Radiofrequency Electromagnetic Fields OET Bulletin 65, Edition 97-01, 1997

Identifying and Controlling Microwave/RF Radiation Hazards

The Office of Environment, Health & Safety (EH&S) will work with you to identify and assess the microwave/RF radiation hazards in your work area. Because of the difficulties of performing actual microwave/RF radiation surveys (near field measurements, cost of equipment, etc.), it is often necessary to use calculations and/or computer models to replace actual measurements in evaluating the hazard.

Antennas and Antenna Arrays

Operation of radio, television, microwave, and other related communication systems using electromagnetic radiation, and carrier-current systems require prior review and approval by Communication and Network Services (CNS) and Environment, Health & Safety (EH&S). Per UC Business and Finance Bulletin IS-5, CNS, in coordination with ORS, will advise you on licensing requirements, operational issues, FCC regulations and the appropriate exposure model to use in your hazard assessment process. Please provide ORS with a copy of your hazard assessment for regulatory review. CNS coordinates all FCC applications with the Office of President and maintains all campus-approved licenses. EH&S, in coordination with CNS, maintains an inventory of all transmission antennas on campus. Please contact EH&S before you place a new transmission antenna in or on any campus building or location.

Wireless Local Area Networks (WLAN)

Radio frequency based wireless local area networks based on the IEEE 802.11b Standard are becoming available on the campus. Wireless LAN systems (indoor and outdoor) are very safe when properly installed and used. WLAN systems operate on extremely low power (less than that of a cell phone). It is important that only approved equipment be used to build a campus operated WLAN.

Construction or Modification of campus operated WLAN equipment must be reviewed and approved by CNS and EH&S in order to prevent potential hazardous conditions from existing. The placement of base station antennas should be high on a wall or on the ceiling. This not only increases the useful range of the system, but also allows for a separation distance of 50 cm, which is sufficient of safe operation. In general, persons should avoid direct contact with antennas attached to computer cards. A separation distance of 10 cm is sufficient for safe operation.

Other Potential Microwave/RF Radiation Sources (Leakage Sources)

For waveguides, co-axial cables, generators, sealers, and ovens, probably the most important aspect of controlling microwave/RF radiation hazards is a careful physical inspection of the source. Leaking sources will normally show misalignment of doors or

plates, missing bolts, or physical damage to plane surfaces. Sources, which are suspected of leaking, should be repaired and then surveyed with appropriate instrumentation to verify they are no longer leaking. Contact EH&S if you need assistance with evaluating microwave/RF radiation leakage hazards.

Microwave Ovens

Because of the large number of microwave ovens used and their presence in nearly every Department, EH&S has special concerns about safety with these devices. Specific guidance on microwave oven safety can be found in the Appendix C in the back of this manual. It is very unusual for a commercial microwave oven to leak, but misuse, damage, and interlock failures have caused ovens to leak. Any microwave oven suspected of leaking will be surveyed, upon request, by EH&S. Please contact EH&S if you would like your ovens surveyed.

Power Supplies

Many high voltage power supplies operate in the microwave or radiofrequency regions. If damaged, or not properly shielded, these sources can leak, producing unintended microwave/RF radiation exposure. Most of the time, the leakage from these sources is minimal and does not present a hazard. However, if you have an indication of microwave/RF radiation leakage (RF interference with other equipment or documentation warning of interference), please contact EH&S for a survey.

Module #3
Extremely Low Frequency Radiation Safety

What is ELF Radiation?

Whenever a current passes through a wire, a magnetic field is produced. Because electric power generation in the United States changes polarity at 60 Hz (cycles per second), the magnetic fields generated also alternate at 60 Hz. Since about 1980, these 60 Hz magnetic fields (and their frequency harmonics) have been suspected of causing various types of negative health effects. These magnetic fields are commonly called extremely low frequency (or ELF) fields.

Does ELF Present a Human Health Hazard?

The most accurate answer is that no one really knows. Although some health effects have been statistically related to ELF exposure, these effects are poorly understood and may exist only as statistical or scientific errors. Some research studies, which originally indicated ELF health effects, could not be duplicated. Much of the data supporting effects

is from epidemiological studies and the effects found were slightly outside the boundaries of statistical error. What can be determined from this information is that any real effect (and the corresponding hazard) must be relatively small.

Are there Protection Standards for ELF Exposure?

In the absence of conclusive data, the International Radiation Protection Association/International Non-Ionizing Radiation Committee (IRPA/INIRC) have produced an interim exposure guideline. Although the US Government and the State of California have no regulations on exposure to ELF, UC Berkeley has adapted the IRPA/INIRC guidelines in order to address employee concerns.

The IRPA/INIRC Interim Guidelines on Limits of Exposure to 50/60 Hz Electric and Magnetic Fields

Exposure Type	Electric Field Strength in kV/m_2	Mag. Flux Density in mT
Occupational		
Working Day (8 hours)	10	0.5 (5 Gauss)
Short Term	30*	5** (50 Gauss)
Extremities (limbs)	---	25 (250 Gauss)
Non-Occupational		
Continual - 24 hours/day***	5	0.1 (1 Gauss)
A few hours/day****	10	1 (10 Gauss)

* The duration of exposure to fields between 10 and 30 kV/m2 may be calculated from the formula **t 0 E**, where **t** is the duration in hours per work day and **E** is the electric field strength in kV/m2.
** Maximum exposure duration is 2 hours per workday.
*** This restriction applies to open spaces in which members of the general public might reasonably be expected to spend a substantial part of the day, such as recreational areas, meeting grounds, and the like.
**** These values can be exceeded for a few minutes each day provided precautions are taken to prevent indirect coupling effects.

What is a normal ELF Field at UC Berkeley?

Since even the wiring for electric lights will generate ELF magnetic fields, these fields are present in virtually every room of every building on campus. The ELF field intensity is a function of the amperage passing through the wiring. In general, transformers and large motors will produce the most intense fields. Mechanical spaces and machine shops normally have the most intense fields and these may (rarely) exceed the non-occupational exposure limit. Laboratories and offices usually do not have intense fields and a reasonable average value for these areas has been measured at about 3 to 5 mG

(milliGauss). So normally, the ELF fields UC Berkeley employees are exposed to are less than 1% of the non-occupational exposure limit.

Who Should I Call if I Have ELF Concerns?

Radiation Safety is available to address questions on ELF exposure. A number of training documents are available to explain what is (and is not) known about ELF exposure and health effects. Please contact EH&S if you would like copies of these documents.

EH&S is also available, upon request, to perform ELF surveys of specific equipment or work areas. Survey reports will characterize the ELF field intensity in the areas surveyed, but cannot specifically address the hazards of fields found to be in excess of the IRPA/INIRP Guidelines.

EH&S will normally recommend that exposure to fields in excess of the guidelines be mitigated so as to prevent exposure above the IRPA/INIRP Guidelines to employees or students. Since there is no legal requirement to control ELF exposure, the implementation of such recommendations is at the discretion of the Department.

Module #4
Static Magnetic Field Safety

Many sources (devices) on the UC Berkeley campus produce static magnetic fields. Static magnetic fields result from either fixed magnets or the magnetic flux resulting from the flow of direct current (DC). Sources producing these fields include (but are not limited to) the following:

- Nuclear Magnetic Resonance (NMR) imaging and spectroscopy devices
- Electron Paramagnetic Resonance (EPR, ESR, EMR) devices
- Helmholtz Coils, Solenoids, DC Motors, etc.

Factors Affecting Static Magnetic Field Hazards

Under certain conditions, sources of static magnetic fields can present health hazards. Factors affecting the potential hazards include:

- Magnetic flux intensity associated with the source
- Design of the magnetic field source
- Accessibility of the magnetic field
- Equipment/hazardous materials associated with the magnetic field source

Sources of large static magnetic fields may require appropriate controls to mitigate potential hazards. For sources intended to produce human exposure to the magnetic field (such as MRI devices), it is critical that safety precautions cover not only the user of the device, but also the research subject.

Bioeffects of Exposure to Static Magnetic Fields

There are no known adverse bioeffects for flux densities within the ACGIH (American Conference of Governmental Industrial Hygienists) exposure limits. Implanted medical devices present a potential hazard to individuals exposed to fields above the ACGIH limits (see following section on kinetic energy hazards).

Kinetic Energy Hazards

Due to the large fields associated with NMR magnets, ferrous objects can be accelerated toward the magnet with sufficient energy to seriously injure persons and/or damage the magnet. As a precaution, even small metal objects (screws, tools, razor blades, paper clips, etc.) should be kept at least 1.5 meters from the magnet (or anywhere the field exceed 30 G). Large ferrous objects (equipment racks, tool dollies, compressed gas cylinders, etc.) should be moved with care whenever the field approaches 300 G. There are many recorded instances in which large objects have been drawn towards and even into the bore of the magnet.

Standards for Exposure to Static Magnetic Fields

The ACGIH and International Council on Non-Ionizing Radiation Protection (ICNIRP) have set guidelines for continuous exposure to static electromagnetic fields as indicated in the table below:

Note: 1 Gauss (G) = 0.1 millitesla (mT)

5 G	Highest allowed field for implanted cardiac pacemakers.
10 G	Watches, credit cards, magnetic tape, computer disks damaged.
30 G	Small ferrous objects present a kinetic energy hazard.
600 G	Allowed TWA for routine exposure (whole body).
6000 G	Allowed TWA for routine exposure (extremities).
20,000 G (2T)	Whole body ceiling limit (no exposure allowed above this limit).
	Extremity ceiling limit (no exposure allowed above this limit).

NOTE: TWA exposure time is normally only a concern for extremely high field exposures to the whole body.

Magnetic Field Measurements

NMR magnets commonly produce core fields from 0.2 T to 20 T. These fields decrease in intensity as the distance from the core increases. A field strength map of the area surrounding the magnet should be developed and posted for use by staff. If the magnetic fields in your laboratory have not yet been evaluated, please call Radiation Safety at (510) 642-3073 to schedule a survey.

Posting of Magnetic Field Hazards

All access points to rooms containing magnets fields in excess of 5 G shall be marked with magnetic field hazard signs (available from Radiation Safety). The 5 G threshold line shall be clearly identified with floor tape or equivalent markings. The location of the 5 G line will vary with the operating frequency and resulting magnetic fields. As an example, one vendor indicates the following values for their NMR spectroscopy equipment:

Operating frequency of 200 MHz - 5 G threshold line @ 1.3 meters

Operating frequency of 500 MHz - 5 G threshold line @ 3.5 meters

Operating frequency of 800 MHz - 5 G threshold line @ 6.0 meters

Access Restrictions

Persons with cardiac pacemakers or other implanted medical devices shall be restricted to areas outside the 5 G threshold line. Security (locked doors) and proper door markings shall be maintained to prevent unauthorized access to the magnet area.

Cryogenic Gas Issues

Types and Expansion Ratios - The cryogenic (liquefied) gases used with NMR magnets are Liquid Nitrogen (-320 deg. F) and Liquid Helium (-452 deg. F). If these liquids are raised to room temperature, the resulting gases expand to hundreds of times their liquid volumes, possibly displacing the air in the room (LN = 694/1, LH = 700/1).

Quench - Quench is the (normally unexpected) loss of superconductivity in a NMR magnet resulting in rapid heating through increased resistance to the high current. This can violently damage the magnet and cause rapid venting of large volumes of He/N gas into the room, quickly resulting in an oxygen deficient atmosphere. To avoid a quench situation, use cryogen level sensors and always refill or de-energize the magnet if low cryogen levels are indicated on the sensors. NOTE: Quench conditions can result from ferrous objects being drawn into the magnet bore.

Personal Protective Equipment (PPE) - When handling cryogens, use insulated gloves and face shields or other splash eye/face protection, closed-toed shoes, and lab coats.

Dewars- The containers used for transporting cryogens should be made of metal. Glass dewars can easily implode, causing seriously injury. All dewars should have appropriate pressure vents. Unvented containers can rupture as the liquid warms and expands. All transfers of cryogens should be continuously attended to prevent spills or frozen valves.

Room Ventilation - Generally speaking, five complete room air changes per hour is considered adequate for managing small spills or releases of cryogens. In the event of a major release, the staff should immediately leave the room and the room doors should be left open. If the risk of a catastrophic release exists, auxiliary ventilation should be considered to prevent the formation of an oxygen deficient atmosphere.

Bioeffects of Cryogen Exposure - Direct contact with the skin or eye tissues can cause severe damage through frostbite (tissue damage from freezing). If the frostbite is severe, the damaged tissues may need to be amputated. Inhalation of concentrated cryogen gases may cause loss of consciousness and (eventually) death through oxygen deprivation (asphyxiation).

Electrical Safety Issues

Power Supplies - Although the power supplies used for NMR magnets operate at relatively low voltages (about 10 V), the current used is very large (about 100A). High amperage is extremely dangerous if allowed to come into contact with tissues.

Cables, Wires, and Connectors - All cables, wires, and connectors should be properly insulated to prevent contact with the operating current. These should be inspected on a regular basis to assure the integrity of the insulation. In order to prevent arcing; never break connections without first turning off the power to the circuit being handled.

LOTO (Lock Out, Tag Out)- Cal-OSHA requires all workers to follow LOTO procedures when working on equipment which is activated by a hazardous energy source. Contact EH&S for information on LOTO requirements.

Qualification of Electrical Workers - Cal-OSHA requires that persons who work on electrical equipment be properly qualified. Contact EH&S for information on qualification requirements.

Home Built Equipment - Must be designed and maintained so as to meet safety standards. Enclosures with proper grounding and safety markings are required for all home built electronics.

Bioeffects of Electrical Exposure - Current moving across a break in an electrical circuit may cause a high temperature arc to occur. Depending on the current, this arc can exceed 10,000 deg. F, causing severe burns. Blast effects resulting from the vaporization of copper or other metals in the arc can throw people and equipment across rooms, causing severe trauma injuries. Even if an arc is not struck, current flowing through tissues can result in burns, “blow out” injuries, and possible cardiac failure (depending on the line

frequency). Every effort must be made to follow good electrical safety practices and avoid direct contact with live current.

Radiofrequency Radiation (RF) Issues

RF Sources - The RF source being used for the NMR should be commercially produced or equivalent quality if assembled in the laboratory. Units that are lab built or modified should be checked to assure they are safe and do not leak radiation.

Waveguides and Coils - Should be carefully checked to assure there are no gaps or loose bolts that will allow leakage of the radiation. Care should be taken to avoid direct contact with coils to avoid RF burns.

RF Measurements - If the RF fields in your laboratory need evaluation, please call Radiation Safety (510) at 642-3073 to obtain a survey.

Bioeffects - Exposure to high level RF fields can cause heating and damage of tissues. Skin burns can occur from direct contact with RF coils.

Other Hazard Issues

Tripping Hazards - Cables and wires lying about on the floor can present tripping hazards. Please make every effort to keep cables in trays or covered by bridges.

Fire Protection - A Class C fire extinguisher should be kept nearby to deal with electrical fires. The power must be shut down before attempting to fight an electrical fire. All staff should be trained in fire protection and evacuation procedures.

Earthquake Concerns - Magnet assemblies may weigh several tons and must be restrained so they will not move about or tip over during an earthquake. Their placement should take into account structural steel support members. Power supplies should also be secured to prevent movement in an earthquake.

Ergonomic Concerns- The prolonged use or improper ergonomic setup of VDT stations may cause eye or neck strain problems. Back injuries may result from the use of improper lifting procedures or lifting heavy objects without assistance

Use of NIR Hazard Signs and Warning Labels

Depending on the accessibility and level of NIR hazards, it may be necessary to mark rooms or other areas with appropriate warning signs (static magnetic fields, UV light, etc.). Please consult with Radiation Safety on the need for such signs prior to placing them. Please refer to Appendix E for the appropriate design of warning signs. Radiation Safety provides these and other custom NIR signs upon request. Please contact Radiation Safety for assistance with warning signs.

Warning labels should be placed on equipment to indicate the presence of specific NIR hazards (UV light, RF fields, etc.). Again, please consult with Radiation Safety on the need for such labels prior to placing them. Radiation Safety provides these labels upon request. Please contact Radiation Safety for assistance with warning labels.

http://agreenroad.blogspot.com/2012/11/symptoms-of-low-dose-radiation-exposure.html

Top Ten Symptoms Of Low Dose Radiation Exposure On Fetus In Utero, Infants, Children, Adults And Seniors, Gene Blood Test Can Show How Much Damage Radiation Caused

Top Ten Symptoms Of Low Dose Radiation Exposure On Fetus In Utero, Infants, Children, Adults And Seniors, Gene Blood Test Can Show How Much Damage Radiation Caused

DR CALDICOTT MD DISCUSSES RADIATION TESTING VIA URINE TESTS, PREVENTION AND FUKUSHIMA RADIATION CONSEQUENCES

Watch the Dr Caldicott Interview in Byron Bay from Spirit Gaia on Vimeo, by clicking on the live link in this sentence.

Dr. Helen Caldicott MD is a pediatrician and nuclear expert. In this interview she talks about the effects of the Fukushima crisis on children specifically. She explores some of the most common symptoms at 6 minutes in. Then she explores the effects of internal emitters, which is a term used for radiation that is taken in by drinking liquids, breathing air, or eating food. She also details that children are much more sensitive to the same radiation that adults are exposed to, and that a fetus is even more sensitive to the same doses.

She concludes that the only safe way to deal with low dose radiation is not to try and chelate it out, but to prevent it from getting into the body in the first place, which means closing down all nuclear power plants and eliminating all nuclear bombs.

She also discusses testing for radiation by testing for it in urine. Certain radioactive elements will show up in the urine. She also talks about testing for radiation effects in the thyroid by getting an ultrasound test of the gland, and then doing a needle biopsy of anything found to determine if it is cancerous. In Japan, medical tests found a very high percentage of children in Fukushima Province had cysts on their thyroid glands, which according to Dr. Caldicott is unheard of. She cannot believe that the Japanese medical authorities are doing nothing for these children.

https://youtu.be/MbwjhXtAg0I

Source: "Chernobyl: Consequences of the Catastrophe for People and the Environment"

According to the video above, health professionals coming from other countries were shocked to see how bad the

situation was and how many negative health symptoms people were having in Japan. The health of people in general was found to have deteriorated since the Fukushima nuclear accident.

The symptoms found by these foreign doctors visiting in Japan were always the same;

Nose bleeds....

Press Conference by Former Official: I'm bleeding from nose every day, many in Fukushima have similar symptoms — Author: My nose bled for days, it wouldn't stop; Staff had same problem… Do people want me to lie? I can only write truth May 11, 2014

Skin disease

Diarrhea

Fatigue
Author had bouts of nosebleeds, plagued by unusual fatigue after Fukushima plant visits — Group of newspaper journalists "confess to suffering similar symptoms" — Official unbearably sick since 3/11, many residents are too they just don't say it openly — Worker: "This is like going to war" May 5, 2014

Respiratory diseases

Viral and bacterial attacks

Pains at the rear of the ears

Thyroid disorders; cysts, tumors, cancer

Sores; Stomatitis (infections and sores in the mouth)

According to Wikipedia; "Stomatitis is an inflammation of the mucous lining of any of the structures in the mouth, which may involve the cheeks, gums, tongue, lips, throat, and roof or floor of the mouth. The inflammation can be caused by conditions in the mouth itself, such as poor oral hygiene, dietary protein deficiency, poorly fitted dentures, or from mouth burns from hot food or drinks, toxic plants, or by conditions that affect the entire body, such as medications, allergic reactions, RADIATION THERAPY, or infections." http://en.wikipedia.org/wiki/Stomatitis

Skin sloughing off or skin sores
http://www.cbsnews.com/pictures/radiation-sickness-8-terrifying-symptoms/5/

Hair loss (can be complete, partial, spotty, or just increased amount over normal)
http://www.cbsnews.com/pictures/radiation-sickness-8-terrifying-symptoms/6/

Severe fatigue
http://www.cbsnews.com/pictures/radiation-sickness-8-terrifying-symptoms/7/

Bottom line, radiation exposure causes sores both in the skin and inside the body, where they are know as lesions. Lesions appear on the heart in the case of cesium contamination. They appear on other organs and glands depending

on the radiation contamination exposure. For more details on internal and external lesions, click on the the following article links..

IMMUNE SYSTEM STRENGTH IS LOWERED OR COMPROMISED, OPPORTUNISTIC INFECTIONS INCREASE

In addition, after exposure to radiation, the immune system strength is compromised, due to loss of white blood cells. Upper respiratory problems are much more common. Ear, nose and throat issues are also common. Bacterial and viral infections are much more common.

2015 - Record Level Of Dying, Sick, Injured California Seals And Sea Lions, Mass Die Offs Continue, Started In 2011 After Fukushima
http://agreenroad.blogspot.com/2014/04/2014-record-level-of-sick-injured.html

When ocean biologists are finding viruses or bacterial infections in animals, they stop there and blame everything on the virus or bacteria. They should be looking deeper, at what causes these mass die offs of many species, all at the same time. It is not ocean water too hot, or ocean water too cold, or too many viruses, or too many bacteria. What they refuse to look at is internal radiation contamination.

Animals, Insects, Birds And Plants - Negative Effects Of Chronic, Cumulative Man Made Radiation
http://agreenroad.blogspot.com/p/animals-and-low-level-radiation-effects.html

TOP TEN SYMPTOMS OF RADIATION EXPOSURE

Here is a short video, show the top ten symptoms of radiation exposure...

https://youtu.be/GQSBh3qvzFM

TOP HEALTH COMPLAINTS FROM CHERNOBYL RADIATION VICTIMS

In the book; "Chernobyl: Consequences of the Catastrophe for People and the Environment", the following symptoms were reported among people exposed to low dose radiation from Chernobyl;

PAGE 44:

Weakness
Dizziness
Headache
Fainting
Nose bleeds
Fatigue
Heart Arythmias

Stomach pain
Vomiting
Heartburn
Loss of appetite
Chronic stomach and intestinal problems
Chronic duodenitis
Chronic gastroduodenitis
Gallbladder inflammation
Vascular dystonia
Heart syndrome
Asthenia-neurosis
Tonsil hypertrophy and chronic tonsillitis
Tooth decay
Chronic periodontitis

PAGE 47:

Neoplasms
Nervous system diseases
Circulatory diseases

PAGE 55:

Premature aging of the eyes
osteoporosis
chronic choleosystitis
pancreatitis
fatty liver
renal dystrophy

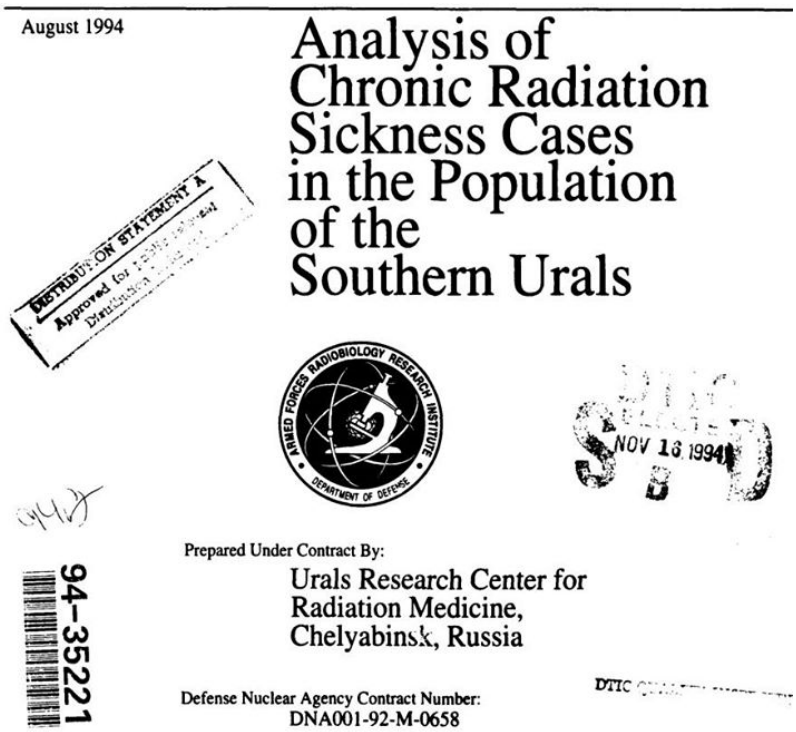
PAGE 56

Cataracts at young age
Decline in higher mental function characteristic of senility
Development of Type II diabetes at young age
Loss of stability in the antioxidant system
Retinal vessel arteriosclerosis
Hearing and vestibular disorders at young ages

According to the Mayo clinic, the symptoms of radiation sickness, as as follows;

Vomiting
Diarrhea
Lethargy
Headaches

For more information click on link below
http://www.mayoclinic.com/health/radiation-sickness/DS00432/DSECTION=symptoms


August 1994

Analysis of Chronic Radiation Sickness Cases in the Population of the Southern Urals

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DTIC

Source/credit

Via Rob Soltysik Chronic Radiation Sickness (CRS) among victims of the Mayak/Techa River radiation catastrophe in the Soviet Union. The nervous system symptoms sounds suspiciously like ME/CFS/SEID. "About half the patients with CRS complained of headaches, and one third of the patients complained of vertigo. Vasomotor reactions and psychoemotional disturbances were identified on the basis of the patients' own accounts of their symptoms: they were questioned by physicians about the occurrence of chills, sensation of hot flushes, syncopes (for evaluating vasomotor reactions), sleep disturbances, failing memory and attention, and increased excitability (for evaluating psychoemotional status). In relation to the frequency of the above-described complaints as well as that of complaints of extreme. unmotivated weakness, no connection with the CRS patients' radiation exposure rates was revealed (table 7.8)."
http://www.ncf-net.org/radiation/AnalysisOfChronicRadiationSicknessCasesInThePopulationOfTheSouthernUrals.pdf

RADIATION-INDUCED IMMUNOSUPPRESSION

Radiation-induced immunosuppression is a critical concern in populations exposed to sublethal to lethal doses of ionizing radiation. Radiation results in a dramatic decrease in peripheral blood cell population, especially granulocytes, lymphocytes, and platelets, due to depletion in hematopoietic stem and progenitor cells.[54,55] However, depletion is often followed by delayed repopulation and recovery as the surviving stem cells reconstitute the hematopoietic system. The delay in repopulation can be correlated to the extent of damage to the stem and progenitor cells, which further depends on the absorbed dose.[56] During this delay, individuals are susceptible to opportunistic infections; thus, accelerated recovery is essential to prevent bone-marrow–related injury and mortality. Radiation-induced stem cell damage was first illustrated in a mouse model by Till and McCulloch; the team demonstrated that bone-marrow stem cells from mice exposed to significant doses of ionizing radiation exhibited lower numbers of stem cell colonies in the spleen and poor capacity to reconstitute the hematopoietic system in recipient animals.[56] Reduction in the reconstitutive capacity of hematopoietic stem cells (HSCs) depended on absorbed dose. Since then, this assay is routinely used to assess stem cell function in animal models and is considered an index of the reconstitutive capacity of HSCs.[57–59]

Bone marrow suppression can be prevented by stimulating hematopoiesis and rapid recovery. In clinical and animal models, such recovery is routinely stimulated by use of various cytokines, cytokine mimetics, and hematopoietic growth factors.[60–64] However, it has become increasingly evident that growth-factor–mediated recovery is not entirely a complete hematopoietic recovery. Radiation-induced damage, such as genotoxic stress, in stem cells is not alleviated by cytokines and growth factors.[65] In contrast, replicative stress is induced upon proliferative stimuli in damaged stem cells that may potentially accumulate genomic instability. Indeed, several studies report higher incidences of malignancies in hematopoietic system in response to ionizing radiation.[66]

Prevalence of long-term immunosuppression is also concerning in patients treated with radio- or chemotherapy years after treatment. It was believed that HSCs have finite capacity to replicate, thus mitotic overload in HSCs potentially leads to accelerated aging and exhaustion of the stem cell pool. However, serial bone-marrow transplant experiments suggest that long-term colony-forming units increased upon serial transplantation in mice, showing practically infinite replicative capacity.[67] Also an increase in telomere length did not increase HSC expansion any further compared to control animals.[68] In some

Credit/Source Rob Soltysik

Medical Consequences of Radiological and Nuclear Weapons

LATE AND LOW-LEVEL EFFECTS OF IONIZING RADIATION
http://www.ncf-net.org/radiation/MedicalConsequencesOfNuclearWarfare9.pdf

MENTAL AND EMOTIONAL HEALTH PROBLEMS ARISE AFTER THYROID IS AFFECTED BY RADIATION

Thyroid problems are common after any nuclear accident. As radioactive iodine levels rise, thyroid problems appear, both in the hyper and hypo side of things. Extreme thyroid issues are more prevalent in infants and fetuses, resulting in still births, birth problems, and increased mortality rate.

Via Nick February 12, 2015 "The Thyroid and the Mind and Emotions
(Summary of an address to the Kitchener-Waterloo Area Chapter)

The psychiatric disturbances which accompany hyperthyroidism and hypothyroidism, the two commonest thyroid disorders, mimic mental illness. People with an overactive thyroid may exhibit marked anxiety and tension, emotional lability, impatience and irritability, distractible overactivity, exaggerated sensitivity to noise, and

fluctuating depression with sadness and problems with sleep and the appetite. In extreme cases, they may appear schizophrenic, losing touch with reality and becoming delirious or hallucinating.

An underactive thyroid can lead to progressive loss of interest and initiative, slowing of mental processes, poor memory for recent events, fading of the personality's colour and vivacity, general intellectual deterioration, depression with a paranoid flavour, and eventually, if not checked, to dementia and permanent harmful effects on the brain. In instances of each condition, some persons have been wrongly diagnosed, hospitalized for months, and treated unsuccessfully for psychosis."
http://www.thyroid.ca/e10f.php

IN UTERO BRAIN DEVELOPMENT AND NEGATIVE EFFECT OF RADIATION

Socrates March 9, 2015 At about ten weeks of gestation, the fetus should develop it's own thyroid gland. In utero exposures to fetuses of radioactive iodone wipes out the fetal thyroid gland during critical periods of fetal brain development. If the timing during early pregnancy prevents enough thyroid hormone, the fetus will die or go on to have cretinism, attention deficit syndrome, mental delays, etc. Many such fetuses will be stillborn or miscarry.

If this is recognized, thyroxin Replacement can be administered in some cases. With government cover ups you would expect higher numbers to go untreated. Many are not disgnosed.

Thyroid cancer is another matter. Papillary thyroid cancer results from genetic changes, often from radioactive exposures, but not always by any means.

There will be an epidemic of learning disabled children from in utero exposures as well as thyroid cysts and thyroid cancers.

WBC AND LOW DOSE RADIATION EXPOSURE

Another way to tell if you have been exposed to radiation is to have a blood culture study done. Have blood taken. The lab will count the different blood cells including your white blood cells (WBC). The WBC count drops within a day of being exposed to even small doses of radiation. Repeating this test will tell a person if they are being persistently exposed or if the radiation is gone. If the WBC count comes back up, good.

If the WBC count keeps dropping, it indicates a huge problem. Either the area is getting worse in terms of radiation or another source of radiation is making things worse... this could be radiation coming into the body with food or water, air, etc.

Doing repeated blood studies is important because it indicates how much radiation one is exposed to. If the WBC level drops to 50% of normal, that indicates a huge exposure, but it is survivable. A drop of 10% of normal WBC indicates an exposure to doses of radiation that should be avoided if possible. The higher the drop off of WBC levels, the higher the exposure of radiation indicated.

MEDICAL DOCTOR SAYS CHILDREN'S BLOOD NEGATIVELY AFFECTED BY FUKUSHIMA RADIATION

Doctor Shigeru Mita says
… Since December 2011, I have conducted thyroid ultrasound examinations, thyroid function tests, general blood tests and biochemical tests on about 2000 people, mostly families in the Tokyo metropolitan area expressing concerns on the effects of radiation. I have observed that white blood cells, especially neutrophils, are decreasing among children under the age of 10. There are cases of significant decline in the number of neutrophils in 0-1 year-olds born after the earthquake …
http://www.save-children-from-radiation.org/2014/07/16/a-tokyo-doctor-who-has-moved-to-western-japan-urges-fellow-doctors-to-promote-radiation-protection-a-message-from-dr-mita-to-his-colleagues-in-kodaira-city-t/

Of course, the pro nuclear apologists will claim that these children are not smiling enough and are suffering from nothing more than stress. But then what about animals? Are they also not smiling enough, and suffering from too much stress?

MONKEYS BLOOD NEGATIVELY AFFECTED BY FUKUSHIMA RADIATION

Guardian: Abnormal blood in monkeys linked to Fukushima disaster — Study: 'Epidemic infectious disease' could occur — "We cannot find other reasons except radiation" — Concern about strontium-90 other radioactive materials besides cesium — "Potential direct relevance to humans
http://enenews.com/study-finds-blood-monkeys-70-km-fukushima-plant-epidemic-infectious-disease-could-occur-find-other-reasons-except-radiation-effects-neurological-development-discovered-other-mammals-potent

Irradiated Monkeys Showing Fukushima Effects | IFLScience
www.iflscience.com/.../irradiated-monkeys-showing-fukushima-effects
Jul 25, 2014 - The affected monkeys also had decreased counts of both red and white blood cells, consistent with results in people living near Chernobyl.

Two years following the incident, these monkeys - which generally boast 20-year life spans - have been living under the long-term influence of low-level radiation. Researchers compared the original 61 subjects to 31 macaques living nearly 230 miles away from Fukushima. They found the Fukushima macaques had significantly lower hemoglobin and blood cell counts compared to the distant monkeys.'
http://www.designntrend.com/articles/17212/20140725/blood-abnormalities-found-in-japanese-monkeys-living-near-fukushima-nuclear-plant.htm

BLOOD WAS NEGATIVELY AFFECTED IN PEOPLE LIVING NEAR CHERNOBYL

Radiation levels now | The Chernobyl Gallery
chernobylgallery.com/chernobyl-disaster/radiation-levels/
During the Chernobyl disaster four hundred times more radioactive material was ...cause radiation sickness, including nausea, lower white blood cell count.

Journal of Exposure Science and Environmental ...
cricket.biol.sc.edu/chernobyl/papers/Lindgren-et-al-JESEE-2013.pdf
Sep 25, 2013 - associated with decreased blood counts in children in the ... log(WBC) activity in the body had significantly decreased hemoglobin, erythrocyte and thrombocyte counts. ... the most contaminated populated areas around the Chernobyl.... long-term effects on red blood cells.. Abnormalities such as a decreased blood cell count in people living in contaminated areas have been reported from Chernobyl as a long-term effect of low-dose radiation exposure,' Shin-ichi Hayama told the Guardian, adding that this study can help further an understanding of the consequences of long-term exposure to even extremely low levels of radiation.
http://www.designntrend.com/articles/17212/20140725/blood-abnormalities-found-in-japanese-monkeys-living-near-fukushima-nuclear-plant.htm

This blood test is an easy test to ask any doctor to perform, and you do not need to talk with him or her about what all of this means or why you are asking for it. If you tell them why, they may refuse, especially in Japan, since the medical industry seems to be taking part in the active cover up and denial of any harm from the Fukushima 'accident'.

No internal radiation test is necessary (although that is one good way to tell if you have been exposed to gamma or beta radiation, but not alpha radiation) and the doctor can be left completely clueless about what you are looking for. Many, if not all hospitals in Japan have refused to do internal radiation tests for people, even those who ask for it, and for those who KNOW that they have been exposed to radiation. The medical doctors in Japan have been told to not discuss negative radiation effects on health with any patients.

Many doctors will see the WBC drop and look for everything EXCEPT low dose radiation exposure, so do not be surprised when this happens, because most medical professionals are NOT trained in this area of low dose radiation exposure and the harm caused by it. Just after reading this article, you will more than likely know MORE than the doctor does about low dose radiation exposure symptoms and harm caused by it.

Many doctors believe that radiation will not hurt anyone, and that it is good for everyone, including children and pregnant women. After all, they use radiation cancer 'therapy', to supposedly heal people. If the radiation does not kill you, it is good for you, seems to be the philosophy of much of the medical and nuclear profession, even if that means polluting the whole world with radioactive contamination and nuclear fallout.

PARALYSIS AS A RESULT OF RADIATION DAMAGE

Heart of the Rose April 19, 2015 "1,142 children paralysed in last 3 months in Pakistan April 19 2015 "Sometimes paralysis can occur because of tuberculosis, radiation therapy and some other infection which damage antibodies, he said."
http://www.netindia123.com/netindia/showdetails.asp?id=2575535&n_date=20150420&cat=World

Radiation THERAPY?
http://www.bing.com/images/search?q=drone+pakistan+children&FORM=HDRSC2

DR. BUSBY ON LOW DOSE RADIATION NEGATIVE EFFECTS

https://youtu.be/rCmP83mgUnk

In the video above, Christopher Busby, a British scientist researching the negative health effects of low-dose ionizing radiation, makes an appearance to talk about the critical situation at the Fukushima nuclear plant in Japan. He finishes his interview by discussing how the nuclear industry sponsored models of how radiation causes harm are flawed and totally fraudulent.

NEUROLOGICAL IMPACT OF LOW DOSE CUMULATIVE RADIATION

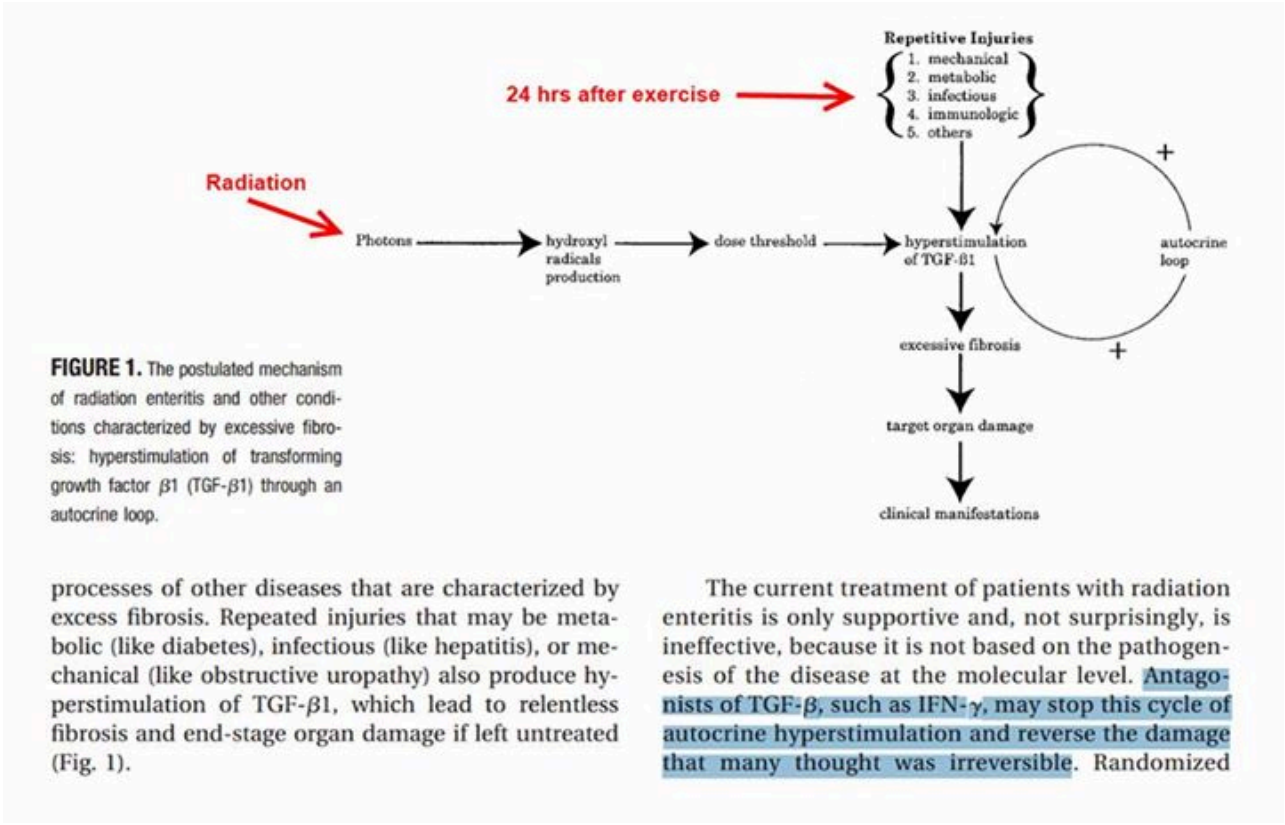

FIGURE 1. The postulated mechanism of radiation enteritis and other conditions characterized by excessive fibrosis: hyperstimulation of transforming growth factor β1 (TGF-β1) through an autocrine loop.

processes of other diseases that are characterized by excess fibrosis. Repeated injuries that may be metabolic (like diabetes), infectious (like hepatitis), or mechanical (like obstructive uropathy) also produce hyperstimulation of TGF-β1, which lead to relentless fibrosis and end-stage organ damage if left untreated (Fig. 1).

The current treatment of patients with radiation enteritis is only supportive and, not surprisingly, is ineffective, because it is not based on the pathogenesis of the disease at the molecular level. Antagonists of TGF-β, such as IFN-γ, may stop this cycle of autocrine hyperstimulation and reverse the damage that many thought was irreversible. Randomized

Source/credit

Rob Soltysik The TGF-beta autocrine loop. The radiation involved could be both ionizing radiation (Fukushima) or non-ionizing radiation (cell phones, cell towers, smart meters). The neurological effects come from the hyperstimulation of TGF-beta, which lowers the levels of the IDO enzyme. IDO dysfunction is implicated in many neurological diseases.

BLOOD TEST CAN MEASURE RADIATION DAMAGE WITHIN 24 HOURS OF RADIATION EXPOSURE

SadieDogMay 13, 2015 Quick test could measure long term radiation damage in people after serious exposure…

"Before now, it's been effectively impossible for a doctor to inspect a patient and accurately diagnose the radiation damage he or she has borne, especially within the first 24 hours. Doctors can estimate radiation poisoning based on where the person was during a disaster, which is inaccurate and hard to do in the chaotic aftermath of a nuclear event. Or they can take a blood sample to check how many white blood cells have died, a metric that can't delineate between a deadly dose of radiation and a excruciatingly high but survivable one.

GENE TEST CAN SHOW HOW MUCH RADIATION A PERSON HAS RECEIVED, AND HOW MUCH DAMAGE THAT DOSE WILL HAVE ON THE BODY

But today a team of scientists at Harvard Medical School and Montefiore Medical Center in New York City has announced an accurate way to immediately identify long-term radiation damage, by peering into blood-bound genes. As they report in the journal Science Translational Medicine, the researchers discovered that a class of tiny, free-floating chunks of genes called microRNAs signal not only how much radiation a person has received, but how much damage that dose will have on the body. The discovery, made in mice, may lead the way to the world's first radiation poisoning test."
http://www.popularmechanics.com/science/health/a15527/blood-test-radiation-damage/

RELATED ARTICLES THAT GO INTO MORE DETAIL

Low Dose Radiation Dangers To Children Start At 10 Bq/Kg; List Of Symptoms And Health Issues Caused By Fukushima, Chernobyl, TMI
http://agreenroad.blogspot.com/2012/03/low-dose-chernobyl-and-fukushima.html

As Little As 10-30 Bq/kg of Radioactive Cesium Internal Radiation In Kids Causes Health Problems
http://agreenroad.blogspot.com/2013/06/as-little-as-10-30-bqkg-of-cesium.html

Children And Adults - Negative Effects Of Chronic, Cumulative Man Made Radiation Exposure
http://agreenroad.blogspot.com/p/low-dose-radiation-dangers-for-children.html

Beta Radiation Burns In Animals, Plants And Humans, From Medical Radiation, Nuclear Bombs, Nuclear Accidents, And More
http://agreenroad.blogspot.com/2014/08/beta-radiation-burns-in-animals-and.html

Seals, Walruses, Polar Bears And Fish ARE Suffering From Fukushima Radiation Caused Effects; via A Green Road
http://agreenroad.blogspot.com/2013/02/seals-walruses-polar-bears-suffering.html

WHAT YOU CAN DO

For more information about how to protect yourself, click on the following link...

Dr. Blaylock MD - How To Protect Yourself From Nuclear Radiation; via A Green Road

http://agreenroad.blogspot.com/2012/05/nuclear-radiation-dr-blaylock-md-how-to.html

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End

Top Ten Symptoms Of Low Dose Radiation Exposure On Fetus In Utero, Infants, Children, Adults And Seniors, Gene Blood Test Can Show How Much Damage Radiation Caused
http://agreenroad.blogspot.com/2012/11/symptoms-of-low-dose-radiation-exposure.html

Posted 30th November 2012 by Dr. Good Heart

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the International Commission of Non-Ionizing Radiation Protection, the International Labour Organization, or the World Health Organization.

Environmental Health Criteria 238

EXTREMELY LOW FREQUENCY FIELDS

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Environmental Health Criteria

CONTENTS

PREAMBLE

The WHO Environmental Health Criteria Programme

In 1973 the World Health Organization (WHO) Environmental Health Criteria Programme was initiated with the following objectives:

(i) to assess information on the relationship between exposure to environmental pollutants and human health, and to provide guidelines for setting exposure limits;

(ii) to identify new or potential pollutants;

(iii) to identify gaps in knowledge concerning the health effects of pollutants;

(iv) to promote the harmonization of toxicological and epidemiological methods in order to have internationally comparable results.

It should be noted in this context that WHO defines health as the state of complete physical, mental and social well being and not merely the absence of disease or infirmity (WHO, 1946).

The first Environmental Health Criteria (EHC) monograph, on mercury, was published in 1976 and since that time an ever-increasing number of assessments of chemical and of physical agents have been produced. In addition, many EHC monographs have been devoted to evaluating toxicological methodology, e.g. for genetic, neurotoxic, teratogenic and nephrotoxic agents. Other publications have been concerned with epidemiological guidelines, evaluation of short-term tests for carcinogens, biomarkers, effects on the elderly and so forth.

The original impetus for the Programme came from World Health Assembly resolutions and the recommendations of the 1972 UN Conference on the Human Environment. Subsequently the work became an integral part of the International Programme on Chemical Safety (IPCS), a cooperative programme of the United Nations Environment Programme (UNEP), the International Labour Office (ILO) and WHO. With the strong support of the new partners, the importance of occupational health and environmental effects was fully recognized. The EHC monographs have become widely established, used and recognized throughout the world.

Electromagnetic Fields

Three monographs on electromagnetic fields (EMF) address possible health effects from exposure to extremely low frequency (ELF) fields, static and ELF magnetic fields, and radiofrequency (RF) fields (WHO, 1984; WHO, 1987; WHO, 1993). They were produced in collaboration with UNEP, ILO and the International Non-Ionizing Radiation Committee (INIRC) of the International Radiation Protection Association (IRPA) and from 1992 the International Commission on Non-Ionizing Radiation Protection (ICNIRP).

EHC monographs are usually revised if new data are available that would substantially change the evaluation, if there is public concern for health or environmental effects of the agent because of greater exposure, or if an appreciable time period has elapsed since the last evaluation. The EHCs on EMF are being revised and will be published as a set of three monographs spanning the relevant EMF frequency range (0–300 GHz); static fields (0 Hz), ELF fields (up to 100 kHz, this volume) and RF fields (100 kHz – 300 GHz).

WHO's assessment of any health risks produced by non-ionizing radiation emitting technologies (in the frequency range 0–300 GHz) falls within the responsibilities of the International EMF Project. This Project was established by WHO in 1996 in response to public concern over health effects of EMF exposure, and is managed by the Radiation and Environmental Health Unit (RAD) which is coordinating the preparation of the EHC Monographs on EMF.

The WHO health risk assessment exercise includes the development of an extensive database that comprises relevant scientific publications. Interpretation of these studies can be controversial, as there exists a spectrum of opinion within the scientific community and elsewhere. In order to achieve as wide a degree of consensus as possible, the health risk assessment also draws on, and in some cases includes sections of, reviews already completed by other national and international expert review bodies, with particular reference to:

- the International Agency for Research on Cancer (IARC) Monograph on static and extremely low frequency (ELF) fields IARC, 2002. In June 2001 IARC formally evaluated the evidence for carcinogenesis from exposure to static and ELF fields. The review concluded that ELF magnetic fields are possibly carcinogenic to humans.
- Reviews on physics/engineering, biology and epidemiology commissioned by WHO to the International Commission on Non-Ionizing Radiation Protection (ICNIRP), a non-governmental organization in formal relations with WHO (ICNIRP, 2003).
- Reviews by the Advisory Group on Non-Ionising Radiation (AGNIR) of the Health Protection Agency (HPA), United Kingdom (AGNIR, 2001a; 2001b; 2004; 2006).

Scope

The EHC monographs are intended to provide critical reviews on the effect on human health and the environment of chemicals, physical and biological agents. As such, they include and review studies that are of direct relevance for the evaluation. However, they do not describe *every* study carried out. Worldwide data are used and are quoted from original studies, not from abstracts or reviews. Both published and unpublished reports are considered but preference is always given to published data. Unpublished data

are only used when relevant published data are absent or when they are pivotal to the risk assessment. A detailed policy statement is available that describes the procedures used for unpublished proprietary data so that this information can be used in the evaluation without compromising its confidential nature (WHO, 1990).

In the evaluation of human health risks, sound human data, whenever available, are generally more informative than animal data. Animal and in vitro studies provide support and are used mainly to supply evidence missing from human studies. It is mandatory that research on human subjects is conducted in full accord with ethical principles, including the provisions of the Helsinki Declaration (WMA, 2004).

All studies, with either positive or negative effects, need to be evaluated and judged on their own merit, and then all together in a weight of evidence approach. It is important to determine how much a set of evidence changes the probability that exposure causes an outcome. Generally, studies must be replicated or be in agreement with similar studies. The evidence for an effect is further strengthened if the results from different types of studies (epidemiology and laboratory) point to the same conclusion.

The EHC monographs are intended to assist national and international authorities in making risk assessments and subsequent risk management decisions. They represent an evaluation of risks as far as the data will allow and are not, in any sense, recommendations for regulation or standard setting. These latter are the exclusive purview of national and regional governments. However, the EMF EHCs do provide bodies such as ICNIRP with the scientific basis for reviewing their international exposure guidelines.

Procedures

The general procedures that result in the publication of this EHC monograph are discussed below.

A first draft, prepared by consultants or staff from a RAD Collaborating Centre, is based initially on data provided from reference databases such as Medline and PubMed and on IARC and ICNIRP reviews. The draft document, when received by RAD, may require an initial review by a small panel of experts to determine its scientific quality and objectivity. Once the document is acceptable as a first draft, it is distributed, in its unedited form, to well over 150 EHC contact points throughout the world who are asked to comment on its completeness and accuracy and, where necessary, provide additional material. The contact points, usually designated by governments, may be Collaborating Centres, or individual scientists known for their particular expertise. Generally some months are allowed before the comments are considered by the author(s). A second draft incorporating comments received and approved by the Coordinator (RAD), is then distributed to Task Group members, who carry out the peer review, at least six weeks before their meeting.

The Task Group members serve as individual scientists, not as representatives of their organization. Their function is to evaluate the accuracy, significance and relevance of the information in the document and to assess the health and environmental risks from exposure to the part of the electromagnetic spectrum being addressed. A summary and recommendations for further research and improved safety aspects are also required. The composition of the Task Group is dictated by the range of expertise required for the subject of the meeting (epidemiology, biological and physical sciences, medicine and public health) and by the need for a balance in the range of opinions on the science, gender and geographical distribution.

The membership of the WHO Task Groups is approved by the Assistant Director General of the Cluster on Sustainable Development and Health Environments. These Task Groups are the highest level committees within WHO for conducting health risk assessments.

Task Groups conduct a critical and thorough review of an advanced draft of the ELF EHC monograph and assess any risks to health from exposure to both electric and magnetic fields, reach agreements by consensus, and make final conclusions and recommendations that cannot be altered after the Task Group meeting.

The World Health Organization recognizes the important role played by non-governmental organizations (NGOs). Representatives from relevant national and international associations may be invited to join the Task Group as observers. While observers may provide a valuable contribution to the process, they can only speak at the invitation of the Chairperson. Observers do not participate in the final evaluation; this is the sole responsibility of the Task Group members. When the Task Group considers it to be appropriate, it may meet *in camera.*

All individuals who as authors, consultants or advisers participate in the preparation of the EHC monograph must, in addition to serving in their personal capacity as scientists, inform WHO if at any time a conflict of interest, whether actual or potential, could be perceived in their work. They are required to sign a conflict of interest statement. Such a procedure ensures the transparency and probity of the process.

When the Task Group has completed its review and the Coordinator (RAD) is satisfied as to the scientific consistency and completeness of the document, it then goes for language editing, reference checking, and preparation of camera-ready copy. After approval by the Director, Department of Protection of the Human Environment (PHE), the monograph is submitted to the WHO Office of Publications for printing. At this time a copy of the final draft is sent to the Chairperson and Rapporteur of the Task Group to check the proofs.

Extremely Low Frequency Environmental Health Criteria

This EHC addresses the possible health effects of exposure to extremely low frequency (>0 Hz – 100 kHz) electric and magnetic fields. By

far the majority of studies concern the health effects resulting from exposure to power frequency (50–60 Hz) magnetic fields; a few studies address the effects of exposure to power frequency electric fields. In addition, a number of studies have addressed the effects of exposure to the very low frequency (VLF, 3–30 kHz) switched gradient magnetic fields used in Magnetic Resonance Imaging, and, more commonly, the weaker VLF fields emitted by visual display units (VDU's) and televisions.

The ELF EHC is organized by disease category; separate expert working groups met in order to develop drafts addressing neurodegenerative disorders (Chapter 7), cardiovascular disorders (Chapter 8), childhood leukaemia (section 11.2.1) and protective measures (Chapter 13). The membership of these expert working groups is given below. Drafts of the other chapters were prepared by consultants, staff from WHO collaborating centres and by RAD Unit staff. These included Prof. Paul Elliot, Imperial College of Science, Technology and Medicine, UK, Prof. Maria Stuchly, University of Victoria, Canada, and Prof. Bernard Veyret, ENSCPB, France, in addition to individuals who were also members of one of the expert working groups and/or the Task Group (see below). The draft chapters were individually reviewed by external referees prior to their collation as a draft document.

The draft EHC was subsequently distributed for external review. Editorial changes and minor scientific points were addressed by a WHO Editorial Group and the final draft was distributed to Task Group members prior to the Task Group meeting.

The Task Group met from October 3–7, 2005 at WHO headquarters in Geneva. The text of the EHC was subsequently edited for clarity and consistency by an Editorial Group consisting of Dr Emilie van Deventer and Dr Chiyoji Ohkubo, both from WHO, Geneva, Switzerland, Dr Rick Saunders, Health Protection Agency, Chilton, UK, Dr Eric van Rongen, Health Council of the Netherlands, Prof. Leeka Kheifets, UCLA School of Public Health, Los Angeles, CA, USA and Dr Chris Portier, NIEHS, Research Triangle Park, NC, USA. Following a final review by the Task Group and scientific and text editing, the EHC was published on the International EMF Projects website on 18 June 2007.

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WHO Neurodegenerative Disorders Workshop, WHO HQ, Geneva. 12–13 December, 2002

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WHO Protective Measures for ELF EMFs Workshop, NIEHS, USA, 9–11 February, 2005

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ABBREVIATIONS

AC	alternating current
ACTH	adrenocorticotropic hormone
AD	Alzheimer's disease
AF	attributable fraction
AGNIR	Advisory Group on Non-Ionising Radiation
ALL	acute lymphocytic leukaemia
ALS	amyotrophic lateral sclerosis
AMI	acute myocardial infarction
AML	acute myeloid leukaemia
aMT6s	6-sulphatoxymelatonin
AN	attributable number
BP	benzo(a)pyrene
CA	chromosomal aberrations
CAM	cell adhesion molecule
CBPI	cytokinesis-blocked proliferation index
CI	confidence interval
CNS	central nervous system
Con-A	concanavalin-A
Cx	connexin
DC	direct current
DENA	diethylnitrosamine
DMBA	7,12-dimethylbenz(a)anthracene
DNA	desoxyribonucleic acid
EAS	electronic access and security system
EBCLIS	electric blanket cancer Long Island study
ECG	electrocardiogram
EEG	electroencephalograms
EHC	Environmental Health Criteria
ELF	extremely low frequency
EM	electromagnetic
EMF	electromagnetic fields
ENU	N-ethyl-N-nitrosourea
ER	estrogen receptor
ERP	evoked or event-related potentials
ES	embryonic stem cells
FDTD	finite-difference time-domain
FFT	fast Fourier transformation
FSH	follicle stimulating hormone
GABA	gamma-aminobutyric acid
GCS	ceramide glucosyltransferase
GH	growth hormone
GJIC	gap junction intercellular communication
H2O2	hydrogenperoxyde
HIOMT	hydroxyindole-O-methyltransferase
HRV	heart rate variability

HSF	heat shock factor
hsp	heat shock protein
IARC	International Agency for Research on Cancer
ICNIRP	International Commission on Non-Ionizing Radiation Protection
IEEE	Institute of Electrical and Electronic Engineers
IEI	idiopathic environmental intolerance
IFN	interferon
Ig	immunoglobulin
IL	interleukin
JEM	job-exposure matrix
LAK	lymphokine activated killer
LH	luteinising hormone
LIBCSP	Long Island breast cancer study project
LPS	lipopolysaccharide
LTP	long-term potentiation
MBM	mouse bone marrow
MN	micronucleus
MRI	magnetic resonance imaging
mRNA	messenger ribonucleic acid
MS	multiple sclerosis
NA	noradrenaline
NADH	nicotinamide adenine dinucleotide
NADPH	nicotinamide adenine dinucleotide phosphate
NAT	N-acetyl-transferase enzyme
NDI	nuclear division index
NGF	nerve growth factor
NHL	non-Hodgkin lymphoma
NIEHS	National Institute for Environmental Health Sciences
NIOHS	National Institute for Occupational Safety and Health
NK	natural killer
NMDA	N-methyl-D-aspartate
NMU	N-methylnitrosurea
NO	nitric oxide
NRPB	National Radiological Protection Board
ODC	ornithine decarboxylase
OHCC	ordinary high current configuration
8-OhdG	8-hydroxydeoxyguanine
OLCC	ordinary low current configuration
OR	odds ratio
PAGE	poly-acrylamide gel electrophoresis
PARP	poly-ADP ribose polymerase
PBMC	peripheral blood mononuclear cells
PHA	phytohemagglutinin
PKC	protein kinase C
RAD	Radiation and Environmental Health Unit
RF	radiofrequency
RFID	radiofrequency identification
RNS	reactive nitrogen species

ROS	reactive oxygen species
RR	relative risk
SCE	sister chromatid exchange
SD	standard deviation
SES	socioeconomic status
SMR	standardized mortality ratio
SIR	standardized incidence ratio
SPFD	scalar potential finite difference
SRR	standardized relative mortality risk ratio
TGFR	transforming growth factor- receptor
TMS	transcranial magnetic stimulation
TNF	tumour necrosis factor
TNFR	tumour necrosis factor receptor
TPA	12-0-tetradecanoylphorbol-13-acetate
TSH	thyroid-stimulating hormone
TWA	time-weighted average
UG	underground
UKCCSI	United Kingdom childhood cancer study investigators
ULF	ultra low frequency
UV	ultraviolet
VDU	visual display unit
VHCC	very high current configuration
VLCC	very low current configuration
VLF	very low frequency
WBC	white blood cell
WHO	World Health Organization

Units

A	ampere
kA	kiloampere, 10^3 ampere
eV	electronvolt
F	farad
µF	microfarad, 10^{-6} farad
Hz	hertz
kHz	kilohertz, 10^3 hertz
MHz	megahertz, 10^9 hertz
J	joule
kJ	kilojoule, 10^3 joule
M	molar
nM	nanomolar,10^{-9} molar
N	newton
pN	piconewton,10^{-12} newton
V	volt
kV	kilovolt, 10^3 volt
mV	millivolt, 10^{-3} volt
µV	microvolt, 10^{-6} volt

T	tesla
kT	kilotesla, 10^3 tesla
mT	millitesla, 10^{-3} tesla
μT	microtesla, 10^{-6} tesla
nT	nanotesla, 10^{-9} tesla
W	watt
kW	kilowatt, 10^3 watt
Ω	ohm
kΩ	kiloohm, 10^3 ohm

1 SUMMARY AND RECOMMENDATIONS FOR FURTHER STUDY

This Environmental Health Criteria (EHC) monograph addresses the possible health effects of exposure to extremely low frequency (ELF) electric and magnetic fields. It reviews the physical characteristics of ELF fields as well as the sources of exposure and measurement. However, its main objectives are to review the scientific literature on the biological effects of exposure to ELF fields in order to assess any health risks from exposure to these fields and to use this health risk assessment to make recommendations to national authorities on health protection programs.

The frequencies under consideration range from above 0 Hz to 100 kHz. By far the majority of studies have been conducted on power-frequency (50 or 60 Hz) magnetic fields, with a few studies using power-frequency electric fields. In addition, there have been a number of studies concerning very low frequency (VLF, 3–30 kHz) fields, switched gradient magnetic fields used in magnetic resonance imaging, and the weaker VLF fields emitted by visual display units and televisions.

This chapter summarizes the main conclusions and recommendations from each section as well as the overall conclusions of the health risk assessment process. The terms used in this monograph to describe the strength of evidence for a given health outcome are as follows. Evidence is termed "limited" when it is restricted to a single study or when there are unresolved questions concerning the design, conduct or interpretation of a number of studies. "Inadequate" evidence is used when the studies cannot be interpreted as showing either the presence or absence of an effect because of major qualitative or quantitative limitations, or when no data are available.

Key gaps in knowledge were also identified and the research needed to fill these gaps has been summarized in the section entitled "Recommendations for research".

1.1 Summary

1.1.1 Sources, measurements and exposures

Electric and magnetic fields exist wherever electricity is generated, transmitted or distributed in power lines or cables, or used in electrical appliances. Since the use of electricity is an integral part of our modern lifestyle, these fields are ubiquitous in our environment.

The unit of electric field strength is volts per metre (V m^{-1}) or kilovolts per metre (kV m^{-1}) and for magnetic fields the flux density is measured in tesla (T), or more commonly in millitesla (mT) or microtesla (μT) is used.

Residential exposure to power-frequency magnetic fields does not vary dramatically across the world. The geometric-mean magnetic field in homes ranges between 0.025 and 0.07 μT in Europe and 0.055 and 0.11 μT in the USA. The mean values of the electric field in the home are in the range of several tens of volts per metre. In the vicinity of certain appliances, the

instantaneous magnetic-field values can be as much as a few hundred microtesla. Near power lines, magnetic fields reach approximately 20 μT and electric fields up to several thousand volts per metre.

Few children have time-averaged exposures to residential 50 or 60 Hz magnetic fields in excess of the levels associated with an increased incidence of childhood leukaemia (see section 1.1.10). Approximately 1% to 4% have mean exposures above 0.3 μT and only 1% to 2% have median exposures in excess of 0.4 μT.

Occupational exposure, although predominantly to power-frequency fields, may also include contributions from other frequencies. The average magnetic field exposures in the workplace have been found to be higher in "electrical occupations" than in other occupations such as office work, ranging from 0.4–0.6 μT for electricians and electrical engineers to approximately 1.0 μT for power line workers, with the highest exposures for welders, railway engine drivers and sewing machine operators (above 3 μT). The maximum magnetic field exposures in the workplace can reach approximately 10 mT and this is invariably associated with the presence of conductors carrying high currents. In the electrical supply industry, workers may be exposed to electric fields up to 30 kV m^{-1}.

1.1.2 Electric and magnetic fields inside the body

Exposure to external electric and magnetic fields at extremely low frequencies induces electric fields and currents inside the body. Dosimetry describes the relationship between the external fields and the induced electric field and current density in the body, or other parameters associated with exposure to these fields. The locally induced electric field and current density are of particular interest because they relate to the stimulation of excitable tissue such as nerve and muscle.

The bodies of humans and animals significantly perturb the spatial distribution of an ELF electric field. At low frequencies the body is a good conductor and the perturbed field lines outside the body are nearly perpendicular to the body surface. Oscillating charges are induced on the surface of the exposed body and these induce currents inside the body. The key features of dosimetry for the exposure of humans to ELF electric fields are as follows:

- The electric field inside the body is normally five to six orders of magnitude smaller than the external electric field.
- When exposure is mostly to the vertical field, the predominant direction of the induced fields is also vertical.
- For a given external electric field, the strongest induced fields are for the human body in perfect contact through the feet with ground (electrically grounded) and the weakest induced fields are for the body insulated from the ground (in "free space").

- The total current flowing in a body in perfect contact with ground is determined by the body size and shape (including posture), rather than tissue conductivity.
- The distribution of induced currents across the various organs and tissues is determined by the conductivity of those tissues
- The distribution of an induced electric field is also affected by the conductivities, but less so than the induced current.
- There is also a separate phenomenon in which the current in the body is produced by means of contact with a conductive object located in an electric field.

For magnetic fields, the permeability of tissue is the same as that of air, so the field in tissue is the same as the external field. The bodies of humans and animals do not significantly perturb the field. The main interaction of magnetic fields is the Faraday induction of electric fields and associated current densities in the conductive tissues. The key features of dosimetry for the exposure of humans to ELF magnetic fields are as follows:

- The induced electric field and current depend on the orientation of the external field. Induced fields in the body as a whole are greatest when the field is aligned from the front to the back of the body, but for some individual organs the highest values are for the field aligned from side to side.
- The weakest electric fields are induced by a magnetic field oriented along the vertical body axis.
- For a given magnetic field strength and orientation, higher electric fields are induced in larger bodies.
- The distribution of the induced electric field is affected by the conductivity of the various organs and tissues. These have a limited effect on the distribution of induced current density.

1.1.3 Biophysical mechanisms

Various proposed direct and indirect interaction mechanisms for ELF electric and magnetic fields are examined for plausibility, in particular whether a "signal" generated in a biological process by exposure to a field can be discriminated from inherent random noise and whether the mechanism challenges scientific principles and current scientific knowledge. Many mechanisms become plausible only at fields above a certain strength. Nevertheless, the lack of identified plausible mechanisms does not rule out the possibility of health effects even at very low field levels, provided basic scientific principles are adhered to.

Of the numerous proposed mechanisms for the direct interaction of fields with the human body, three stand out as potentially operating at lower field levels than the others: induced electric fields in neural networks, radical pairs and magnetite.

Electric fields induced in tissue by exposure to ELF electric or magnetic fields will directly stimulate single myelinated nerve fibres in a biophysically plausible manner when the internal field strength exceeds a few volts per metre. Much weaker fields can affect synaptic transmission in neural networks as opposed to single cells. Such signal processing by nervous systems is commonly used by multicellular organisms to detect weak environmental signals. A lower bound on neural network discrimination of 1 mV m^{-1} has been suggested, but based on current evidence, threshold values around 10–100 mV m^{-1} seem to be more likely.

The radical pair mechanism is an accepted way in which magnetic fields can affect specific types of chemical reactions, generally increasing concentrations of reactive free radicals in low fields and decreasing them in high fields. These increases have been seen in magnetic fields of less than 1 mT. There is some evidence linking this mechanism to navigation during bird migration. Both on theoretical grounds and because the changes produced by ELF and static magnetic fields are similar, it is suggested that power-frequency fields of much less than the geomagnetic field of around 50 μT are unlikely to be of much biological significance.

Magnetite crystals, small ferromagnetic crystals of various forms of iron oxide, are found in animal and human tissues, although in trace amounts. Like free radicals, they have been linked to orientation and navigation in migratory animals, although the presence of trace quantities of magnetite in the human brain does not confer an ability to detect the weak geomagnetic field. Calculations based on extreme assumptions suggest a lower bound for the effects on magnetite crystals of ELF fields of 5 μT.

Other direct biophysical interactions of fields, such as the breaking of chemical bonds, the forces on charged particles and the various narrow bandwidth “resonance” mechanisms, are not considered to provide plausible explanations for the interactions at field levels encountered in public and occupational environments.

With regard to indirect effects, the surface electric charge induced by electric fields can be perceived, and it can result in painful microshocks when touching a conductive object. Contact currents can occur when young children touch, for example, a tap in the bathtub in some homes. This produces small electric fields, possibly above background noise levels, in bone marrow. However, whether these present a risk to health is unknown.

High-voltage power lines produce clouds of electrically charged ions as a consequence of corona discharge. It is suggested that they could increase the deposition of airborne pollutants on the skin and on airways inside the body, possibly adversely affecting health. However, it seems unlikely that corona ions will have more than a small effect, if any, on long-term health risks, even in the individuals who are most exposed.

None of the three direct mechanisms considered above seem plausible causes of increased disease incidence at the exposure levels generally encountered by people. In fact they only become plausible at levels orders of

magnitude higher and indirect mechanisms have not yet been sufficiently investigated. This absence of an identified plausible mechanism does not rule out the possibility of adverse health effects, but it does create a need for stronger evidence from biology and epidemiology.

1.1.4 Neurobehaviour

Exposure to power-frequency electric fields causes well-defined biological responses, ranging from perception to annoyance, through surface electric charge effects. These responses depend on the field strength, the ambient environmental conditions and individual sensitivity. The thresholds for direct perception by 10% of volunteers varied between 2 and 20 kV m^{-1}, while 5% found 15–20 kV m^{-1} annoying. The spark discharge from a person to ground is found to be painful by 7% of volunteers in a field of 5 kV m^{-1}. Thresholds for the discharge from a charged object through a grounded person depend on the size of the object and therefore require specific assessment.

High field strength, rapidly pulsed magnetic fields can stimulate peripheral or central nerve tissue; such effects can arise during magnetic resonance imaging (MRI) procedures, and are used in transcranial magnetic stimulation. Threshold induced electric field strengths for direct nerve stimulation could be as low as a few volts per metre. The threshold is likely to be constant over a frequency range between a few hertz and a few kilohertz. People suffering from or predisposed to epilepsy are likely to be more susceptible to induced ELF electric fields in the central nervous system (CNS). Furthermore, sensitivity to electrical stimulation of the CNS seems likely to be associated with a family history of seizure and the use of tricyclic antidepressants, neuroleptic agents and other drugs that lower the seizure threshold.

The function of the retina, which is a part of the CNS, can be affected by exposure to much weaker ELF magnetic fields than those that cause direct nerve stimulation. A flickering light sensation, called magnetic phosphenes or magnetophosphenes, results from the interaction of the induced electric field with electrically excitable cells in the retina. Threshold induced electric field strengths in the extracellular fluid of the retina have been estimated to lie between about 10 and 100 mV m^{-1} at 20 Hz. There is, however, considerable uncertainty attached to these values.

The evidence for other neurobehavioural effects in volunteer studies, such as the effects on brain electrical activity, cognition, sleep, hypersensitivity and mood, is less clear. Generally, such studies have been carried out at exposure levels below those required to induce the effects described above, and have produced evidence only of subtle and transitory effects at best. The conditions necessary to elicit such responses are not well-defined at present. There is some evidence suggesting the existence of field-dependent effects on reaction time and on reduced accuracy in the performance of some cognitive tasks, which is supported by the results of studies on the gross electrical activity of the brain. Studies investigating whether magnetic fields affect sleep quality have reported inconsistent results. It is possible that these

inconsistencies may be attributable in part to differences in the design of the studies.

Some people claim to be hypersensitive to EMFs in general. However, the evidence from double-blind provocation studies suggests that the reported symptoms are unrelated to EMF exposure.

There is only inconsistent and inconclusive evidence that exposure to ELF electric and magnetic fields causes depressive symptoms or suicide. Thus, the evidence is considered inadequate.

In animals, the possibility that exposure to ELF fields may affect neurobehavioural functions has been explored from a number of perspectives using a range of exposure conditions. Few robust effects have been established. There is convincing evidence that power-frequency electric fields can be detected by animals, most likely as a result of surface charge effects, and may elicit transient arousal or mild stress. In rats, the detection range is between 3 and 13 kV m^{-1}. Rodents have been shown to be aversive to field strengths greater than 50 kV m^{-1}. Other possible field-dependent changes are less well-defined; laboratory studies have only produced evidence of subtle and transitory effects. There is some evidence that exposure to magnetic fields may modulate the functions of the opioid and cholinergic neurotransmitter systems in the brain, and this is supported by the results of studies investigating the effects on analgesia and on the acquisition and performance of spatial memory tasks.

1.1.5 Neuroendocrine system

The results of volunteer studies as well as residential and occupational epidemiological studies suggest that the neuroendocrine system is not adversely affected by exposure to power-frequency electric or magnetic fields. This applies particularly to the circulating levels of specific hormones of the neuroendocrine system, including melatonin, released by the pineal gland, and to a number of hormones involved in the control of body metabolism and physiology, released by the pituitary gland. Subtle differences were sometimes observed in the timing of melatonin release associated with certain characteristics of exposure, but these results were not consistent. It is very difficult to eliminate possible confounding by a variety of environmental and lifestyle factors that might also affect hormone levels. Most laboratory studies of the effects of ELF exposure on night-time melatonin levels in volunteers found no effect when care was taken to control possible confounding.

From the large number of animal studies investigating the effects of power-frequency electric and magnetic fields on rat pineal and serum melatonin levels, some reported that exposure resulted in night-time suppression of melatonin. The changes in melatonin levels first observed in early studies of electric field exposures up to 100 kV m^{-1} could not be replicated. The findings from a series of more recent studies, which showed that circularly-polarised magnetic fields suppressed night-time melatonin levels, were weakened by inappropriate comparisons between exposed animals and his-

torical controls. The data from other experiments in rodents, covering intensity levels from a few microtesla to 5 mT, were equivocal, with some results showing depression of melatonin, but others showing no changes. In seasonally breeding animals, the evidence for an effect of exposure to power-frequency fields on melatonin levels and melatonin-dependent reproductive status is predominantly negative. No convincing effect on melatonin levels has been seen in a study of non-human primates chronically exposed to power-frequency fields, although a preliminary study using two animals reported melatonin suppression in response to an irregular and intermittent exposure.

The effects of exposure to ELF fields on melatonin production or release in isolated pineal glands were variable, although relatively few in vitro studies have been undertaken. The evidence that ELF exposure interferes with the action of melatonin on breast cancer cells in vitro is intriguing. However this system suffers from the disadvantage that the cell lines frequently show genotypic and phenotypic drift in culture that can hinder transferability between laboratories.

No consistent effects have been seen in the stress-related hormones of the pituitary-adrenal axis in a variety of mammalian species, with the possible exception of short-lived stress following the onset of ELF electric field exposure at levels high enough to be perceived. Similarly, while few studies have been carried out, mostly negative or inconsistent effects have been observed in the levels of growth hormone and of hormones involved in controlling metabolic activity or associated with the control of reproduction and sexual development.

Overall, these data do not indicate that ELF electric and/or magnetic fields affect the neuroendocrine system in a way that would have an adverse impact on human health and the evidence is thus considered inadequate.

1.1.6 Neurodegenerative disorders

It has been hypothesized that exposure to ELF fields is associated with several neurodegenerative diseases. For Parkinson disease and multiple sclerosis the number of studies has been small and there is no evidence for an association with these diseases. For Alzheimer disease and amyotrophic lateral sclerosis (ALS) more studies have been published. Some of these reports suggest that people employed in electrical occupations might have an increased risk of ALS. So far, no biological mechanism has been established which can explain this association, although it could have arisen because of confounders related to electrical occupations, such as electric shocks. Overall, the evidence for the association between ELF exposure and ALS is considered to be inadequate.

The few studies investigating the association between ELF exposure and Alzheimer disease are inconsistent. However, the higher quality studies that focused on Alzheimer morbidity rather than mortality do not

indicate an association. Altogether, the evidence for an association between ELF exposure and Alzheimer disease is inadequate.

1.1.7 Cardiovascular disorders

Experimental studies of both short-term and long-term exposure indicate that while electric shock is an obvious health hazard, other hazardous cardiovascular effects associated with ELF fields are unlikely to occur at exposure levels commonly encountered environmentally or occupationally. Although various cardiovascular changes have been reported in the literature, the majority of effects are small and the results have not been consistent within and between studies. With one exception, none of the studies of cardiovascular disease morbidity and mortality has shown an association with exposure. Whether a specific association exists between exposure and altered autonomic control of the heart remains speculative. Overall, the evidence does not support an association between ELF exposure and cardiovascular disease.

1.1.8 Immunology and haematology

Evidence for the effects of ELF electric or magnetic fields on components of the immune system is generally inconsistent. Many of the cell populations and functional markers were unaffected by exposure. However, in some human studies with fields from 10 μT to 2 mT, changes were observed in natural killer cells, which showed both increased and decreased cell numbers, and in total white blood cell counts, which showed no change or decreased numbers. In animal studies, reduced natural killer cell activity was seen in female mice, but not in male mice or in rats of either sex. White blood cell counts also showed inconsistency, with decreases or no change reported in different studies. The animal exposures had an even broader range of 2 μT to 30 mT. The difficulty in interpreting the potential health impact of these data is due to the large variations in exposure and environmental conditions, the relatively small numbers of subjects tested and the broad range of endpoints.

There have been few studies carried out on the effects of ELF magnetic fields on the haematological system. In experiments evaluating differential white blood cell counts, exposures ranged from 2 μT to 2 mT. No consistent effects of acute exposure to ELF magnetic fields or to combined ELF electric and magnetic fields have been found in either human or animal studies.

Overall therefore, the evidence for effects of ELF electric or magnetic fields on the immune and haematological system is considered inadequate.

1.1.9 Reproduction and development

On the whole, epidemiological studies have not shown an association between adverse human reproductive outcomes and maternal or paternal exposure to ELF fields. There is some evidence for an increased risk of mis-

carriage associated with maternal magnetic field exposure, but this evidence is inadequate.

Exposures to ELF electric fields of up to 150 kV m^{-1} have been evaluated in several mammalian species, including studies with large group sizes and exposure over several generations. The results consistently show no adverse developmental effects.

The exposure of mammals to ELF magnetic fields of up to 20 mT does not result in gross external, visceral or skeletal malformations. Some studies show an increase in minor skeletal anomalies, in both rats and mice. Skeletal variations are relatively common findings in teratological studies and are often considered biologically insignificant. However, subtle effects of magnetic fields on skeletal development cannot be ruled out. Very few studies have been published which address reproductive effects and no conclusions can be drawn from them.

Several studies on non-mammalian experimental models (chick embryos, fish, sea urchins and insects) have reported findings indicating that ELF magnetic fields at microtesla levels may disturb early development. However, the findings of non-mammalian experimental models carry less weight in the overall evaluation of developmental toxicity than those of corresponding mammalian studies.

Overall, the evidence for developmental and reproductive effects is inadequate.

1.1.10 Cancer

The IARC classification of ELF magnetic fields as "possibly carcinogenic to humans" (IARC, 2002) is based upon all of the available data prior to and including 2001. The review of literature in this EHC monograph focuses mainly on studies published after the IARC review.

Epidemiology

The IARC classification was heavily influenced by the associations observed in epidemiological studies on childhood leukaemia. The classification of this evidence as limited does not change with the addition of two childhood leukaemia studies published after 2002. Since the publication of the IARC monograph the evidence for other childhood cancers remains inadequate.

Subsequent to the IARC monograph a number of reports have been published concerning the risk of female breast cancer in adults associated with ELF magnetic field exposure. These studies are larger than the previous ones and less susceptible to bias, and overall are negative. With these studies, the evidence for an association between ELF magnetic field exposure and the risk of female breast cancer is weakened considerably and does not support an association of this kind.

In the case of adult brain cancer and leukaemia, the new studies published after the IARC monograph do not change the conclusion that the overall evidence for an association between ELF magnetic fields and the risk of these diseases remains inadequate.

For other diseases and all other cancers, the evidence remains inadequate.

Laboratory animal studies

There is currently no adequate animal model of the most common form of childhood leukaemia, acute lymphoblastic leukaemia. Three independent large-scale studies of rats provided no evidence of an effect of ELF magnetic fields on the incidence of spontaneous mammary tumours. Most studies report no effect of ELF magnetic fields on leukaemia or lymphoma in rodent models. Several large-scale long-term studies in rodents have not shown any consistent increase in any type of cancer, including haematopoietic, mammary, brain and skin tumours.

A substantial number of studies have examined the effects of ELF magnetic fields on chemically-induced mammary tumours in rats. Inconsistent results were obtained that may be due in whole or in part to differences in experimental protocols, such as the use of specific sub-strains. Most studies on the effects of ELF magnetic field exposure on chemically-induced or radiation-induced leukaemia/lymphoma models were negative. Studies of pre-neoplastic liver lesions, chemically-induced skin tumours and brain tumours reported predominantly negative results. One study reported an acceleration of UV-induced skin tumourigenesis upon exposure to ELF magnetic fields.

Two groups have reported increased levels of DNA strand breaks in brain tissue following in vivo exposure to ELF magnetic fields. However, other groups, using a variety of different rodent genotoxicity models, found no evidence of genotoxic effects. The results of studies investigating non-genotoxic effects relevant to cancer are inconclusive.

Overall there is no evidence that exposure to ELF magnetic fields alone causes tumours. The evidence that ELF magnetic field exposure can enhance tumour development in combination with carcinogens is inadequate.

In vitro studies

Generally, studies of the effects of ELF field exposure of cells have shown no induction of genotoxicity at fields below 50 mT. The notable exception is evidence from recent studies reporting DNA damage at field strengths as low as 35 μT; however, these studies are still being evaluated and our understanding of these findings is incomplete. There is also increasing evidence that ELF magnetic fields may interact with DNA-damaging agents.

There is no clear evidence of the activation by ELF magnetic fields of genes associated with the control of the cell cycle. However, systematic studies analysing the response of the whole genome have yet to be performed.

Many other cellular studies, for example on cell proliferation, apoptosis, calcium signalling and malignant transformation, have produced inconsistent or inconclusive results.

Overall conclusion

New human, animal and in vitro studies, published since the 2002 IARC monograph, do not change the overall classification of ELF magnetic fields as a possible human carcinogen.

1.1.11 Health risk assessment

According to the WHO Constitution, health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity. A risk assessment is a conceptual framework for a structured review of information relevant to estimating health or environmental outcomes. The health risk assessment can be used as an input to risk management that encompasses all the activities needed to reach decisions on whether an exposure requires any specific action(s) and the undertaking of these actions.

In the evaluation of human health risks, sound human data, whenever available, are generally more informative than animal data. Animal and in vitro studies can support evidence from human studies, fill data gaps left in the evidence from human studies or be used to make a decision about risks when human studies are inadequate or absent.

All studies, with either positive or negative effects, need to be evaluated and judged on their own merit and then all together in a weight-of-evidence approach. It is important to determine to what extent a set of evidence changes the probability that exposure causes an outcome. The evidence for an effect is generally strengthened if the results from different types of studies (epidemiology and laboratory) point to the same conclusion and/or when multiple studies of the same type show the same result.

Acute effects

Acute biological effects have been established for exposure to ELF electric and magnetic fields in the frequency range up to 100 kHz that may have adverse consequences on health. Therefore, exposure limits are needed. International guidelines exist that have addressed this issue. Compliance with these guidelines provides adequate protection for acute effects.

Chronic effects

Scientific evidence suggesting that everyday, chronic low-intensity (above 0.3–0.4 μT) power-frequency magnetic field exposure poses a health

risk is based on epidemiological studies demonstrating a consistent pattern of increased risk for childhood leukaemia. Uncertainties in the hazard assessment include the role that control selection bias and exposure misclassification might have on the observed relationship between magnetic fields and childhood leukaemia. In addition, virtually all of the laboratory evidence and the mechanistic evidence fail to support a relationship between low-level ELF magnetic fields and changes in biological function or disease status. Thus, on balance, the evidence is not strong enough to be considered causal, but sufficiently strong to remain a concern.

Although a causal relationship between magnetic field exposure and childhood leukaemia has not been established, the possible public health impact has been calculated assuming causality in order to provide a potentially useful input into policy. However, these calculations are highly dependent on the exposure distributions and other assumptions, and are therefore very imprecise. Assuming that the association is causal, the number of cases of childhood leukaemia worldwide that might be attributable to exposure can be estimated to range from 100 to 2400 cases per year. However, this represents 0.2 to 4.9% of the total annual incidence of leukaemia cases, estimated to be 49 000 worldwide in 2000. Thus, in a global context, the impact on public health, if any, would be limited and uncertain.

A number of other diseases have been investigated for possible association with ELF magnetic field exposure. These include cancers in both children and adults, depression, suicide, reproductive dysfunction, developmental disorders, immunological modifications and neurological disease. The scientific evidence supporting a linkage between ELF magnetic fields and any of these diseases is much weaker than for childhood leukaemia and in some cases (for example, for cardiovascular disease or breast cancer) the evidence is sufficient to give confidence that magnetic fields do not cause the disease.

1.1.12 Protective measures

It is essential that exposure limits be implemented in order to protect against the established adverse effects of exposure to ELF electric and magnetic fields. These exposure limits should be based on a thorough examination of all the relevant scientific evidence.

Only the acute effects have been established and there are two international exposure limit guidelines (ICNIRP, 1998a; IEEE, 2002) designed to protect against these effects.

As well as these established acute effects, there are uncertainties about the existence of chronic effects, because of the limited evidence for a link between exposure to ELF magnetic fields and childhood leukaemia. Therefore the use of precautionary approaches is warranted. However, it is not recommended that the limit values in exposure guidelines be reduced to some arbitrary level in the name of precaution. Such practice undermines the scientific foundation on which the limits are based and is likely to be an expensive and not necessarily effective way of providing protection.

Implementing other suitable precautionary procedures to reduce exposure is reasonable and warranted. However, electric power brings obvious health, social and economic benefits, and precautionary approaches should not compromise these benefits. Furthermore, given both the weakness of the evidence for a link between exposure to ELF magnetic fields and childhood leukaemia, and the limited impact on public health if there is a link, the benefits of exposure reduction on health are unclear. Thus the costs of precautionary measures should be very low. The costs of implementing exposure reductions will vary from one country to another, making it very difficult to provide a general recommendation for balancing the costs against the potential risk from ELF fields.

In view of the above, the following recommendations are given.

- Policy-makers should establish guidelines for ELF field exposure for both the general public and workers. The best source of guidance for both exposure levels and the principles of scientific review are the international guidelines.
- Policy-makers should establish an ELF EMF protection programme that includes measurements of fields from all sources to ensure that the exposure limits are not exceeded either for the general public or workers.
- Provided that the health, social and economic benefits of electric power are not compromised, implementing very low-cost precautionary procedures to reduce exposure is reasonable and warranted.
- Policy-makers, community planners and manufacturers should implement very low-cost measures when constructing new facilities and designing new equipment including appliances.
- Changes to engineering practice to reduce ELF exposure from equipment or devices should be considered, provided that they yield other additional benefits, such as greater safety, or little or no cost.
- When changes to existing ELF sources are contemplated, ELF field reduction should be considered alongside safety, reliability and economic aspects.
- Local authorities should enforce wiring regulations to reduce unintentional ground currents when building new or rewiring existing facilities, while maintaining safety. Proactive measures to identify violations or existing problems in wiring would be expensive and unlikely to be justified.
- National authorities should implement an effective and open communication strategy to enable informed decision-making by all stakeholders; this should include information on how individuals can reduce their own exposure.

- Local authorities should improve planning of ELF EMF-emitting facilities, including better consultation between industry, local government, and citizens when siting major ELF EMF-emitting sources.
- Government and industry should promote research programmes to reduce the uncertainty of the scientific evidence on the health effects of ELF field exposure.

1.2 Recommendations for research

Identifying the gaps in the knowledge concerning the possible health effects of exposure to ELF fields is an essential part of this health risk assessment. This has resulted in the following recommendations for further research (summarized in Table 1).

As an overarching need, further research on intermediate frequencies (IF), usually taken as frequencies between 300 Hz and 100 kHz, is required, given the present lack of data in this area. Very little of the required knowledge base for a health risk assessment has been gathered and most existing studies have contributed inconsistent results, which need to be further substantiated. General requirements for constituting a sufficient IF database for health risk assessment include exposure assessment, epidemiological and human laboratory studies, and animal and cellular (in vitro) studies (ICNIRP, 2003; ICNIRP, 2004; Litvak, Foster & Repacholi, 2002).

For all volunteer studies, it is mandatory that research on human subjects is conducted in full accord with ethical principles, including the provisions of the Helsinki Declaration (WMA, 2004).

For laboratory studies, priority should be given to reported responses (i) for which there is at least some evidence of replication or confirmation, (ii) that are potentially relevant to carcinogenesis (for example, genotoxicity), (iii) that are strong enough to allow mechanistic analysis and (iv) that occur in mammalian or human systems.

1.2.1 Sources, measurements and exposures

The further characterization of homes with high ELF exposure in different countries to identify relative contributions of internal and external sources, the influence of wiring/grounding practices and other characteristics of the home could give insights into identifying a relevant exposure metric for epidemiological assessment. An important component of this is a better understanding of foetal and childhood exposure to ELF fields, especially from residential exposure to underfloor electrical heating and from transformers in apartment buildings.

It is suspected that in some cases of occupational exposure the present ELF guideline limits are exceeded. More information is needed on exposure (including to non-power frequencies) related to work on, for example, live-line maintenance, work within or near the bore of MRI magnets

(and hence to gradient-switching ELF fields) and work on transportation systems. Similarly, additional knowledge is needed about general public exposure which could come close to guideline limits, including sources such as security systems, library degaussing systems, induction cooking and water heating appliances.

Exposure to contact currents has been proposed as a possible explanation for the association of ELF magnetic fields with childhood leukaemia. Research is needed in countries other than the USA to assess the capability of residential electrical grounding and plumbing practices to give rise to contact currents in the home. Such studies would have priority in countries with important epidemiological results with respect to ELF and childhood leukaemia.

1.2.2 Dosimetry

In the past, most laboratory research was based on induced electric currents in the body as a basic metric and thus dosimetry was focused on this quantity. Only recently has work begun on exploring the relationship between external exposure and induced electric fields. For a better understanding of biological effects, more data on internal electric fields for different exposure conditions are needed.

Computation should be carried out of internal electric fields due to the combined influence of external electric and magnetic fields in different configurations. The vectorial addition of out-of-phase and spatially varying contributions of electric and magnetic fields is necessary to assess basic restriction compliance issues.

Very little computation has been carried out on advanced models of the pregnant woman and the foetus with appropriate anatomical modelling. It is important to assess possible enhanced induction of electric fields in the foetus in relation to the childhood leukaemia issue. Both maternal occupational and residential exposures are relevant here.

There is a need to further refine micro-dosimetric models in order to take into account the cellular architecture of neural networks and other complex suborgan systems identified as being more sensitive to induced electric field effects. This modelling process also needs to consider influences in cell membrane electrical potentials and on the release of neurotransmitters.

1.2.3 Biophysical mechanisms

There are three main areas where there are obvious limits to the current understanding of mechanisms: the radical pair mechanism, magnetic particles in the body and signal-to-noise ratios in multicell systems, such as neuronal networks.

The radical pair mechanism is one of the more plausible low-level interaction mechanisms, but it has yet to be shown that it is able to mediate significant effects in cell metabolism and function. It is particularly impor-

tant to understand the lower limit of exposure at which it acts, so as to judge whether this could or could not be a relevant mechanism for carcinogenesis. Given recent studies in which reactive oxygen species were increased in immune cells exposed to ELF fields, it is recommended that cells from the immune system that generate reactive oxygen species as part of their immune response be used as cellular models for investigating the potential of the radical pair mechanism.

Although the presence of magnetic particles (magnetite crystals) in the human brain does not, on present evidence, appear to confer a sensitivity to environmental ELF magnetic fields, further theoretical and experimental approaches should explore whether such sensitivity could exist under certain conditions. Moreover, any modification that the presence of magnetite might have on the radical pair mechanism discussed above should be pursued.

The extent to which multicell mechanisms operate in the brain so as to improve signal-to-noise ratios should be further investigated in order to develop a theoretical framework for quantifying this or for determining any limits on it. Further investigation of the threshold and frequency response of the neuronal networks in the hippocampus and other parts of the brain should be carried out using in vitro approaches.

1.2.4 Neurobehaviour

It is recommended that laboratory-based volunteer studies on the possible effects on sleep and on the performance of mentally demanding tasks be carried out using harmonized methodological procedures. There is a need to identify dose-response relationships at higher magnetic flux densities than used previously and a wide range of frequencies (i.e. in the kilohertz range).

Studies of adult volunteers and animals suggest that acute cognitive effects may occur with short-term exposures to intense electric or magnetic fields. The characterization of such effects is very important for the development of exposure guidance, but there is a lack of specific data concerning field-dependent effects in children. The implementation of laboratory-based studies of cognition and changes in electroencephalograms (EEGs) in people exposed to ELF fields is recommended, including adults regularly subjected to occupational exposure and children.

Behavioural studies on immature animals provide a useful indicator of the possible cognitive effects on children. The possible effects of pre- and postnatal exposure to ELF magnetic fields on the development of the nervous system and cognitive function should be studied. These studies could be usefully supplemented by investigations into the effects of exposure to ELF magnetic fields and induced electric fields on nerve cell growth using brain slices or cultured neurons.

There is a need to further investigate potential health consequences suggested by experimental data showing opioid and cholinergic responses in animals. Studies examining the modulation of opioid and cholinergic

responses in animals should be extended and the exposure parameters and the biological basis for these behavioural responses should be defined.

1.2.5 Neuroendocrine system

The existing database of neuroendocrine response does not indicate that ELF exposure would have adverse impacts on human health. Therefore no recommendations for additional research are given.

1.2.6 Neurodegenerative disorders

Several studies have observed an increased risk of amyotrophic lateral sclerosis in "electrical occupations". It is considered important to investigate this association further in order to discover whether ELF magnetic fields are involved in the causation of this rare neurodegenerative disease. This research requires large prospective cohort studies with information on ELF magnetic field exposure, electric shock exposure as well as exposure to other potential risk factors.

It remains questionable whether ELF magnetic fields constitute a risk factor for Alzheimer's disease. The data currently available are not sufficient and this association should be further investigated. Of particular importance is the use of morbidity rather than mortality data.

1.2.7 Cardiovascular disorders

Further research into the association between ELF magnetic fields and the risk of cardiovascular disease is not considered a priority.

1.2.8 Immunology and haematology

Changes observed in immune and haematological parameters in adults exposed to ELF magnetic fields showed inconsistencies, and there are essentially no research data available for children. Therefore, the recommendation is to conduct studies on the effects of ELF exposure on the development of the immune and haematopoietic systems in juvenile animals.

1.2.9 Reproduction and development

There is some evidence of an increased risk of miscarriage associated with ELF magnetic field exposure. Taking into account the potentially high public health impact of such an association, further epidemiological research is recommended.

1.2.10 Cancer

Resolving the conflict between epidemiological data (which show an association between ELF magnetic field exposure and an increased risk of childhood leukaemia) and experimental and mechanistic data (which do not support this association) is the highest research priority in this field. It is recommended that epidemiologists and experimental scientists collaborate on this. For new epidemiological studies to be informative they must focus on new aspects of exposure, potential interaction with other factors or on high exposure groups, or otherwise be innovative in this area of research. In addi-

tion, it is also recommended that the existing pooled analyses be updated, by adding data from recent studies and by applying new insights into the analysis.

Childhood brain cancer studies have shown inconsistent results. As with childhood leukaemia, a pooled analysis of childhood brain cancer studies should be very informative and is therefore recommended. A pooled analysis of this kind can inexpensively provide a greater and improved insight into the existing data, including the possibility of selection bias and, if the studies are sufficiently homogeneous, can offer the best estimate of risk.

For adult breast cancer more recent studies have convincingly shown no association with exposure to ELF magnetic fields. Therefore further research into this association should be given very low priority.

For adult leukaemia and brain cancer the recommendation is to update the existing large cohorts of occupationally exposed individuals. Occupational studies, pooled analyses and meta-analyses for leukaemia and brain cancer have been inconsistent and inconclusive. However, new data have subsequently been published and should be used to update these analyses.

The priority is to address the epidemiological evidence by establishing appropriate in vitro and animal models for responses to low-level ELF magnetic fields that are widely transferable between laboratories.

Transgenic rodent models for childhood leukaemia should be developed in order to provide appropriate experimental animal models to study the effect of ELF magnetic field exposure. Otherwise, for existing animal studies, the weight of evidence is that there are no carcinogenic effects of ELF magnetic fields alone. Therefore high priority should be given to in vitro and animal studies in which ELF magnetic fields are rigorously evaluated as a co-carcinogen.

With regard to other in vitro studies, experiments reporting the genotoxic effects of intermittent ELF magnetic field exposure should be replicated.

1.2.11 Protective measures

Research on the development of health protection policies and policy implementation in areas of scientific uncertainty is recommended, specifically on the use of precaution, the interpretation of precaution and the evaluation of the impact of precautionary measures for ELF magnetic fields and other agents classified as “possible human carcinogens”. Where there are uncertainties about the potential health risk an agent poses for society, precautionary measures may be warranted in order to ensure the appropriate protection of the public and workers. Only limited research has been performed on this issue for ELF magnetic fields and because of its importance, more research is needed. This may help countries to integrate precaution into their health protection policies.

Further research on risk perception and communication which is specifically focused on electromagnetic fields is advised. Psychological and sociological factors that influence risk perception in general have been widely investigated. However, limited research has been carried out to analyse the relative importance of these factors in the case of electromagnetic fields or to identify other factors that are specific to electromagnetic fields. Recent studies have suggested that precautionary measures which convey implicit risk messages can modify risk perception by either increasing or reducing concerns. Deeper investigation in this area is therefore warranted.

Research on the development of a cost–benefit/cost-effectiveness analysis for the mitigation of ELF magnetic fields should be carried out. The use of cost–benefit and cost-effectiveness analyses for evaluating whether a policy option is beneficial to society has been researched in many areas of public policy. The development of a framework that will identify which parameters are necessary in order to perform this analysis for ELF magnetic fields is needed. Due to uncertainties in the evaluation, quantifiable and unquantifiable parameters will need to be incorporated.

Table 1. Recommendations for further research

Sources, measurements and exposures	**Priority**
Further characterization of homes with high ELF magnetic field exposure in different countries	Medium
Identify gaps in knowledge about occupational ELF exposure, such as in MRI	High
Assess the ability of residential wiring outside the USA to induce contact currents in children	Medium
Dosimetry	
Further computational dosimetry relating external electric and magnetic fields to internal electric fields, particularly concerning exposure to combined electric and magnetic fields in different orientations	Medium
Calculation of induced electric fields and currents in pregnant women and in the foetus	Medium
Further refinement of microdosimetric models taking into account the cellular architecture of neural networks and other complex suborgan systems	Medium
Biophysical mechanisms	
Further study of radical pair mechanisms in immune cells that generate reactive oxygen species as part of their phenotypic function	Medium
Further theoretical and experimental study of the possible role of magnetite in ELF magnetic field sensitivity	Low
Determination of threshold responses to internal electric fields induced by ELFs on multicell systems, such as neural networks, using theoretical and in vitro approaches	High

Table 1. Continued

Neurobehaviour	
Cognitive, sleep and EEG studies in volunteers, including children and occupationally exposed subjects, using a wide range of ELF frequencies at high flux densities	Medium
Studies of pre- and post-natal exposure on subsequent cognitive function in animals	Medium
Further study of opioid and cholinergic responses in animals	Low
Neurodegenerative disorders	
Further studies of the risk of amyotrophic lateral sclerosis in "electric" occupations and in relation to ELF magnetic field exposure and of Alzheimer's disease in relation to ELF magnetic field exposure	High
Immunology and haematology	
Studies of the consequences of ELF magnetic field exposure on immune and haematopoietic system development in juvenile animals.	Low
Reproduction and development	
Further study of the possible link between miscarriage and ELF magnetic field exposure	Low
Cancer	
Update existing pooled analyses of childhood leukaemia with new information	High
Pooled analyses of existing studies of childhood brain tumour studies	High
Update existing pooled and meta-analyses of adult leukaemia and brain tumour studies and of cohorts of occupationally exposed individuals	Medium
Development of transgenic rodent models of childhood leukaemia for use in ELF studies	High
Evaluation of co-carcinogenic effects using in vitro and animal studies	High
Attempted replication of in vitro genotoxicity studies	Medium
Protective measures	
Research on the development of health protection policies and policy implementation in areas of scientific uncertainty	Medium
Further research on risk perception and communication focused on electromagnetic fields	Medium
Development of a cost–benefit/cost-effectiveness analysis for the mitigation of ELF fields	Medium

2 SOURCES, MEASUREMENTS AND EXPOSURES

2.1 Electric and magnetic fields

This chapter describes the nature of electric and magnetic fields, provides information on sources and exposures, and discusses the implications for exposure assessment for epidemiology. Generation and measurement of fields in experimental laboratory settings is outside the scope of this chapter.

2.1.1 The field concept

The field concept is very general in physics and describes for each point in a region of space the specific state of a physical quantity. Although a field can be defined for almost any physical quantity, it is in common use only for those which are capable of exerting a force. The gravitational field, for example, describes the force exerted on a unit mass at each point in space. Accordingly, the electric field describes the force exerted on a unit electric charge, and the magnetic field is defined in terms of the force exerted on a moving unit charge.

Electric fields are produced by electric charges, irrespective of their state of motion. A single charge at a point produces an electric field in all directions in a pattern with spherical symmetry and infinite dimension. A line of charges (e.g. a power line) produces an electric field around the line in a pattern with cylindrical symmetry. In practice, it is not possible to have a single isolated charge or a single isolated charged object, and instead of indefinitely long field lines, they will terminate on another charge (which could be another charge already present in a conductor or could be a charge induced by the field itself in a conducting object). The overall shape of the pattern of electric field experienced at any point thus depends on the distribution of charges and of objects in the vicinity. In technical systems, electric charges are related to voltages, and not to currents or power.

Magnetic fields are produced by moving charges and thus are proportional to electric currents in a system, irrespective of the voltage used. A current flowing in any conductor, no matter how complicated the shape of the conductor, can be broken down into a series of infinitesimally small segments, joined end-to-end. The magnetic field produced by a short element of current is given by the Biot-Savart law:

$$\frac{|dH|}{dl} = \frac{i}{4\pi r^2}\sin(\varphi)$$

where dH is the element of magnetic field produced by the current element i in the conductor element dl at a position r in space, and φ is the angle between dl and r.

As long as charges and currents are static, electricity and magnetism are distinct phenomena. Time varying charge distributions however result in a coupling of electric and magnetic fields that become stronger with increasing frequency. The characteristics and interactions of electric and magnetic fields are completely described by Maxwell's equations.

In addition to the "quasi static fields" from resting and moving charges, accelerating charges produce a radiation component. At extremely low frequencies the radiating field of a source is negligible. In practical exposure situations, radiation is absolutely negligible in the ELF range. Radiation only becomes dominant at distances that are large compared to the wavelength.

The wavelength is the distance between two successive cycles of the wave. In free space it is related to the frequency by the formula wavelength = speed of light / frequency. At 50 Hz, the wavelength is very long, 6000 km (60 Hz: 5000 km). In comparison, a radio wave with a frequency of 100 kHz has a wavelength of 3 km.

2.1.2 Quantities and units

For magnetic fields, there are two different quantities: the magnetic flux density, usually designated *B*, and the magnetic field strength, usually designated *H*. The distinction between *B* and *H* becomes important for the description of magnetic fields in matter, especially for materials which have certain magnetic (ferromagnetic) properties, such as iron. Biological tissue generally has no such properties and for practical purposes, either *B* or *H* can be used to describe magnetic fields outside and inside biological tissues.

Similarly, for the description of electric fields there are also different quantities: the electric field strength *E* and the dielectric displacement *D*. *D* is not useful for the description of electric fields in biological tissue. All these parameters are vectors; vectors are denoted in italics in this Monograph (see also paragraph 3.1).

The SI unit of magnetic flux density (*B*) is the tesla (T), and of magnetic field strength (*H*) is the ampere per metre (A m^{-1}). In the absence of magnetic material, 1 μT = $4\pi\times10^{-7}$ A m^{-1}. Either *B* or *H* can be used to describe fields, but *B* (i.e. tesla) is more common and is used here. Older literature, especially American, often uses the Gauss (G): 1 μT = 10^4 G (1 μT= 10 mG).

The SI unit of the electric field strength (*E*) is volt per metre (V m^{-1}).

2.1.3 Polarization

Electric and magnetic fields are vector quantities; they are characterized by an intensity (field strength) and a direction. In static (direct current, DC) fields, direction and intensity are constant over time. A time varying (alternating current, AC) field usually has a constant direction but a variable intensity. The field oscillates in a defined direction. This is often referred to as linear polarization.

In complex exposure scenarios, fields with different vector quantities may overlap. The resultant field is the addition of the two or more field vectors. In DC fields the result is a field with a different intensity and in most cases a different orientation. In AC fields, the situation becomes more complex because the vector addition may result in a time varying orientation of the resulting field. The field vector rotates in space; with the varying intensity of AC fields, the tip of the vector traces out an ellipse in a plane. This is often referred to as elliptical or circular polarization. This situation needs to be considered with respect to field measurement.

2.1.4 Time variation, harmonics and transients

The basic AC field can be described as a sine wave over time. The peak field strength is called the amplitude and the number of wave cycles within a second is called the frequency. The most common frequencies used in the electricity system of many countries are 50 Hz and 60 Hz. When fields of more than one frequency are combined, the resultant field is no longer a sine wave when plotted against time. Depending on the parameters of the combined fields (amplitude, frequency) any time course of the resultant field can be achieved, for example a square wave or a triangular wave. Conversely, any shape waveform can be split into a number of sinusoidal components at different frequencies. The process of splitting a waveform into its component frequencies is known as Fourier analysis, and the components are called the Fourier components.

In many electrical systems, sinusoidal signals are distorted by a non-linear behaviour of the loads. This happens when the electrical properties of the system depend on the signal strength. Such distortions introduce Fourier components in addition to the fundamental frequency of the signal, which are called harmonics. Harmonics are a precise multiple of the fundamental frequency. Given a 50 Hz fundamental frequency, 100 Hz is the second harmonic, 150 Hz is the third harmonic, and so forth.

Note that the terminology used in electrical engineering is different to musical terminology: a frequency of twice the fundamental is the second harmonic to the engineer but only the first harmonic to the musician. In electrical engineering, “fundamental” and “first harmonic” are equivalent terms.

The term “harmonic” is generally used only for those components of the current or voltage with a frequency which is an integral multiple of the power frequency (and is locked into that frequency) and that are produced as part of the operation of the electricity system. These will produce harmonic frequencies in the magnetic or electric fields produced. If there are currents or voltages at other frequencies, which are not tied to the power frequency, these frequencies will also appear in the magnetic or electric fields produced.

There is a number of possible sources of such currents and voltages, particularly at frequencies rather higher than the power frequencies. With regard to exposure of the public, the main sources are the 16 2/3(20 or sometimes 15) Hz used by some electric transport systems, 400 Hz used by most aeroplanes, the screen-refresh frequencies of video display units (VDUs)

(which have varied over the years with advances in computer design but is typically 50–160 Hz), and the variable frequencies increasingly used by variable-speed traction drives for trains and trams. It can be seen that these are all specific to particular situations, and, with the exception of the VDU, it would not be expected to find fields at these frequencies in normal domestic settings. In a normal domestic setting, any non-harmonic frequencies are generally negligible. There are many other sources in occupational settings related to specific industrial processes.

All the frequency components of the field so far considered are periodic: that is, although the amplitude of the field varies over time, the pattern of the variation repeats itself at fixed intervals (e.g. at 20 ms intervals for signals with a fundamental frequency of 50 Hz).

Natural and man made field sources often produce signals which are not repeated periodically but rather occur only once. The resulting time variation of the field is called transient. Over the course of a period of time, say a day, there may be a number of transients, but there is no regularity or periodicity to them, and they are sufficiently far apart to be treated as separate isolated events.

Transients accompany virtually all switching operations and are characterized by a high rate of change of the field. In fact there is a wide range of events which fit the basic definition of a transient as a non-periodic event. The characteristics of transients are numerous, which makes measurement complex.

2.1.5 Perturbations to fields, shielding

Magnetic fields are perturbed by materials that have a very high relative permeability. This effectively means they are perturbed only by ferromagnetic materials, and the most common example is iron and its compounds or alloys. An object made of such material will produce a region of enhanced field where the field enters and leaves the object, with a corresponding reduction in the field to the sides.

Shielding of ELF magnetic fields with such material is in practice only an option to protect small areas, for example VDU's from magnetic interference. Another option with only little practical relevance for field reduction purposes is the compensation of the magnetic field with a specially designed field source.

Electric fields, in contrast to magnetic fields, are readily perturbed by materials with a high relative permittivity (dielectrics) and even more significantly by conducting objects. A conducting enclosure eliminates the electric field within it. A conducting object also perturbs the field outside it, increasing it in line with the field and reducing it to the sides. At power frequencies, a metal box is effectively a perfect screen, and buildings are sufficiently conducting to reduce the electric field within them from an external source by factors of 10–100 or more.

Electric fields are particularly affected by earthed conducting objects including not just the ground, but also trees, hedges, fences, many buildings, and human beings. Any conducting object has a charge induced on it by the electric field. This induced charge itself then becomes part of the set of charges which constitutes the field. The consequence is that to determine the electric field produced by, say, a transmission line it is necessary to consider not just the positions of the conductors of the line but the position of the ground relative to them and the positions of any other conducting objects. In terms of human exposure to power lines, the main effect is that close to a vertical object that is tall compared to a person – e.g. a tree or a house – field exposure on the ground is reduced.

2.2 Sources of alternating fields

2.2.1 Electric fields

2.2.1.1 Naturally occurring fields

The natural electric field encountered above the surface of the Earth varies greatly with time and location. The primary cause of the field is the charge separation that occurs between the Earth and the ionosphere, which acts as a perfect conductor separated by air of negligible conductivity (König et al., 1981). The field near the surface in fair weather has a typical strength of about 130 V m^{-1} (Dolezalek, 1979). The strength generally depends on height, local temperature, humidity profile and the presence of ions in the atmosphere. Deviations of up to 200% from fair-weather levels have been recorded in the presence of fog or rain. Daily changes are attributed to meteorological phenomena, such as thunderstorms, which affect the rate of charge transfer between the ground and the upper atmosphere.

Variations of up to 40 kV m^{-1} occur near thunderstorms, although even in the absence of local lightning, fields can reach up to 3 kV m^{-1}. Because the dominant component usually changes very slowly, the phenomenon is often described as “electrostatic”. However a variety of processes in the atmosphere and magnetosphere produce a wide range of signals with frequencies reaching up to several megahertz. Atmospheric inversion layer phenomena produce electric fields at the lower end of the ELF range (König et al., 1981). Atmospheric fields related to lightning discharges have spectral components below 1 Hz but the largest amplitude components have frequencies between 1 and 30 kHz. Generally the range of frequencies and field strengths vary widely with geographical location, time of day and season. Characteristics of the Earth's electric field in the ELF range are summarized in Table 2. The intensity of time-varying fields related to atmospherics such as lightning between 5 Hz and 1 kHz are typically less than 0.5 V m^{-1} and amplitudes generally decrease with increasing frequency. The natural electric field strength at the power frequencies of 50 or 60 Hz is about 10^{-4} V m^{-1} (EC, 1996).

Table 2. Characteristics of the Earth's electric field in the ELF range		
Frequency range (Hz)	**Electric field strength ($V\ m^{-1}$)**	**Comment**
0.001–5	$0.2–10^3$	Short duration pulses of magnetohydrodynamic origin
7.5–8.4 and 26–27	$0.15–0.6\times10^{-6}$	Quasi-sinusoidal pulses of underdetermined origin
5–1000	$10^{-4}–0.5$	Related to atmospheric changes (atmospherics)

The Earth-atmosphere system approximates electromagnetically to a three conductive layer radial shell, denoted as the Earth-ionosphere cavity, in which electromagnetic radiation is trapped. In this cavity broadband electromagnetic impulses, like those from lightning flashes, create globally the so-called Schumann resonances at frequencies 5–50 Hz (Bliokh, Nickolaenko & Filippov, 1980; Schumann, 1952; Sentman, 1987). Electric fields of up to a few tenths of a millivolt per metre can be attributed to the Schumann resonances (König et al., 1981).

2.2.1.2 Artificial fields

The dominant sources of ELF electric fields are invariably the result of human activity, in particular, the operation of power systems or the operation of mains appliances within a home.

2.2.1.2.1 Overhead power lines

The electric field at a point near a power line depends on the voltage of the line, its distance, and how close together the various charged conductors making up the line are. The radius of the conductors is also relevant. Other factors being equal, thicker conductors result in larger electric fields at ground level. In addition, electric fields are affected by conducting objects.

Electric fields are lower and fall more rapidly with distance for point symmetric systems than for others. Electric fields are lowest when the three phases are balanced and rise with the unbalance. At ground level, electric fields are highest towards the middle of a span where the sag of the conductors brings them nearest the ground and reduce towards the end of the span.

The highest electric field strength at ground level from overhead lines is typically around 10 kV m^{-1} (AGNIR, 2001b; NIEHS, 1995).

2.2.1.2.2 House wiring and appliances

The electric field produced by any source outside the home will be attenuated considerably by the structure of the home. All common building

materials are sufficiently conducting to screen fields, and the ratio of the field outside to the field inside typically ranges from 10 to 100 or more (AGNIR, 2001b).

Within homes, however, there are sources of electric field just as there are sources of magnetic field. House wiring can produce electric fields, which are clearly strongest close to the wiring but which can be significant over the volume of a house as well. The electric field produced by wiring depends partly on how it is installed; wiring installed in metal trunking or conduit produces very small external fields, and the fields produced by wiring installed within walls is attenuated by an amount depending on the building materials (AGNIR, 2001b).

The other main source of electric fields within a home is mains appliances. Any mains appliance produces power-frequency electric fields whenever it is connected to the mains (in contrast to magnetic fields, which are produced only when current is being drawn), and appliances are often left plugged in even when not operating. The size of the electric field depends on the wiring of the appliance, and on how much of the wiring is enclosed by metal which will screen the electric field. The electric field from an appliance falls rapidly with distance from the appliance, just as the magnetic field does. The magnetic field from an appliance typically merges into the background magnetic field within a metre or two. With electric fields, except in those few homes very close to a source of high electric field, there is no background field from sources outside the home. Therefore the electric field from an appliance is still appreciable, albeit rather small, at greater distances from the appliance than is the case for magnetic fields.

Because electric fields are so easily perturbed by conducting objects, fields within the volume of a room are rarely uniform or smoothly varying. Many objects, in particular metal objects, perturb the field and can create local areas of high electric field strength.

2.2.1.2.3 Underground cables and substations

When a cable is buried underground, it still produces a magnetic field above the ground (see section 2.2.2.2.2). By contrast, a buried cable produces no electric field above ground, partly because of the screening effect of the ground itself, but mainly because underground cables practically always include a metal sheath which screens the electric field.

Substations also rarely produce significant electric fields outside their perimeter. In the case of a ground-mounted final distribution substation, this is because all the busbars and other equipment are contained either in metal cabinets and pillars or in a building, both of which screen electric fields. Higher-voltage substations are not so rigorously enclosed, but are usually surrounded by a security fence, which because it is metal again screens the electric field.

2.2.1.2.4 Electric power industry

Bracken and colleagues have characterized the electric field environment within towers of transmission lines rated between 230 and 765 kV. During various operations that include climbing the towers, electric fields may reach anywhere from 10 to 30 kV m^{-1}.These fields would not typically be oriented parallel to the body (Bracken, Senior & Dudman, 2005; Bracken, Senior & Tuominen, 2004). In some operations, such as bare hand live line work, linemen wear a conductive suit, which shields the individual from the electric field.

2.2.2 Magnetic fields

2.2.2.1 Naturally occurring fields

The Earth's magnetic field changes continually at periods ranging from a few milliseconds up to 10^{12} seconds. The broad spectrum of variation is summarized in Table 3. The main feature of the geomagnetic field is its close resemblance to a dipole field aligned approximately with the spin axis of the Earth. The dipole field is explained by electrical currents that flow in the core. The vertical component of the field reaches a maximum of about 70 μT at the magnetic poles, and approaches zero at the magnetic equator; conversely the horizontal component is close to zero at the poles and has a maximum just over 30 μT at the magnetic equator. Changes of the dipole field with periods of the order of 100 years or so constitute the secular variation, and are explained by eddy currents located near the core boundary (Bullard, 1948).

Table 3. The broad spectrum of variation in the Earth's magnetic field

Type	Period (seconds)	Typical amplitudes	Origin	Comment
Reversals	~10^{12}	100 μT	Internal	Current systems in the earth
Secular change	10^{9}–10^{10}	10 μT		
Magnetic storms	10^{8}–10^{9}	hundreds nT	External	11 year period of maximum
Sunspot activity	10^{6}			
Storm repetition				27 day period
Diurnal	10^{5}	tens nT		24 hour period
Lunar	10^{5}			25 hour period
Pulsations	10^{-1}–10^{2}	0.02–100 nT		Solar-terrestrial interaction
Cavity resonances	10^{-2}–10^{-1}	10^{-2} nT		Solar-terrestrial interaction
Atmospherics	10^{-6}–10^{0}	10^{-2} nT (ELF)		Lightning discharges

Table 4. Characteristics of the Earth's magnetic field across the ELF part of the spectrum

Nature and origin	Amplitude changes (μT)	Typical frequency (Hz)	Comment
Regular solar and lunar variations	0.03–0.05 (solar) 0.005–0.006 (lunar)	10^{-5} 10^{-5}	Increases in energy during summer and towards the equator. Also increases at a period of 11 years due to sunspot activity.
Irregular disturbances, such as magnetic storms related to sunspot activity	0.8–2.4	Wide range of frequencies	Repetition after 27 day period corresponding to the sun's rotation time on its axis.
Geomagnetic pulsations (micropulsations) related to changes in the magnetosphere	2×10^{-5}–8×10^{-2}	0.002–5 Hz	Amplitudes quoted for moderate activity at mid-latitudes.
Cavity resonances	2×10^{-5}–5×10^{-5}	5–50 Hz	Schumann resonance oscillations excited by broadband lightning discharges
Atmospherics related to lightning discharges	5×10^{-5}	< 1–2 kHz	Energy peak at 100–200 Hz. Some spectral components < 1 Hz and VLF components in the range 1–30 kHz.

The main characteristics of the Earth's magnetic field across the ELF and VLF part of the spectrum are summarized in Table 4. All of the spectrum of time variations of period shorter than the most rapid secular change have their primary cause outside the Earth, associated with processes in the ionosphere and magnetosphere (Garland, 1979). These include the regular solar and lunar daily variations upon which more irregular disturbances are superimposed. The typical solar diurnal cycle shows variations of no more than a few tens of nanoteslas depending on magnetic latitude. Large magnetic disturbances known as storms show typical variations of 0.5 μT over 72 hours and are closely related to sunspot activity and the sun's rotation time. Geomagnetic pulsations arise from effects in the magnetosphere and typically cover the frequency range from 1 MHz to 1 Hz. At mid-latitudes during periods of moderate activity up to several tens of nanotesla can be attributed to pulsations (Allan & Pouler, 1992; Anderson, 1990).

The ELF variations arise mainly from the effects of solar activity in the ionosphere and atmospheric effects such as lightning discharges which cause resonance oscillations in the Earth-ionosphere cavity. Changes in ELF

signals over 11-year and 27-day periods and circadian variations reflect the solar influences (EC, 1996). The electromagnetic fields that arise from lightning discharges, commonly known as atmospherics, have a very broad frequency range with spectral components from below 1 Hz up to a few megahertz. In the ELF range the peak intensity from lightning discharges occurs typically at 100–200 Hz. The Schumann resonances are a source of ELF magnetic fields of the order of 10^{-2} nT at frequencies of up to a few tens of hertz (König et al., 1981). The measurement of signals with frequencies below 100 Hz is extremely difficult because of the interference from man-made signals. At 50 Hz or 60 Hz the natural magnetic field is typically of the order of 10^{-6} μT (Polk, 1974).

2.2.2.2 Artificial fields

2.2.2.2.1 Transmission lines

Factors affecting fields

The magnetic field produced by a transmission line depends on several factors.

- The number of currents carried by the line (usually three for a single-circuit line, 6 for a two-circuit line, etc.).
- The arrangement of those currents in space, including:
  - *The separation of the currents*. This is usually determined by the need to avoid sparkover between adjacent conductors, including an allowance for displacement of conductors caused by wind. The separation therefore usually increases as the voltage of the line increases.
  - *The relative phasing of multiple circuits*. Suppose the three phases of one circuit are arranged in the order a-b-c from top to bottom. If the second circuit is similarly arranged a-b-c, the two circuits produce magnetic fields which are aligned with each other and reinforce each other. But if the second circuit is arranged in the opposite order, c-b-a, its magnetic field will be in the opposite direction and the two fields will partially cancel each other. The resultant field falls more nearly as the reciprocal of distance cubed instead of squared. This is variously known as transposed, reversed, or rotated phasing. Other arrangements of the relative phasing are clearly possible and generally produce higher fields at ground level.
- The currents carried by the line, which include:
  - the load current;
  - any out of balance currents.
- Any currents carried by the earth conductor or in the ground itself.

- The height of the currents above ground: the minimum clearance allowed for a given voltage line is usually determined by the need to avoid sparkover to objects on the ground.

Higher voltage lines usually carry higher currents and have larger spacing between conductors. They therefore usually produce higher magnetic fields, even though the magnetic field itself does not depend on the voltage.

Currents in power lines vary over the course of a day, seasonally and from year to year as electricity demand varies. This affects the magnetic field both directly and also because the load carried affects the conductor temperature and hence sag and ground clearance. Lines usually operate at significantly less load than their rating, and therefore average magnetic fields encountered are usually significantly less than the theoretical maximum field a line is capable of producing.

Harmonics and transients

The nature of the electricity system and the use of electricity means that some harmonics are more prevalent than others. In particular, the third harmonic, 150 (180) Hz, is usually the strongest, and even harmonics (2nd, 4th, 6th etc.) are usually smaller than odd harmonics (3rd, 5th, 7th etc.). In many situations, harmonics are very small, perhaps a few percent or less of the fundamental. In some situations, however, particularly in buildings with certain types of apparatus, or near certain industrial users of electricity, the harmonic content can increase, and on occasion the third harmonic can be comparable in magnitude to the fundamental. In general, harmonics above the third or fifth are very small, but there are certain processes which lead to harmonics as high as the 23rd and 25th. Some harmonics occur as a result of the operation of the electricity system itself – for instance, small amounts of 11th, 13th, 23rd and 25th harmonics are produced by common types of AC-to-DC conversion equipment – but most occur as a result of the loads consumers connect to the electricity system. A particular example is dimmer switches used in lighting applications. Harmonics are regarded as undesirable on an efficiently operated electricity system. Harmonics tend to be lower in the transmission system, higher in the distribution system, and highest in final-distribution circuits and homes.

Transients also occur in electrical systems. Transients in the voltage (and hence in the electric field) are produced by the following causes.

- *Lightning strikes to an overhead power line*. Most lightning strikes hit the earth conductor (where one is present). If the lightning hits a phase conductor instead, or jumps across to the phase conductor having initially hit something else, a very high voltage can be applied to that phase conductor. This voltage rapidly dissipates, not least over the spark gaps which are installed partly for this very purpose.

- *Switching events*. When a switch in a circuit carrying a current is opened and the current is interrupted, a voltage is generated in that circuit. The voltage dissipates over a period of time determined by the electrical characteristics of the circuit. Switching surges occur whenever circuits are interrupted, so also occur in distribution systems and in homes.
- *Short circuits*. These can occur either between two phase conductors or from a phase conductor to earth or to an earthed conductor. Examples of how short circuits occur with overhead lines include when two phase conductor, both oscillating in the wind, clash, or when an object such as a tree or a hot-air balloon bridges the gap between a phase conductor and another conductor or the earth. With underground circuits and circuits in homes, short circuits can occur when a drill cuts the cable, or as a result of corroded insulation. Short circuits should usually result in the circuit concerned being rapidly disconnected (by the operation of a circuit breaker or by the blowing of a fuse). For the duration of the short circuit, which could be as short as 40 ms on parts of the transmission system or as long as a second on parts of the distribution system, the voltage of the circuit concerned is forced by the fault to a different value from normal.

Transients in the current (and in the resulting magnetic field) result from the following causes.

- *Short circuits*. For the duration of the short circuit (until either the short circuit is removed, or more usually, until the circuit is disconnected by the fuse or circuit breaker) abnormally high currents will be flowing. On the UK transmission system, the highest "fault current" that is allowed to flow is 63 kA. At lower voltages, the "fault level" (the amount of current that can flow in the event of a short circuit) is lower, but can still be many times the normal current in the circuit.
- *Switching events*. Transient currents can be produced when a circuit is first switched on (such currents are often called "inrush" currents which describes their nature quite well).

Some transients affect only the circuit they are generated on. More usually, they affect neighbouring circuits as well, but to a lesser extent. For instance, at high voltages, a lightning strike to a transmission circuit may cause a sufficiently large transient voltage on that circuit to cause the protection circuits to operate the circuit breaker and to disconnect the circuit. On other nearby circuits, it may cause a large transient voltage, but not large enough to cause the protection to operate. On circuits further away, the transient may still be present but may be much smaller and for practical purposes negligible. At low voltages, switching an appliance in one home may produce a transient that affects adjoining homes as well. Thus it is only transient

voltages or currents which are generated close to a given point which are likely to produce significant transient electric or magnetic fields at that point.

Field levels

Transmission lines can produce maximum magnetic flux densities of up to a few tens of microteslas during peak demand, however mean levels are usually no more than a few microteslas. The magnetic flux density reduces typically to a few hundred nanotesla at distances of several tens of metres from a transmission line. The magnetic flux density decreases in lower voltage systems, mainly due to progressively smaller currents and conductor separations used.

Overhead transmission lines operate at various voltages up to 1150 kV. In the UK, the largest power lines in use operate at 400 kV with ratings up to 4 kA per circuit and a minimum ground clearance of 7.6 m. This theoretically produces up to 100 µT directly beneath the conductors. In practice, because the load is rarely the maximum and the clearance rarely the minimum, the typical field at ground level directly beneath the conductors is 5 µT. Table 5 gives more detail on the average magnetic field at various distances from a typical National Grid line. These figures were calculated from one year's recorded load data and are the average for a representative sample of 43 different lines.

Table 5. Average magnetic field at various distances from National Grid line [a]

Distance (m)	Average field (µT)
0	4.005
50	0.520
100	0.136
200	0.034
300	0.015

[a] Source: National Grid, 2007b.

Table 6. Typical magnetic field levels in µT for power transmission lines [a]

Type of line	Usage	Maximum on right-of-way	Distance from lines			
			15 m	30 m	61 m	91 m
115 kV	Average	3	0.7	0.2	0.04	0.02
	Peak	6.3	1.4	0.4	0.09	0.04
230 kV	Average	5.8	2.0	0.7	0.18	0.08
	Peak	11.8	4.0	1.5	0.36	0.16
500 kV	Average	8.7	2.9	1.3	0.32	0.14
	Peak	18.3	6.2	2.7	0.67	0.30

[a] Source: NIEHS, 1995.

tances from a typical National Grid line. These figures were calculated from one year's recorded load data and are the average for a representative sample of 43 different lines. Typical values for the US at various distances, voltages, and power usage are summarized in Table 6.

2.2.2.2.2 Underground cables

When a high-voltage line is placed underground, the individual conductors are insulated and can be placed closer together than with an overhead line. This tends to reduce the magnetic field produced. However, the conductors may only be 1 m below ground instead of 10 m above ground, so can be approached more closely. The net result is that to the sides of the underground cable the magnetic field is usually significantly lower than for the equivalent overhead line, but on the line of the route itself the field can be higher. Examples of fields for UK underground cables are given in Table 7.

Table 7. Examples of fields for underground cables calculated at 1 m above ground level [a]

Voltage	Specifics	Location	Load	Magnetic field in μT at distance from centreline			
				0 m	5 m	10 m	20 m
400 kV and 275 kV	trough	0.13 m spacing 0.3 m depth	maximum	83.30	7.01	1.82	0.46
			typical	20.83	1.75	0.46	0.12
	direct buried	0.5 m spacing 0.9 m depth	maximum	96.17	13.05	3.58	0.92
			typical	24.06	3.26	0.90	0.23
132 kV	separate cores	0.3 m spacing 1 m depth	typical	9.62	1.31	0.36	0.09
	single cable	1 m depth	typical	5.01	1.78	0.94	0.47
33 kV	single cable	0.5 m depth	typical	1.00	0.29	0.15	0.07
11 kV	single cable	0.5 m depth	typical	0.75	0.22	0.11	0.06
400 V	single cable	0.5 m depth	typical	0.50	0.14	0.07	0.04

[a] Source: National Grid, 2007a.

Depending on the voltage of the line, the various conductors can be contained within an outer sheath to form a single cable. Not only is in that case the separation of the conductors further reduced, but they are usually wound helically, which produces a further significant reduction in the magnetic field produced.

2.2.2.2.3 Distribution lines

In power system engineering, it is common to distinguish between transmission lines and distribution lines. Transmission lines are high voltage (more than a few tens of kV), usually carried on lattice steel towers or substantial metal or concrete structures, capable of carrying large currents (hundreds or sometimes thousands of amps), and used for long-distance bulk transmission of power. Distribution lines are usually lower voltage (less than a few tens of kV), more often carried on wood poles or simpler structures, designed to carry lower currents, and used for more local distribution of power, including the final distribution of power to individual homes. Distribution lines may also have a neutral conductor whereas transmission lines rarely do.

Viewed from the standpoint of production of electric and magnetic fields, the difference between transmission lines and distribution lines is one of degree rather than kind. As the voltage of a circuit reduces, generally so does the spacing of the conductors and the load. All of these factors tend to mean that as the voltage decreases, so do both the electric and magnetic fields. Thus, conceptually, a distribution line without grounding currents is no different to a transmission line, it simply produces lower fields. In practice, the main difference between transmission and distribution lines is often that distribution lines do carry grounding currents but transmission lines do not.

The situation described for transmission lines also applies for a distribution circuit where the neutral is isolated from ground for most of its length. The neutral is often connected to the earth once at or near the transformer or substation which supplies the line, but that is the only earth connection. However, it was realised in various countries that by connecting the earth to the neutral at further points along their length other than just at the transformer/substation, extra security and safety could be obtained. When this is done, the neutral is usually connected to the mass of earth itself at various points, and in some configurations, there is a combined neutral-and-earth conductor rather than separate neutral and earth conductors.

This is the basis of much distribution wiring round the world. Practical systems are more complicated than this simple description, and there are usually numerous regulations and practices associated with them. However, for the present purposes, it is sufficient to note that much distribution wiring results in the neutral conductor being earthed at various points along its length. The situation in different countries is summarized in Table 8.

Each time the neutral conductor is earthed, there is the possibility that neutral current can divert out of the line into the earth itself (or more likely, into a convenient conducting earthed utility such as a water pipe) and return to the transformer/substation by a different route altogether. As soon as any neutral current diverts out of the lines, the currents left in the line are no longer exactly balanced. This can be expressed in various ways, for instance by saying that the neutral current is no longer equal and opposite to

Table 8. Wiring practices in different countries		
Country	**What is known about distribution earthing practices**	**Source of information**
Australia	Neutral is earthed at entrance to each house	Rauch et al., 1992
France	Multiple earthing should not occur	
Germany	Cities: neutral multiply earthed (optional but common). Rural: neutral not normally earthed.	Rauch et al., 1992
Japan	Multiple earthing not normal but can occur with certain motors and telecommunications equipment	Rauch et al., 1992
Norway	Multiple earthing should not occur	Vistnes et al., 1997b
UK	Multiple earthing becoming more common. Over 64% of circuits with multiple earthing.	Swanson, 1996
USA	Multiple earthing of neutral universal	Rauch et al., 1992

the zero-sequence current. The commonest and most useful way of describing the situation is to say that the line now has a net current, that is, a non-zero vector sum of all the currents flowing within the line.

Grounding currents – diverted neutral currents – flow on various conducting services, such as water pipes, and these may pass through a home. Where this happens there can be a region of elevated field within the home.

The net current clearly has a return path (all currents must flow in complete circuits). However, the return path, comprising water pipes, the ground, and maybe other distribution circuits or the same circuit further along its length, are likely to be rather distant from the line with the net current. So at any given point, for instance in a home supplied by the line, there is likely to be rather poor cancellation between the magnetic fields produced by the net current in the line and its return path. Often, it is accurate enough to calculate the magnetic field in a home based just on the net current in the distribution line supplying it, ignoring the return current altogether.

Net currents tend to be low — typically varying from a fraction of an amp to a few amps — and so these magnetic fields produced by net currents are also rather low compared to the magnetic fields produced directly underneath transmission lines. However, in homes which are distant from transmission lines (which is in fact the majority of homes in most countries), and from heavily loaded 3 phase distribution lines, there are no other significant sources of magnetic field outside the home, so it is the field produced by the net current which constitutes the dominant source of field, usually referred to as the “background field”. If the return path is distant and we are regarding the field as produced by a single net current, it falls as one over the

distance from the source, so varies comparatively little over the volume of a typical home.

Note that, although the concept of a net current was introduced by reference to deliberate multiple earthing of a neutral conductor, there are two other ways net currents can arise. These are, firstly, where two adjacent distribution circuits meet and their neutral conductors are connected; and secondly, where faulty house wiring or a faulty appliance results in an unintended earth connection to the neutral (this probably occurs in 20% or more of homes in the UK and is also common in the USA). Both have the effect of allowing neutral current to divert out of the line, and thus of creating a net current. In practical situations, a net current could be created by any of these three mechanisms, or more likely by a combination of two or all three of them, and the magnetic field it produces is unaffected by which of the mechanisms produced it (Maslanyj et al., 2007).

With overhead distribution, the phase conductors are sometimes close together in a single cable. Often, however, they are not as close together as they are with underground distribution, and significant fields may arise from load currents as well as net currents. Net currents still exist, and the magnetic field is produced by both net current and the currents in the phase conductors.

The size of a net current depends on the size of the neutral current, which in turn depends on the size of the currents in the phase conductors. These vary over time, as loads are switched on and off. In fact, electricity use shows characteristic variations both diurnally and annually. Because net currents do not depend directly on loads, they do not vary over time in exactly the same way, but net currents (and hence the background magnetic fields in homes produced by them) do usually show characteristic variations over time.

Supplies to houses in the USA have two phases each at 110 V. Appliances connected at 220 V between the two phases do not contribute neutral current and therefore do not contribute to net currents. Appliances connected between one or other phase and earth do contribute to neutral current. The neutral current, and hence the net current and magnetic field, depends on the difference between the loads connected to the two phases rather than to the total load.

Another wiring source of magnetic field within homes is two-way switching of lights. If wired in orthodox fashion, no net currents are produced by two-way switched lights. However, the layout of the lighting circuits, switches and lights in a home often makes it tempting to wire the light in a way which effectively creates a loop of net current connecting the light and the two switches and enclosing part of the rest of the volume of the home. This loop of net current constitutes a source of magnetic field. Again, this source only operates when the relevant light is switched on.

Spatial distribution

EMF strength from any source diminishes as the distance from the source increases. Quite often, fields decrease with a power of the distance, depending on the configuration of the source (Kaune & Zafanella, 1992).

The field strength at any distance r is proportional to $1/r$, $1/r^2$, or $1/r^3$. The higher the power of r, the steeper the decrease of the field. When the field strength is proportional to one over the distance cubed ($1/r^3$), the field is reduced to an eighth with every doubling of the distance. Although good approximations, in practice, fields rarely follow these power laws exactly, departing from them particularly at very small distances or very large distances.

Within homes, the background field – the general level of field over the volume of the home – varies relatively little, as it usually comes from sources outside the home, and the inverse distance or inverse distance square relationship with distance does not produce great variation over a limited volume. However, superimposed on that background variation, there are local areas of higher fields, from appliances, or house wiring. The fields from such devices tend to decay at $1/r^3$.

Temporal variation

Because magnetic fields stem from currents, they vary over time as electricity demand varies over time. The relationship is not precise, as magnetic fields usually depend on net currents, which may not be precisely proportional to loads. Nonetheless, magnetic fields do show daily, weekly and annual variations. The magnetic field in a home in the UK can vary typically by a factor of 2 during the day above and below the daily average and by 25% during the year above and below the annual average.

Direct measurements of fields in the same property are available only up to about 5 years apart. Dovan et al. (Dovan, Kaune & Savitz, 1993) conducted measurements in a sample of homes from the childhood cancer study of Savitz et al. (1988) five years after they were first measured and reported a correlation of 0.7 between the spot measurements for the two periods. For longer periods, changes in fields have to be estimated from models, taking account of changes in loads, numbers of consumers, lengths of circuits, etc. Kaune et al. (1998) examined the correlation of loads over time for over one hundred transmission circuits in Sweden. The correlation decayed substantially over time (after about ten years) and thus, contemporaneous measurements are not reliable for retrospective estimation of ambient residential fields. Simple models look just at some measure of per capita consumption. Swanson (1996) developed a more sophisticated model which looks at changes in electricity systems and wiring practices as well. Even so, there are some changes which such models cannot easily take into account, so the results should be interpreted with caution. The models all suggest that average fields have increased over time, for example by a factor of 4.2 in the UK from 1949 to 1989.

Data on fields in different countries

Several authors (e.g. Kaune et al., 1994; Kaune & Zaffanella, 1994; Merchant, Renew & Swanson, 1994a; Merchant, Renew & Swanson, 1994c; Perry et al., 1981; Silva et al., 1989; UKCCSI, 2000) have found that the distribution of fields in domestic settings was approximately lognormal, and other published data also appear to exhibit this structure. It is therefore assumed here that all distributions are approximately lognormal and, thus, are better characterised by their geometric mean (GM) and geometric standard deviation (GSD) than by their arithmetic mean (AM) and standard deviation (SD). For a log-normal distribution, GM and GSD can be calculated from AM and SD using the following formulae (Swanson & Kaune, 1999):

$$GM = \frac{AM^2}{\sqrt{AM^2 + SD^2}}$$

$$GSD = e^{\sqrt{\ln\left[1 + \left(\frac{SD}{AM}\right)^2\right]}}$$

Data from various countries show, that the geometric mean of spot measurements in homes do not vary dramatically. Geometric means of the data provided range between 48 nT and 107 nT in Canada (Donnelly & Agnew, 1991; Mader et al., 1990; McBride, 1998), 60 nT in Finland (Juutilainen, 1989), 26 nT to 29 nT in Germany (Michaelis et al., 1997; Schüz et al., 2000), 29 nT in New Zealand (Dockerty et al., 1998; 1999), 37 nT to 48 nT in Sweden (Eriksson et al., 1987; Tomenius, 1986), 29 nT to 64 nT in the UK (Coghill, Steward & Philips, 1996; Merchant, Renew & Swanson, 1994c; Preece et al., 1996; UKCCSI, 1999), and 47 nT to 99 nT in the USA (Banks et al., 2002; Bracken et al., 1994; Davis, Mirick & Stevens, 2002; Kaune et al., 1987; Kaune et al., 1994; Kaune & Zaffanella, 1994; Kavet, Silva & Thornton, 1992; Linet et al., 1997; London et al., 1991; Zaffanella, 1993; Zaffanella & Kalton, 1998). There is a tendency of higher fields in countries with lower distribution voltage. These data should, however, be interpreted with care, given great differences in the evaluation conditions (e.g. number of homes included).

2.2.2.2.4 Electrical equipment, appliances, and devices

The commonest source of magnetic field within a home is not the fixed wiring of the home but mains appliances. Every mains appliance produces a magnetic field when it is drawing current (and with some appliances, the mains transformer is still connected and drawing current whenever the appliance is plugged in, regardless of whether it is switched on or not). In a typical home the magnetic field consists of the background field with "peaks" of field surrounding each appliance. Exposure to magnetic fields from home appliances can sometimes usefully be considered separately from

exposure to fields due to power lines. Power lines produce relatively low-intensity, small-gradient fields that are always present throughout the home, whereas fields produced by appliances are invariably more intense, have much steeper spatial gradients, and are, for the most part, experienced only sporadically. The appropriate way of combining the two field types into a single measure of exposure depends critically on the exposure metric considered.

Magnetic fields from appliances are produced by electric current used by the devices. Currents in an appliance can often be approximated as small closed loops. Appliances of that type usually produce a comparatively small field, because any current within the appliance is balanced by a return current a comparatively short distance away. It is usually only in some appliances such as kettles, convection fires, electric blankets, that the current flows in the heating element round a reasonably large loop.

However, many appliances contain an electric motor, a transformer, or a choke or inductor. These all depend on magnetic fields for their operation: that is, they deliberately create a magnetic field inside the appliance. The magnetic field around those appliances (stray field) depends strongly on the design, which aims to keep stray fields as low as possible. If the design priorities are not efficiency but low cost, small size or low weight, the result will be an appliance that produces higher magnetic fields.

Thus higher fields are often produced by small and cheap transformers (e.g. mains adaptors, transistor radios) and small, cheap and compact motors (e.g. mains razors, electric can openers). A survey of 57 mains appliances conducted for National Grid in 1992 (Swanson, 1996) found that the field produced by an appliance was, on average, independent of the power consumed by the appliance.

Whether it is produced directly by the currents or indirectly by leakage field from a transformer or motor, the magnetic field produced by an appliance usually falls as one over the distance cubed. In consequence, magnetic fields from appliances tend to be significant only close to the appliance itself. More than a metre or two away, they have usually become so small that they have effectively merged into the background field. Very close to an appliance, the fields can rise to quite high levels; hundreds of microteslas on the surface of many mains radios, and over a millitesla on the surface of some mains razors. Exactly how high the field rises depends not just on the size of the field produced by the source (motor or transformer) inside the appliance, but also on how close the source can be approached. This depends on where within the volume of the appliance the source is located.

Examples of the field levels likely to be encountered at short distances from various appliances are presented in Table 9.

Table 9. Examples of magnetic flux densities from 50 and 60 Hz domestic electrical appliances [a]

	Source	Magnetic flux densities (μT)			
		60 Hz at 30 cm [b]		50 Hz at 50 cm [c]	
		Median	Range [d]	Computed field	SD
Bathroom	Hair dryers	1	bg***–7	0.12	0.1
	Electric shavers	2	bg–10	0.84	
	Electric showers			0.44	0.75
	Shaver socket			1.24	0.27
Kitchen	Blenders	1	0.5–2	0.97	1.05
	Can openers	15	4–30	1.33	1.33
	Coffee makers	bg	bg–0.1	0.06	0.07
	Dishwashers	1	0.6–3	0.8	0.46
	Food processors	0.6	0.5–2	0.23	0.23
	Microwave ovens	0.4	0.1–20	1.66	0.63
	Mixers	1	0.5–10	0.69	0.69
	Electric ovens	0.4	0.1–0.5	0.39	0.23
	Refrigerators	0.2	bg–2	0.05	0.03
	Freezers			0.04	0.02
	Toasters	0.3	bg–0.7	0.09	0.08
	Electric knives			0.12	0.05
	Liquidisers			0.29	0.35
	Kettle			0.26	0.11
	Extractor fan			0.5	0.93
	Cooker hood			0.26	0.10
	Hobs			0.08	0.05
Laundry/Utility	Clothes dryers	0.2	bg–0.3	0.34	0.42
	Washing machines	0.7	0.1–3	0.96	0.56
	Irons	0.1	0.1–0.3	0.03	0.02
	Portable heaters	2	0.1–4	0.22	0.18
	Vacuum cleaners	6	2–20	0.78	0.74
	Central heating boiler			0.27	0.26
	Central heating timer			0.14	0.17
Living room	TVs	0.7	bg–2	0.26	0.11
	VCRs			0.06	0.05
	Fish tank pumps			0.32	0.09
	Tuners/tape players	bg	bg–0.1	0.24	

Table 9. Continued.					
	Audio systems			0.08	0.14
	Radios			0.06	0.04
	Bedroom				
	Clock alarm	0-50		0.05	0.05
Office	Air cleaners	3.5	2–5		
	Copy machines	2	0.2–4		
	Fax machines	bg	bg–0.2		
	Fluorescent lights	0.6	bg–3		
	VDUs	0.5	0.2–0.6	0.14	0.07
Tools	Battery chargers	0.3	0.2-0.4		
	Drills	3	2-4		
	Power saws	4	0.9-30		
Miscellaneous	Central heating pump			0.51	0.47
	Burglar alarm			0.18	0.11

[a] Source: ICNIRP, 2003.

[b] Source: EPA, 1992.

[c] Source: Preece et al., 1997.

[d] bg: background.

Preece et al. (1997) assessed broadband magnetic fields at various distances from domestic appliances in use in the United Kingdom. The magnetic fields were calculated from a mathematical model fitted to actual measurements made on the numbers of appliances. They reported that few appliances generated fields in excess of 0.2 μT at 1 meter distance: microwave cookers 0.37 ± 0.14 μT; washing machines 0.27 ± 0.14 μT; dishwashers 0.23 ± 0.13 μT; some electric showers 0.11 ± 0.25 μT and can openers 0.20 ± 0.21 μT.

Gauger (1984) and Zaffanella & Kalton (1998) reported narrow band and broadband data, respectively, for the USA. In Gauger's analysis of hand held hair dryers, at 3 cm from their surfaces, magnetic felds of about 6, 15, and 22 μT were produced for three types of hair dryers. Zaffanella (1993) found that at a distance of 27 cm from digital and analog clocks/clock radios, the median fields were 0.13 μT and 1.5 μT for digital and analog clocks, respectively. Preece et al. (1997) also measured the magnetic fields produced by hair dryers and electric clocks. At distances of 5 and 50 cm from hair dryers field measurements were 17 and 0.12 μT, respectively, and from electric clocks 5.0 and 0.04 μT, respectively.

Florig & Hoburg (1990) characterized fields from electric blankets, using a three-dimensional computer model; maximum, minimum, and volume-average fields within human forms were presented as a function of blanket type and geometric factors such as body size, body-blanket separation,

and lateral body position. They reported that when blankets are heating, typical flux densities range from a few tenths of microtesla on the side of the body farthest from the blanket to a few tens of microtesla on the side closest to the blanket. Wilson et al. (1996) used spot measurements made in the home and in the laboratory. They reported that the average magnetic fields from electric blankets to which the whole body is exposed are between 1 and 3T. More recently, from eight-hour measurements, Lee et al. (2000) estimated that the time-weighted average magnetic field exposures from overnight use of electric blankets ranged between 0.1 and 2 μT.

It should be noted that many appliances produce a wide range of harmonics. The interpretation of results from broad band measurements can be misleading, if the spectral content of the fields is not known. Another problem with the interpretation of field measurements from appliances may result from the huge spatial and temporal variability of the fields.

2.2.2.2.5 Distribution substations and transformers

Overhead lines and underground cables at whatever voltage usually terminate at substations. All substations usually contain apparatus to perform similar functions: transforming, switching metering and monitoring. Substations range from large complexes several hundred metres in extent at one end of the scale to simple pole-mounted transformers at the other end of the scale. One feature they all have in common is that members of the general public are excluded from most of the functional regions of the substation, either by a perimeter fence or enclosure (for ground-based substations) or by the height of the pole (for pole-mounted substations).

Although substations vary in their complexity and size, the principles which determine the magnetic fields they produce are common. Firstly, in all substations, there are a number of components which produce a negligible magnetic field outside the confines of the substation. These include the transformers, virtually all switches and circuit breakers, and virtually all metering and monitoring equipment. Secondly, in many cases the largest fields in publicly accessible regions are produced by the overhead lines and underground cables running in and out of the substation. Thirdly, all substations contain a system of conductors (often referred to as ‘busbars’) which connect the various components within it, and these busbars usually constitute the main source of magnetic field within the substation producing appreciable field outside.

The size of the currents and the separation of the busbars are both larger in higher-voltage substations than in lower-voltage ones. However, the perimeter fence also tends to be further away from the busbars in higher-voltage substations. Therefore, the resulting field to which the public can be exposed can be somewhat greater at higher-voltage substations than at lower-voltage ones. In both cases, the magnetic field falls very rapidly with distance from the substation.

Typical values in the United Kingdom for substations of 275 and 400 kV at the perimeter fence is 10 μT, and 1.6 μT for an 11 kV substation. Renew, Male & Maddock found the mean field at the substation boundary, measured at about 0.5 m above ground level, to be 1.6 μT (range: 0.3–10.4 μT) (Renew, Male & Maddock, 1990). They also found (for the 19 substations where the background field was low enough to enable this measurement to be made) the mean distance at which the field at the substation boundary was halved to be 1.4 m (range: 0.6–2.0 m). NRPB has performed similar measurements on 27 substations in the UK with similar findings (Maslanyj, 1996). The mean field at the substation boundary was 1.1 μT, with a field of 0.2 μT at between 0–1.5 m from the boundary and a field of 0.05 μT at between 1–5 m.

2.2.2.2.6 Transport

Dietrich & Jacobs (1999) have reported magnetic fields associated with various transportation systems across a range of frequencies. AC currents of several hundred amperes are commonly used in electric railway systems, and magnetic fields are highly variable with time, the maxima often occurring during braking and acceleration. Up to a few millitesla can be generated near motor equipment, and up to a few tens of microteslas elsewhere on the trains (Table 10). Elevated ELF exposure levels also occur in the areas adjacent to electrified rail lines. Peak magnetic flux densities up to a few tens of microteslas have been recorded on the platform of a local city railway line (EC, 1996). Magnetic flux densities of a few microteslas were measured at 5 m from the line reducing to a microtesla or so at 10 m. In France, measurements inside a high-speed train and at a distance of 10 m outside the train showed peak values around 6 to 7 μT during high-speed drive (Gourdon, 1993). In a Swedish study (Anger, Berglund & Hansson Mild, 1997) field values in the driver cabinet range from a few to over 100 μT with mean values for a working day between a few to up to tens of microteslas depending on the engine. Some UK results are summarized in Table 10.

The magnetic fields encountered in electrified rail systems vary considerably because of the large variety of possible arrangements of power supply and traction. Many of the conventional rail systems use DC traction motors and AC power supplies with frequencies of 16 2/3 Hz or 50 Hz AC power in Europe and 25 Hz or 60 Hz in North America. Such systems often rely on pulse rectification either carried out on board or prior to supply and this gives rise to a significant alternating component in the static or quasi–static magnetic fields from the traction components of the trains (Chadwick & Lowes, 1998). Major sources of static and alternating magnetic fields are the smoothing and line filter inductors and not the motors themselves, which are designed to minimise flux leakage. Alternatively where DC supplies are used, voltage choppers are used to control the power by switching the power supply on and off regularly. Recently AC motors have become more common with the advances in high capacity solid-state technologies. When the required frequency differs from that of the supply frequency, converters are used to supply the correct frequency, or inverters are used when the power supply is DC (Muc, 2001).

Table 10. Alternating magnetic fields from UK electrified rail systems [a]

System and Source	AC magnetic flux density	Frequency	Comments
London underground	Up to 20 μT	100 Hz	In the driver's cab; arising from traction components and on board smoothing inductors
Suburban trains			
750 DC Electric	Up to 1 mT	100 Hz	Floor level
Motor Units	16–64 μT	100 Hz	In passenger car at table height
	16-48 μT	100 Hz	Outside train on platform
Mainline trains			
Electric Motor Units	Up to 15 mT	100 Hz	Floor level above inductor
Mainline trains			
Locomotives	Up to 2.5 mT	100 Hz	0.5 m above floor in equipment car
	5–50 μT	50 Hz	In passenger coaches

[a] Source: Allen et al., 1994; Chadwick & Lowes, 1998.

Train drivers and railway workers incur higher exposures than passengers because they often work closer to important sources. Nordenson et al. (2001) reported that engine drivers were exposed to 16 2/3 Hz magnetic fields ranging from a few to more than 100 μT. Hamalainen et al. (1999) reported magnetic fields ranging in frequency from 10 Hz to 2 kHz measured in local and long distance electrified trains in Finland where roughly more than half of the rail network is electrified with 50 Hz. Average levels to which workers and passengers were exposed varied by a factor of 1000 (0.3–290 μT for passengers and 10–6000 μT for workers). On Swedish trains, Nordenson et al. (2001) found values ranging from 25 to 120 μT for power-frequency fields in the driver's cabin, depending on the type (age and model) of locomotive. Typical daily average exposures were in the range of 2–15 μT.

Wenzl (1997) reported measurements on a 25 Hz AC electrified portion of the Northeast Rail Corridor in Maryland and Pennsylvania. Averages for workers were found to range between 0.3 and 1.8 μT , although 60 Hz and 100 Hz fields were also present from transmission lines suspended above the railway catenaries and from the railway safety communications and signalling system respectively. Chadwick & Lowes (1998) reported flux densities of up to 15 mT modulated at 100 Hz at floor level on British Electric Motor Units and 100 Hz fields of up to 2.5 mT in mainline locomotives (Table 10).

Other forms of transport, such as aeroplanes and electrified road vehicles are also expected to increase exposure, but have not been investi-

gated extensively. Other possible ELF exposures associated with transport are discussed in 2.2.2.2.8.

2.2.2.2.7 Heating

The magnetic fields associated with underfloor heating systems depend on the configuration and depth of the cables, and the current flowing in them (Allen et al., 1994). Typically magnetic flux densities of up to a few microtesla can occur at floor level falling to a few tenths of a microtesla at 1 m above the floor. Systems operating at commercial premises can give up to a few hundred microtesla at floor level falling to a few tens of microtesla at 1 m above the floor. Many systems only draw current overnight, relying on off-peak electricity, and the heat capacity of the floor to provide warmth during the day.

2.2.2.2.8 Miscellaneous sources of ELF fields (other than power frequencies)

ELF magnetic fields are also generated in the home by petrol engine-powered devices such as lawnmowers, strimmers and chainsaws. Personal localised exposures of up to a few hundred microteslas can result when using such equipment (EC, 1996).

The pulsating battery current in the mobile phone generates a low-frequency nonsinusoidal magnetic field in the vicinity of the phone (Jokela, Puranen & Sihvonen, 2004). The time course is approximately a square wave with a pulse cycle similar to the radiation pattern of the phone (pulse width 0.7 to 1 ms with a repetition period of 4.6 ms). As the current drawn by the phones investigated (seven different types) was up to 3 A and the devices are used very close to the brain (approximately 10 mm), the field may exceed 50 μT.

Occupational exposure to ELF electric and magnetic fields from video display units (VDUs) has recently received attention. VDUs produce both power-frequency fields and higher-frequency fields ranging from about 50 Hz up to 50 kHz (NIEHS, 1998). Sandström et al. (1993) measured magnetic fields from VDUs in 150 offices and found that rms values measured at 50 cm from the screen ranged up to 1.2 μT (mean: 0.21 μT) in the ELF range (0–3 kHz) and up to 142 nT (mean: 23 nT) in the VLF range (3–30 kHz).

Cars are another source of ELF magnetic field exposure. Vedholm (1996) measured the field in 7 different cars (two of them with the battery underneath the back seat or in the trunk), engines running idle. In the left front seat the magnetic field, at various ELF frequencies ranged from 0.05 to 3.9 μT and in the left back seat from 0.02 to 3.8 μT. The highest values where parts of the body are likely to be were found at the left ankle at the left front seat, 0.24–13 μT. The higher values were found in cars with the battery located underneath the back seat or in the trunk.

Another source of ELF magnetic fields result from the steel belts in car tires that are permanently magnetized. Depending on the speed of the car,

this may cause magnetic fields in the frequency range below 20 Hz. The field has a fundamental frequency determined by the speed (rotation rate of the tire) and a high harmonic content. At the tread fields can exceed 500 μT and on the seats the maximum is approximately 2 μT (Milham, Hatfield & Tell, 1999).

2.2.2.2.9 Occupational exposure in the electric power industry

Strong magnetic fields are encountered mainly in close proximity to high currents (Maddock, 1992). In the electric power industry, high currents are found in overhead lines and underground cables, and in busbars in power stations and substations. The busbars close to generators in power stations can carry currents up to 20 times higher than those typically carried by the 400-kV transmission system (Merchant, Renew & Swanson, 1994b).

Exposure to the strong fields produced by these currents can occur either as a direct result of the job, e.g. a lineman or cable splicer, or as a result of work location, e.g. when office workers are located on a power station or substation site. It should be noted that job categories may include workers with very different exposures, e.g. linemen working on live or dead circuits. Therefore, although reporting magnetic-field exposure by job category is useful, a complete understanding of exposure requires a knowledge of the activities or tasks and the location as well as measurements made by personal exposure meters.

The average magnetic fields to which workers are exposed for various jobs in the electric power industry have been reported as follows: 0.18–1.72 μT for workers in power stations, 0.8–1.4 μT for workers in substations, 0.03–4.57μT for workers on lines and cables and 0.2–18.48 μT for electricians (AGNIR, 2001b; NIEHS, 1998).

2.2.2.2.10 Other occupational sources

Exposure to magnetic fields varies greatly across occupations. The use of personal dosimeters has enabled exposure to be measured for particular types of job.

Measurements by the National Institute for Occupational Safety and Health (NIOSH) in various industries are summarized in Table 11 (NIOSH, 1996).

In some cases the variability is large. This indicates that there are instances in which workers in these categories are exposed to far stronger fields than the means listed here.

Floderus et al. (1993) investigated sets of measurements made at 1015 different workplaces. This study covered 169 different job categories, and participants wore the dosimeters for a mean duration of 6.8 h. The most common measurement was 0.05 μT and measurements above 1 μT were rare.

Table 11. Magnetic flux densities from equipment in various industries [a]

Industry	Source	ELF magnetic flux density (μT)	Comments	Other frequencies
Manufacturing	Electrical resistance heater	600–1400	Tool exposures measured at operator's chest	VLF
	Induction heater	1–46		
	Hand-held grinder	300		
	Grinder	11		
	Lathe, drill press etc	0.1–0.4		
Electrogalvanizing	Rectification	200–460	Rectified DC current (with an ELF ripple) galvanized metal parts	Static fields
	Outdoor electric line and substation	10–170		
Aluminum refining	Aluminum pot rooms	0.34–3	Highly-rectified DC current (with an ELF ripple) refines aluminum	Static field
	Rectification room	30–330		Static field
Steel foundry	Ladle refinery, electrodes active	17–130	Highest ELF field was at the chair of control room operator	ULF from ladle's magnetic stirrer
	Electrodes inactive	0.06–0.37		
	Electrogalvanizing unit	0.2–110		VLF
Television broadcasting	Video cameras (studio and minocam)	0.72–2.4	Measured at 30 cm	VLF
	Video tape degaussers	16–330		
	Light control centres	0.1–30		
	Studios and newsrooms	0.2–0.5	Walk-through surveys	

Table 11. Continued.

Telecommunications	Relay switching racks	0.15–3.2	Measured 5-7 cm from relays	Static fields and ULF-ELF transients
	Switching rooms (relay and electronic switches)	0.01–130	Walk-through survey	Static fields and ULF-ELF transients
	Underground phone vault	0.3–0.5	Walk-through survey	Static fields and ULF-ELF transients
Hospitals	Intensive care unit	0.01–22	Measured at nurse's chest position	VLF
	Post anaesthesia care unit	0.01–2.4		VLF
	Magnetic resonance imaging	0.05–28	Measured at technician's work locations	Static, VLF and RF
Government offices	Desk work locations	0.01–0.7	Peaks due to laser printers	
	Desks near power centre	1.8-5		
	Power cables in floor	1.5–17		
	Computer centre	0.04–0.66		
	Desktop cooling fan	100	Appliances measured at 15 cm	
	Other office appliances	1–20		
	Building power supplies	2.5–180		

[a] Source: (NIOSH, 1996).

2.2.2.2.11 Arc and spot welding

In arc welding, metal parts are fused together by the energy of a plasma arc struck between two electrodes or between one electrode and the metal to be welded. A power-frequency current usually produces the arc but higher frequencies may be used in addition to strike or to maintain the arc. A feature of arc welding is that the insulated welding cable, which can carry currents of hundreds of amperes, can touch the body of the operator. Magnetic flux densities in excess of 1 mT have been measured at the surface of a welding cable and 100 μT close to the power supply (Allen et al., 1994).

Stuchly & Lecuyer (1989) surveyed the exposure of arc welders to magnetic fields and determined the exposure at 10 cm from the head, chest, waist, gonads, hands and legs. Whilst it is possible for the hand to be exposed to fields in excess of 1 mT, the trunk is typically exposed to several hundred microtesla. Once the arc has been struck, these welders work with comparatively low voltages and this is reflected in the electric field strengths measured; i.e. up to a few tens of volts per metre (AGNIR, 2001b).

Bowman et al. (1988) measured exposure for a tungsten-inert gas welder of up to 90 μT. Similar measurements reported by the National Radiological Protection Board indicate magnetic flux densities of up to 100 μT close to the power supply, 1 mT at the surface of the welding cable and at the surface of the power supply and 100–200 μT at the operator position (AGNIR, 2001b). London et al. (1994) reported the average workday exposure of 22 welders and flame cutters to be much lower (1.95 μT).

2.2.2.2.12 Induction furnaces

Electrically conducting materials such as metals and crystals can be heated as a consequence of eddy current losses induced by alternating magnetic fields. Typical applications include drying, bonding, zone refining, melting, surface hardening, annealing, tempering, brazing and welding. The main sources of electromagnetic fields in induction heaters are the power supply, the high frequency transformer and the induction heater coil, and the product being processed. The latter is positioned within a coil, which acts like a primary winding of a transformer. This coil generates magnetic fields that transfer power to the load, which behaves like a single turn short-circuited secondary winding.

The frequency determines the penetration of the field, a lower frequency being used for volume heating and a higher frequency for surface heating. For example frequencies of a few tens of hertz are used for heating copper billets prior to forging, whereas frequencies of a few megahertz are used for sealing bottle tops. The heating coils range in size depending on the application. Small single turn devices of a few centimetres diameter are used for localised heating of a product, and large multi-turn systems of 1 or 2 m diameter are used in furnaces capable of melting several tons of iron. Power requirements also depend on the application, and range from about 1 kW for small items to several megawatt for induction furnaces (Allen et al., 1994).

Studies of magnetic flux densities in the vicinity of induction furnaces and equipment heaters have shown that operators may have some of the highest maximum exposure levels found in industry (Table 12). Typical maximum flux densities for induction heaters operating at frequencies up to 10 kHz are presented in Table 13. Somewhat higher levels of 1–60 mT have been reported in Sweden (Lövsund, Öberg & Nilsson, 1982), at distances of 0.1–1 m.

Table 12. Maximum exposures to power frequency magnetic flux densities in the workplace [a]

Workplace	Occupation / source	Magnetic flux density (μT)
Industry	Induction workers	10^4
	Railway workers	10^3
	Power industry	10^3
	Arc welders	10^2
Office	Tape erasers	10^2
	VDUs	1
General	Underfloor heating	10
	Electric motors	10

[a] Source: Allen et al., 1994.

Table 13. Examples of magnetic fields produced by induction heaters operating up to 10 kHz [a]

Machine	Input power	Frequency	Position	Maximum magnetic flux density (μT)
Copper billet heater	Up to 6 MW	50 Hz	1 m from coil line	540
Steel billet heater	~ 800 kW	1.1 kHz	1 m from coil	125
Axle induction hardener	140 kW	1.65 kHz	Operator position	29
Copper tube annealer	600 kW	2.9 kHz	0.5 m from coil	375
Chain normalisers	20 kW	8.7–10 kHz	0.5 m from coils	25

[a] Source: Allen et al., 1994.

Electric field strengths in the vicinity of induction heaters that operate in the frequency range of interest are usually no more than several volts per metre.

2.2.2.2.13 Induction cooking equipment

Originally induction cooking equipment was restricted largely to commercial catering environments where three phase power supplies were available; however, single phase domestic varieties are now common (IEC, 2000). Induction cooking hobs normally operate at frequencies of a few tens of kilohertz. In domestic environments a frequency of over 20 kHz is necessary to avoid pan noise and below 50 kHz to have a maximum efficiency and comply with electromagnetic compatibility product standards. Powers normally range between 1–3 kW used for domestic appliances and 5–10 kW for commercial equipment. Under worst-case exposure conditions, corresponding to poor coupling between the coil and pan, maximum magnetic flux den-

sities are usually less than a few microtesla at a few tens of centimetres from the front edge of the hobs. Electric field strengths are usually no more than a few tens of volt per metre because the appliances do not use high voltage electricity. Usually the fundamental frequency induction dominates the magnetic field; however, some models produce harmonic components comparable in magnitude to that of the fundamental (Allen et al., 1994).

2.2.2.2.14 Security and access control systems

A number of devices generate electromagnetic fields for security purposes and for controlling personal access. These include metal detectors, radiofrequency identification (RFID) equipment and electronic article surveillance (EAS) systems, also known as anti-theft systems. RFID and EAS equipment use a broad range of frequencies, ranging from sub-kilohertz frequencies to microwave frequencies.

Metal detectors

Metal detectors are used for security, e.g. at airports. The two main types are the free-standing walk-through systems and the hand-held detectors. Walk-through detectors usually consist of two columns, one which houses the transmitter unit and uses conducting coils to produce a pulsed magnetic field, and the other which contains a receiver which employs a set of coils to detect the electric currents induced in metallic objects by the pulsed field. The magnetic field waveforms from both detectors consist of a train of bipolar pulses and fast Fourier transforms (FFTs) of the pulses exhibit broad spectral content with an amplitude peak in the region of 1 kHz. Peak magnetic fields are usually a few tens of microtesla (Cooper, 2002).

Hand-held detectors normally contain a coil, which carries an alternating current, at frequencies of a few tens of kilohertz. If electrically conducting material is brought within the detection range of the device, eddy currents are produced in the material that disturb the configuration of the magnetic field. The corresponding change in the behaviour of the coil, which may be resonant, can then be detected by the instrument.

The magnetic fields from hand-held metal detectors tend to be weaker and more localised than those from walk-through devices. The maximum magnetic flux density encountered near the casing is typically a few microtesla (Cooper, 2002).

Electronic access and security systems (EAS)

EAS systems use electromagnetic fields to prevent unauthorised removal of items from shops, libraries and supermarkets and are even used in hospitals to stop abduction of babies. The detection panels are the most significant source of electromagnetic fields. The tags or labels serve only to cause a slight perturbation of the fields in the detection systems and are usually passive in the sense that they do not contain any power source, although they may contain a small number of electronic components such as diodes.

The third component of EAS systems is known as “deactivators”. These are used to “switch off” disposable tags or to remove re-usable tags. The deactivator fields are usually higher in absolute amplitude than the main detection fields, though they are confined to a small region.

There are two main types of EAS system that operate within the ELF-VLF range. Both use inductive fields, so the field is almost completely magnetic in nature, and the field propagation is negligible (ICNIRP, 2002; IEC, 2000).

The electromagnetic (EM) type operates at frequencies of 20 Hz–20 kHz and detects harmonics in the detection field that are set up during the non-linear magnetisation of the magnetically soft tag. The magnetic flux density at the point midway through panels normally placed 1–3 m apart is from a few tens of microtesla up to about 100 μT. Typical field strengths fall as the operating frequency rises and some systems use more than one frequency simultaneously.

The resonant acousto-magnetic (AM) type operates at typical frequencies around 60 kHz, and detects the ringing of the tag’s magnetic field caused by an element that resonates in the presence of a specific frequency pulsed magnetic field that occurs in the detection zone.

Some examples of maximum magnetic flux densities inside EAS gates are reported in Table 14.

Table 14. Examples of peak magnetic flux densities within magnetic type EAS gates

Type	Frequency (waveform [a])	Magnetic flux density (μT)	Distance from transmitter (cm)
Electromagnetic (EM)	73 Hz (SCW)	146	31.5
	219 Hz (SCW)	122	36
	230 Hz (SCW)	93	42
	535.7 Hz (SCW)	72	36
	6.25 kHz (SCW)	39	45
	5 kHz / 7.5 kHz (CW)	43	48.5
	1 kHz (PMS)	100	41
	6.25 kHz (CW)	58	25.7
Acoustomagnetic (AM)	58 kHz (PMS)	65	36
	58 kHz (PMS)	17.4	62.5
	58 kHz (CW)	52	37.2

[a] CW = Continuous Wave, SCW = Sinusoidal Continuous Wave, PMS = Pulsed Modulated Sinusoid.

Members of the public receive transient exposure to the main detection field because of the method of use of EAS systems; workers receive longer-term whole body exposure to lower amplitude fields outside the detection system and transient localised exposures from the deactivators.

2.2.2.2.15 Sewing machines

Hansen et al. (2000) reported higher-than-background magnetic fields near industrial sewing machines, because of proximity to motors, with field strengths ranging from 0.32–11.1 μT at a position corresponding approximately to the sternum of the operator. The average exposure for six workers working a full work-shift in the garment industry ranged from 0.21–3.20 μT. A more extensive study of the personal exposures of 34 workers using sewing machines reported exposures (Kelsh et al., 2003) at the waist, where the mean 60-Hz magnetic field was 0.9 μT with a range between 0.07–3.7 μT.

2.3 Assessment of exposure

2.3.1 General considerations

Electric and magnetic fields are complex and can be characterized by many different physical parameters. Some of these parameters are discussed more fully in section 2.1. In general, they include transients, harmonic content, peak values and time above thresholds, as well as average levels. It is not known which of these parameters or what combination of parameters, if any, are relevant for the induction of health effects. If there were a known biophysical mechanism of interaction for e.g. carcinogenesis, it would be possible to identify the critical parameters of exposure, including relevant timing of exposure. However, in the absence of a generally accepted mechanism, most exposure assessments in epidemiological studies are based on a time-weighted average of the field, a measure that is also related to some, but not all field characteristics (Zaffanella & Kalton, 1998).

The physical characteristics of electric and magnetic fields have been described in detail in section 2.1. Some of the characteristics of exposure to electric and magnetic fields which make exposure assessment for the purposes of epidemiological studies particularly difficult are listed below.

- *Prevalence of exposure*. Everyone in the population is exposed to some degree to ELF electric and magnetic fields and therefore exposure assessment can only separate the more from the less exposed individuals, as opposed to separating individuals who are exposed from those who are not.
- *Inability of subjects to identify exposure.* Exposure to electric and magnetic fields, whilst ubiquitous, is usually not detectable by the exposed person nor memorable, and hence epidemiological studies cannot rely solely on questionnaire data to characterize past exposures adequately.

- *Lack of clear contrast between "high" and "low" exposure*. The difference between the average field strengths to which "highly exposed" and "less highly exposed" individuals in a population are subjected is not great. The typical average magnetic fields in homes appear to be about 0.05–0.1 μT. Pooled analyses of childhood leukaemia and magnetic fields, such as that by Ahlbom et al. (2000), have used 0.4 μT as a high-exposure category. Therefore, an exposure assessment method has to separate reliably exposures which may differ by factors of only 2 or 4. Even in most of the occupational settings considered to entail "high exposures" the average fields measured are only one order of magnitude higher than those measured in residential settings (Kheifets et al., 1995).
- *Variability of exposure over time*: *short-term*. Fields (particularly magnetic fields) vary over time-scales of seconds or longer. Assessing a person's exposure over any period involves using a single summary figure for a highly variable quantity.
- *Variability of exposure over time: long-term*. Fields are also likely to vary over time-scales of seasons and years. With the exception of historical data on loads carried by high-voltage power lines, data on such variation are rare. Therefore, when a person's exposure at some period in the past is assessed from data collected later, an assumption has to be made. The usual assumption is that the exposure has not changed. Some authors (e.g. Jackson, 1992; Petridou et al., 1993; Swanson, 1996) have estimated the variations of exposure over time from available data, for example, on electricity consumption. These apply to population averages and are unlikely to be accurate for individuals.
- *Variability of exposure over space*. Magnetic fields vary over the volume of, for example, a building so that, as people move around, they may experience fields of varying intensity. Personal exposure monitoring captures this, but other assessment methods generally do not.

People are exposed to fields in different settings, such as at home, at school, at work, while travelling and outdoors. Current understanding of the contributions to exposure from different sources and in different settings is limited. Most studies make exposure assessments within a single environment, typically at home for residential studies and at work for occupational studies. Some recent studies have included measures of exposure from more than one setting (e.g. Feychting, Forssen & Floderus, 1997; Forssén et al., 2000; UKCCSI, 1999).

In epidemiological studies, the distribution of exposures in a population has consequences for the statistical power of the study. Most populations are characterized by an approximately log-normal distribution with a heavy preponderance of low-level exposure and much less high-level expo-

sure. Pilot studies of exposure distribution are important for developing effective study designs.

Since most epidemiological studies have investigated magnetic rather than electric fields, the next six sections will deal with aspects of magnetic field exposure and section 2.3.7 with electric field exposure.

2.3.2 Assessing residential exposure to magnetic fields: methods not involving measurement

2.3.2.1 Distance

The simplest possible way of assessing exposure is to record proximity to a facility (such as a power line or a substation) which is likely to be a source of field. This does provide a very crude measure of exposure to both electric and magnetic fields from that source, but takes no account of other sources or of how the fields vary with distance from the source (which is different for different sources). Distances reported by study subjects rather than measured by the investigators tend to be unreliable. Recently over half of the time-averaged magnetic field exposures above 0.4 μT in the UKCCS were attributable to sources other than high-voltage power lines (Maslanyj et al., 2007).

2.3.2.2 Wire code

Wire coding is a non-intrusive method of classifying dwellings on the basis of their distance from visible electrical installations and the characteristics of these installations. This method does not take account of exposure from sources within the home. Wertheimer & Leeper (1979) devised a simple set of rules to classify residences with respect to their potential for having a higher-than-usual exposure to magnetic fields. Their assumptions were simple:

- the field strength decreases with distance from the source;
- current flowing in power lines decreases at every pole from which "service drop" wires deliver power to houses;
- if both thick and thin conductors are used for lines carrying power at a given voltage, and more than one conductor is present, it is reasonable to assume that more and thicker conductors are required to carry greater currents; and
- when lines are buried in a conduit or a trench, their contribution to exposure can be neglected. This is because buried cables are placed close together and the fields produced by currents flowing from and back to the source cancel each other much more effectively than when they are spaced apart on a cross beam on a pole (see section 2.2.2.2.2).

Wertheimer & Leeper (1979) used these four criteria to define two and later four (Wertheimer & Leeper, 1982), then five (Savitz et al., 1988)

classes of home: VHCC (very high current configuration), OHCC (ordinary high current configuration), OLCC (ordinary low current configuration), VLCC (very low current configuration) and UG (underground, i.e. buried). The houses with the higher classifications were assumed to have stronger background fields than those with lower classifications. According to this classification scheme, residences more than 40 m from power lines were considered to be not exposed to magnetic fields.

Wire coding, in the original form developed by Wertheimer and Leeper, has been used in a number of studies. The ranges of measurements by wire code category for five substantial data sets – the control groups from the Savitz et al. (1988) and London et al. (1991) studies, the HVTRC survey (Zaffanella, 1993), the EMDEX Residential Project (Bracken et al., 1994) and the NCI study (Tarone et al., 1998) – indicate a positive relationship between the mean of the distributions and the wire code (i.e. higher averages are seen for higher wire code categories), but there is a large overlap among the various categories.

Kheifets, Kavet & Sussman (1997) evaluated relationships between wire codes and measured fields in the data sets available to them (EMDEX; HVTRC and London). The relationships were quite similar across data sets; thus only selected examples are presented below. Log-transformed spot measurement data for all 782 single and duplex residences and for all wire codes, except VLCC, from the HVTRC survey, were distributed log-normally. The data indicate a 10th-to-90th percentile interval of about an order of magnitude for all the wire codes, considerable overlap in the field range across wire codes (as mentioned above), equivalent fields for UG and VLCC (which are sometimes grouped as referent categories), and a trend of increasing field with wire code. For this data, wire code explains 14.5% of the total variance in the log of the spot-measured fields (Kheifets, Kavet & Sussman, 1997).

There are many reasons for a discordance between wire codes and measurement classifications (for simplicity, a dichotomous classification scheme is used). For example, while number and thickness of wires reflect the total current carrying capacity of a system of wires, this does not take into account differences in geometry, phasing schemes in multi-circuit systems that enhance field cancellation, and actual loading patterns. Thus high wire code homes may actually have relatively low fields. Similarly, low wire code homes may exhibit high readings due to high field levels from non-power line sources, or from very heavily loaded external sources. Data available to date shows that the "high wire code–low measurement" situation is far more prevalent than the "low wire code–high measurement" circumstance.

While wire codes explain little of the variance of measured residential magnetic fields, they are useful in identifying homes with potentially high magnetic fields. In particular, the majority of homes with high interior measurements fell into the VHCC category. And although most of the misclassification occurs from homes in high wire code categories having low measurements, the VHCC category still performs reasonably well in excluding homes with low measurements (Kheifets, Kavet & Sussman, 1997).

The concept of wire coding has been shown to be a usable crude surrogate even when tailored to local wiring practices. For example, the correlation between wiring code and measured magnetic fields in homes in the Savitz et al. (1988) study accounted for only 16% of the variance in the measured field values. Rankin et al. (2002) report that wire code predicts < 21% of the variance in magnetic field measurements. The wire code is overall an imperfect surrogate for magnetic field exposure in a variety of environments. In general, wire codes have been used only in North American studies, as their applicability is limited in other countries, where power drops to homes are mostly underground.

2.3.2.3 Calculated historical fields

Feychting & Ahlbom (1993) carried out a case–control study nested in a cohort of residents living in homes within 300 m of power lines in Sweden. The geometry of the conductors on the power line, the distance of the houses from the power lines and historical records of currents, were all available. This special situation allowed the investigators to calculate the fields to which the subjects' homes were exposed at various times (e.g. prior to diagnosis) (Kheifets et al., 1997).

The common elements between wire coding and the calculation model used by Feychting & Ahlbom (1993) are the reliance on the basic physical principles that the field increases with the current and decreases with the distance from the power line, and the fact that both neglect magnetic-field sources other than visible power lines. There is, however, one important difference: in the Wertheimer and Leeper code, the line type and thickness are a measure of the potential current carrying capacity of the line. In the Feychting & Ahlbom (1993) study, the approximate yearly average current was obtained from utility records; thus the question of temporal stability of the estimated fields did not even arise: assessment carried out for different times, using different load figures, yielded different estimates.

The approach of Feychting & Ahlbom (1993) has been used in various Nordic countries and elsewhere, although the likely accuracy of the calculations has varied depending in part on the completeness and precision of the available information on historical load. The necessary assumption that other sources of field are negligible is reasonable only for subjects relatively close to high-voltage power lines. The validity of the assumption also depends on details such as the definition of the population chosen for the study and the size of average fields from other sources to which the relevant population is exposed.

There is some evidence from Feychting & Ahlbom (1993) that their approach may work better for single-family homes than for apartments. When Feychting & Ahlbom (1993) validated their method by comparing calculations of present-day fields with present-day measurements, they found that virtually all homes with a measured field < 0.2 μT, whether single-family or apartments, were correctly classified by their calculations. However,

for homes with a measured field > 0.2 μT, the calculations were able to classify correctly 85% of single-family homes, but only half of the apartments.

The difference between historical calculations and contemporary measurements was also evaluated by Feychting & Ahlbom (1993) who found that calculations using contemporary current loads resulted in a 45% increase in the fraction of single-family homes estimated to have a field > 0.2 μT, compared with calculations based on historical data. If these calculations of historical fields do accurately reflect exposure, this implies that present-day spot measurements overestimate the number of exposed homes in the past.

When fields are calculated from transmission lines and then used as an estimate of the exposure of a person, the assumption is made that fields from other sources are negligible. Close to the transmission line where the field from the line is high, it would be rare for other (principally distribution) sources to produce as high a field, and this is a valid assumption. As the distance from the power line is increased (or equivalently as the threshold between exposed and non-exposed is lowered), the assumption becomes less valid, and misclassification will result. An example of this can be seen in the Feychting & Ahlbom (1993) study where it has been observed that there is substantial calculation error by comparing their contemporary calculations and measurements (Jaffa, Kim & Aldrich, 2000). This error was more pronounced in the lower exposure categories (Feychting & Ahlbom, 2000). These calculation errors in the lower exposure categories are likely the result of not including the field contribution from local sources, which make a greater contribution to exposures at larger distances from transmission lines. This error can negate the value of estimating historical exposures such that contemporary measurements can be a more reliable metric for effect estimates (Jaffa, 2001; Maslanyj et al., 2007; Mezei & Kheifets, 2001).

2.3.3 Assessing residential exposure to magnetic fields using measurements

Following the publication of the Wertheimer & Leeper (1979; 1982) studies, doubt was cast on the reported association between cancer and electrical wiring configurations on the grounds that exposure had not been measured. Consequently, many of the later studies included measurements of various types.

All measurements have the advantage that they capture exposure from whatever sources are present, and do not depend on prior identification of sources, as wire codes and calculated fields do. Furthermore, because measurements can classify fields on a continuous scale rather than in a limited number of categories, they provide greater scope for investigating different thresholds and exposure–response relationships.

2.3.3.1 Spot measurements in the home

The simplest form of measurement is a reading made at a point in time at one place in a home. To capture spatial variations of field, some studies have made multiple spot measurements at different places in or around

the home. In an attempt to differentiate between fields arising from sources inside and outside the home, some studies have made spot measurements under "low-power" (all appliances turned off) and "high-power" (all appliances turned on) conditions. Neither of these alternatives truly represents the usual exposure conditions in a home, although the low-power conditions are closer to the typical conditions.

The major drawback of spot measurements is their inability to capture temporal variations. As with all measurements, spot measurements can assess only contemporary exposure, and can yield no information about historical exposure, which is an intrinsic requirement for retrospective studies of cancer risk. An additional problem of spot measurements is that they give only an approximation even for the contemporary field, because of short-term temporal variation of fields, and unless repeated throughout the year do not reflect seasonal variations.

A number of authors have compared the time-stability of spot measurements over periods of up to five years (reviewed in Kheifets et al., 1997; UKCCSI, 2000). The correlation coefficients reported were from 0.7–0.9, but even correlation coefficients this high may result in significant misclassification (Neutra & Del Pizzo, 1996).

2.3.3.2 Longer-term measurements in homes

Because spot measurements capture short-term temporal variability poorly, many studies have measured fields at one or more locations for longer periods, usually 24–48h, most commonly in a child's bedroom, which is an improvement on spot measurements. Comparisons of measurements have found only a poor-to-fair agreement between long-term and short-term measurements. This was mainly because short-term increases in fields caused by appliances or indoor wiring do not affect the average field measured over many hours (Schüz et al., 2000).

Measurements over 24–48 h cannot account for longer-term temporal variations. One study (UKCCSI, 1999) attempted to adjust for longer-term variation by making 48-h measurements, and then, for subjects close to high-voltage power lines, modifying the measurements by calculating the fields using historical load data. In a study in Germany, Schüz et al. (2001) identified the source of elevated fields by multiple measurements, and attempted to classify these sources as to the likelihood of their being stable over time. Before beginning the largest study in the USA (Linet et al., 1997), a pilot study was conducted (Friedman et al., 1996) to establish the proportion of their time children of various ages spent in different parts of the home. These estimates were used to weight the individual room measurements in the main study (Linet et al., 1997) for the time-weighted average measure. In addition, the pilot study documented that magnetic fields in dwellings rather than schools accounted for most of the variability in children's exposure to magnetic fields.

Table 15. Exposure distribution of the arithmetic mean based on exposure of controls in a case-control study or all respondents in an exposure survey

Country	Authors	Study type	Measure-ment	Magnetic field category (μT)				N
				≤ 0.1	> 0.1–≤ 0.2	> 0.2–≤ 0.3	> 0.3	
Belgium	Decat, Van den Heuvel & Mulpas, 2005	Exposure survey	24-hr personal	81.9%	11.5%	1.6%	5.1%	251
Canada	McBride et al., 1999[a]	Case-control	48-hr personal	59.0%	29.2%	8.5%	3.3%	329
Germany	Michaelis et al., 1998	Case-control	24-hr bedroom	89.9%	7.0%	1.7%	1.4%	414
	Brix et al., 2001	Exposure survey	24-hr personal	73.6%	17.8%	4.1%	4.5%	1952
	Schüz et al., 2001[b]	Case-control	24-hr bedroom	93.0%	5.6%	0.9%	0.5%	1301
Japan	Kabuto et al.,2006[b]	Case-control	7-day home	89.9%	6.0%	2.5%	1.6%	603
Korea	Yang, Ju & Myung, 2004	Exposure survey	24-hr personal	64.0%	24.2%	4.0%	7.8%	409
UK	UKCCSI, 1999[b]	Case-control	48-hr home	92.3%	5.8%	1.2%	0.8%	2226
USA	London et al., 1991[a]	Case-control	24-hr bedroom	69.2%	19.6%	4.2%	7.0%	143
	Linet et al., 1997	Case-control	24-hr bedroom	65.7%	23.2%	6.6%	4.5%	620
	Zaffanella & Kalton, 1998	Exposure survey	24-hr personal	64.2%	21.1%	7.8%	4.2%	995
	Zaffanella, 1993	Exposure survey	24-hr home	72.3%	17.5%	5.6%	4.6%	987

[a] Based on the distribution for pooled analysis reported by Greenland et al., 2000.

[b] Given exposure categories: < 0.1, 0.1–< 0.2, 0.2–< 0.4, > 0.4 μT; approximated categories in the table by applying the ratios of exposures in the high categories of the EMF Rapid Survey (Zaffanella & Kalton, 1998).

Five extensive exposure surveys have been conducted to evaluate ELF exposures of the general population (Brix et al., 2001; Decat, Van den Heuvel & Mulpas, 2005; Yang, Ju & Myung, 2004; Zaffanella, 1993; Zaffanella & Kalton, 1998). As indicated in Tables 15 and 16, these surveys gen-

erally estimate that approximately 4–5% had mean exposures above 0.3 μT, with the exception of Korea where 7.8% had mean exposures above 0.3 μT (Kheifets, Afifi & Shimkhada, 2006). Only 1–2% have median exposures in excess of 0.4 μT.

Estimating exposures using the control-exposures from case-control studies allows a look at a broader spectrum of countries and results in a range of 0.5–7.0 % having mean exposures greater than 0.3? μT and 0.4–3.3% having median exposures above 0.4 μT. Two countries, the USA and Germany, had both exposure surveys and case-control studies. In the USA, the mean exposures were virtually equal from the two methods but for the case-control median eight estimates were less than the survey median estimates. In Germany, the case-control mean exposure estimates were substantially smaller than the survey estimates (median estimates were not available for the case-control study), which could be due to regional differences and the inclusion of occupational exposures in the survey estimates. In some studies, the exposure distribution for 0.2–0.3 μT and 0.3–0.4 μT had to be estimated since only data for the 0.2–0.4 μT intervals were given; the ratio from the EMF Rapid Survey from the USA was used to calculate these estimates.

Table 16. Exposure distribution of the geometric mean based on exposure of controls in a case-control study or all respondents in an exposure survey

Country	Authors	Study type	Measurement	Magnetic field category (μT)				N
				≤ 0.1	> 0.1– ≤ 0.2	> 0.2– ≤ 0.4	> 0.4	
Belgium	Decat, Van den Heuvel & Mulpas, 2005	Exposure survey	24-hr personal	91.9%	4.1%	2.8%	1.2%	251
Canada	McBride et al., 1999[a]	Case-control	48-hr personal	70.7%	17.4%	8.6%	3.3%	304
Germany	Michaelis et al., 1998[a]	Case-control	24-hr bedroom	92.9%	5.1%	1.5%	0.5%	409
UK	UKCCSI, 1999[a]	Case-control	48-hr home	94.4%	4.1%	1.2%	0.4%	2224
USA	Zaffanella & Kalton, 1998	Exposure survey	24-hr personal	72.6%	17.6%	7.5%	2.3%	995
	Linet et al., 1997[a]	Case-control	24-hr bedroom	72.8%	17.9%	8.3%	0.9%	530

[a] Based on the distribution for pooled analysis reported by Ahlbom et al., 2000.

2.3.3.3 *Personal exposure monitoring*

Monitoring the personal exposure of a subject by a meter worn on the body is attractive because it captures exposure to fields from all sources and at all places the individual encounters. Because all sources are included, the average fields measured tend to be higher than those derived from spot or long-term measurements in homes. However, the use of personal exposure monitoring in case–control studies could be problematic, due to age- or disease-related changes in behaviour. The latter could introduce differential misclassification in exposure estimates. However, personal exposure monitoring can be used to validate other types of measurements or estimates.

Table 17 summarizes results from studies which have measured the personal exposure of representative samples of people in different countries. Geometric mean and geometric standard deviation are given on the assumption of log-normal distributions.

Table 17. Summary of measurements of residential personal exposure [a]

Authors	Area	Sample type	Measurement type	Time of year	Sample size	Type of statistics [b]	Geometric mean (nT)	Geometric standard deviation
Donnelly & Agnew, 1991	Toronto, Canada	Utility employees, contacts, and general public, chosen for variety of exposure environments	Roughly 48 h, single axis	June–October	31	Children at home (D)	117	2.98
						Adults at home (D)	133	2.80
Skotte, 1994	Denmark	From industry. Homes near power lines excluded for this analysis.	Personal exposure, 24 h		298 (includes some duplication)	"Non-work" (P)	50	2.08
Brix et al., 2001	Bavaria, Germany	Volunteers recruited for exposure assessment	Personal exposure, 24 h		1952	(U)	6.4	2.41
Vistnes et al., 1997a	Suburb of Oslo, Norway	Children from two schools. This analysis only of homes > 275 m from power line	Personal exposure, 24 h		6	At home (P,A)	15	2.40

Table 17. Continued

Merchant, Renew & Swanson, 1994a	England and Wales, UK	Volunteers from electricity industry. HV lines excluded for this analysis	3–7 days	Spread over year	204	At home (P,F)	54	2.05
Preece et al., 1996	Avon, UK	Random selection from mothers with surviving children	24 h	Dec–May	44	(A)	42	2.65
Kavet, Silva & Thornton, 1992	Maine, USA	Random-digit dialing; adults	24 h	June/August	15	At home (D)	134	1.80
Zaffanella & Kalton, 1998	USA	Random-digit dialling	24 h personal measurement (bedroom & home)		994	(D)	92	1.36
Bracken et al., 1994	USA	Employees of EPRI member utilities, weighted to random samples of wire codes	24 h		396	At home, not in bed (F)	111	1.88
Kaune et al., 1994	Washing-ton DC, USA	Children of volunteers from NCI and private daycare facility, overhead wiring	24 h	Spring	29	Residential (P)	96	2.38
Kaune & Zaffanella, 1994	California and Mass., USA	Children from volunteers from industry, chosen for variety of distribution arrangements	24 h		31	(P)	96	2.45

[a] Source: Swanson & Kaune, 1999.

[b] P = geometric statistics are given in Swanson & Kaune, 1999; A = calculated from arithmetic statistics given in Swanson & Kaune, 1999 using the equations given in Section 2.2.2.2.3 Distribution lines, subsection Data on fields in different countries; D =calculated from data given in Swanson & Kaune, 1999; F = fitted to statistics given in Swanson & Kaune, 1999 using least-squares procedure; U = calculated from unpublished data.

Table 18. Comparisons of personal exposure and background fields

Country	Authors	Subjects	Sample size	Personal exposures: geometric mean (nT)	Long-term background field: geometric mean (nT)	Ratio personal exposure / background
USA	Kavet, Silva & Thornton, 1992	Adults, at home	15	134	58	2.3
	Bracken et al., 1994	Adults, at home, not in bed	396	111	74	1.5
	Kaune et al., 1994	Children, residential	29	96	99	1.0
	Kaune & Zaffanella, 1994	Children	31	96	67	1.4
Canada	Donnelly & Agnew, 1991	Children, at home	31	117	107	1.1
		Adults, at home	31	133		1.2
UK	Merchant, Renew & Swanson, 1994a	Adults, at home	204	54	37	1.5
	Preece et al., 1996	Adults	44	42	29	1.5

In general, personal-exposure measurements are higher than fields measured away from appliances, largely because of the extra contributions of appliances and any other sources within the home. Seven studies that include both personal exposure measurements and long-term measurements of fields away from appliances in the homes of the subjects are compared in Table 18. The ratio of average personal exposure to average field away from appliances varies from 1.0 to 2.3, with an average of 1.44. This shows the relative magnitude of short-term exposure to appliances emitting relatively high magnetic fields compared with background exposure. There may be a tendency for the ratio to be smaller for children than for adults, but it would be unwise to draw firm conclusions from these limited data.

2.3.4 Assessing exposure to magnetic fields from appliances

Only little is known about the magnitude and distribution of EMF exposures from appliances. The contribution to overall exposure by appli-

ances depends, among other things, on the type of appliance, its age, its distance from the person using it, and the pattern and duration of use. The assessment of appliance use in epidemiological studies has generally relied on questionnaires, sometimes answered by proxies such as other household members (Mills et al., 2000). These questionnaires ascertain some (but not usually all) of these facts, and are subject to recall bias. It is not known how well data from even the best questionnaire approximate to the actual exposure. Mezei et al. (2001) reported that questionnaire-based information on appliance use, even when focused on use within the last year, has limited value in estimating personal exposure to magnetic fields. Limited attempts have been made (e.g. UKCCSI, 1999) to include some measurements as well as questionnaire data.

According to Mader & Peralta (1992), appliances are not a significant source of whole-body exposure, but they may be the dominant source of exposure of extremities. Delpizzo (1990) suggested that common domestic electrical appliances were responsible for an exposure comparable to that from power lines. Recently, Mezei et al. (2001) showed that computers contributed appreciablyto overall exposure while other appliances each contributed less than 2%. Most of the time, a low contribution was the result of infrequent and short duration of appliance use. When limited to only those subjects who actually used certain appliances, the analysis showed that computers (16%) and cellular phones (21%) could contribute appreciablyto total daily exposure.

Because exposure to magnetic fields from appliances tends to be short-term and intermittent, the appropriate method for combining assessments of exposure from different appliances and chronic exposure from other sources would be particularly dependent on assumptions made about exposure metrics. Such methods have yet to be developed.

2.3.5 Assessing exposure at schools

Exposure to ELF electric and magnetic fields while at school seldom represents a major fraction of a child's total exposure.

A study involving 79 schools in Canada took a total of 43009 measurements of 60-Hz magnetic fields (141–1543 per school) (Sun et al., 1995). Only 7.8% of all the fields measured were above 0.2 μT. For individual schools, the average magnetic field was 0.08 μT (SD: 0.06 μT). In the analysis by use of room, only typing rooms had magnetic fields that were above 0.2 μT. Hallways and corridors were above 0.1 μT and all other room types were below 0.1 μT. The percentage of classrooms above 0.2 μT was not reported. Magnetic fields above 0.2 μT were mostly associated with wires in the floor or ceiling, proximity to a room containing electrical appliances or movable sources of magnetic fields such as electric typewriters, computers and overhead projectors. Eight of the 79 schools were situated near high-voltage power lines. The survey showed no clear difference in overall magnetic field strength between the schools and domestic environments.

Kaune et al. (1994) measured power-frequency magnetic fields in homes and in the schools and daycare centres of 29 children. Ten public shools, six private schools and one daycare centre were included in the study. In general, the magnetic field strengths measured in schools and daycare centres were smaller and less variable than those measured in residential settings.

The UKCCSI (1999) carried out an epidemiological study of children in which measurements were made in schools as well as homes. Only three of 4452 children aged 0–14 years who spent 15 or more hours per week at school during the winter, had an average exposure during the year above 0.2 μT as a result of exposure at school.

2.3.6 Assessing non-occupational exposure to magnetic fields: discussion

One crucial question in case-control studies in general, and of magnetic fields and childhood cancer in particular, is how to span time. By definition, all exposures of interest in these studies are historical. Thus, measurements, wire codes, and historic models are only surrogates for the critical exposure, which occurred at some unknown time in the past. The question is then, what is a better surrogate for historic exposure: wire codes, area measurements or personal exposure? Each method has distinct advantages. Wire codes are relatively simple categorical scales that are thought to be stable over time. This method allows magnetic fields to be estimated without resident participation, thus reducing potential bias due to non-participation and maximizing study size. Measured fields, on the other hand, are more appealing because they can account for all sources within the residence and entail fewer implicit assumptions. However, one would expect measurements taken soon after diagnosis to be better surrogates than measurements taken long after diagnosis. Although it is generally considered that such long term measurements are the best available estimate of average magnetic field exposure, wire codes may be better indicators of high historical exposure because they may be less biased, and may produce less misclassification and measurement error. This might be especially true when one has to estimate exposure that has occurred several years to decades in the past. Epidemiological studies with personal measurements are yet to be completed. However, in case-control settings personal measurements could be problematic due to age or disease-related changes in behavior and thus, exposure.

Epidemiological studies that estimated the historical exposures of subjects to magnetic fields from power lines by calculations did not usually report using documented computer programs or publish the details of the computation algorithms, e.g. Olsen, Nielsen & Schulgen (1993), Verkasalo et al. (1993; 1996), Feychting & Ahlbom (1994), Tynes & Haldorsen (1997), though others, e.g. UKCCSI (2000), did. However, for exposure assessment in these studies, it is important to consider how accurate the calculations are in a specific study when interpreting results. For example in the seminal Feychting & Ahlbom study (1993), the calculation error (contemporary calculations vs. contemporary measurements) is greater than any advantage that

might have been gained by estimating exposure at the time of diagnosis with historical calculations. As a result, contemporary spot measurements appear to provide better estimates of historical exposures in this study (Jaffa, Kim & Aldrich, 2000).

2.3.7 Assessing occupational exposure to magnetic fields

Following Wertheimer and Leeper's report of an association between residential magnetic fields and childhood leukaemia, Milham (1982; 1985a; 1985b) noted an association between cancer and some occupations (often subsequently called the "electrical occupations") intuitively expected to involve proximity to sources of electric and magnetic fields. However, classification based on job title is a very coarse surrogate. Critics (Guenel et al., 1993; Loomis & Savitz, 1990; Theriault et al., 1994) have pointed out that, for example, many electrical engineers are basically office workers and that many electricians work on disconnected wiring.

Much less is known about exposures in non-electrical occupations. Little data, if any, is available for many jobs and industrial environments. Of note in the few surveys conducted are high exposures among railway engine drivers (about 4 μT) and seamstresses (about 3 μT). The best information on work exposures is available in a survey conducted by Zaffannela (Zaffanella & Kalton, 1998). The survey included 525 workers employed in a variety of occupations (Table 19).

Table 19. Parameters of the distributions of average magnetic field during work for different types of occupations [a]

Description	Sample size	Mean (μT)	Standard deviation (μT)	Geometric mean (μT)	Geometric standard deviation
Managerial and professional speciality occupations	204	0.164	0.282	0.099	2.47
Technical, sales, and administrative supports occupation	166	0.158	0.167	0.109	2.03
(Protective, food, health, cleaning, and personal) service occupations	71	0.274	0.442	0.159	2.55
Farming, forestry, and fishing occupations	19	0.091	0.141	0.045	2.97
Precision production, craft, and repair occupations, and operators, fabricators, and laborers	128	0.173	0.415	0.089	2.80
Electrical occupations [b]	16	0.215	0.162	0.161	2.25

[a] Source: Zaffanella & Kalton, 1998.

[b] As classified by Milham (1982; 1985a; 1985b): electronic technicians, radio and telegraph operators, electricians, linemen (power and telephone), television and radio repairmen, power station operators, aluminium workers, welders and flame cutters, motion picture projectionists, electrical enigineers and subway motormen.

The largest geometric mean (0.161 μT) for magnetic field exposure during work occurred in electrical occupations. Service occupations followed at 0.159 μT. Technical, sales, and administrative support positions had a geometric mean of 0.109 μT; managerial and professional specialty occupations, 0.099 μT; and precision production, craft and repair work, operation, fabrication, and labor, 0.089 μT. At 0.045 μT, farming, forestry, and fishing occupations had the lowest geometric mean. Work exposures were often significantly higher and more variable than other exposures: people spent significantly more time, for example, in fields exceeding 1.6 μT at work than at home. Nevertheless, average work exposures for the general population are low, with only 4% exposed to magnetic fields above 0.5 μT.

Intuitive classification of occupations by investigators can be improved upon by taking account of judgements made by appropriate experts (e.g. Loomis et al., 1994), and by making measurements in occupational groups (e.g. Bowman et al., 1988).

A study by Forssén et al. (2004) provides a first attempt to comprehensively evaluate occupational magnetic field exposure assessment among women. The results for the work-site environments are presented in Table 20. "Large scale kitchens" and "Shops and stores" are both environments with high exposure.

Table 20. Exposures to extremely low frequency magnetic fields by occupational environment [a]

Environment	Sample size	Arithmetic/geometric means (arithmetic standard deviations) (μT)		Proportion of time spent at exposure level (n)			
		Time-weighted average	Maximum	< 0.1 μT	0.1–0.2 μT	0.2–0.3 μT	≥ 0.3 μT
Health care	67	0.11 / 0.10 (0.07)	2.62 / 2.10 (1.90)	66% (29)	20% (18)	8% (10)	7% (10)
Hospitals	27	0.09 / 0.08 (0.05)	3.01 / 2.37 (2.26)	77% (21)	13% (14)	6% (8)	4% (6)
Elsewhere	40	0.13 / 0.11 (0.08)	2.35 / 1.94 (1.58)	59% (31)	24% (20)	9% (11)	9% (12)
Schools and childcare	55	0.15 / 0.12 (0.10)	5.41 / 2.12 (16.49)	62% (27)	20% (16)	8% (8)	10% (12)
Large scale kitchens	34	0.38 / 0.28 (0.43)	5.97 / 4.67 (4.55)	30% (27)	20% (11)	15% (12)	36% (27)
Offices	127	0.16 / 0.12 (0.13)	2.41 / 1.73 (2.32)	55% (38)	25% (26)	9% (14)	12% (22)
Shops and stores	33	0.31 / 0.26 (0.17)	5.84 / 2.55 (18.21)	26% (29)	17% (13)	17% (13)	40% (30)

[a] Source: Forssén et al., 2004.

A further improvement is a systematic measurement programme to characterize exposure in a range of jobs corresponding as closely as possible to those of the subjects in a study, thus creating a "job-exposure matrix", which links measurement data to job titles.

Forssén et al. (2004) constructed a job-exposure matrix for women. Analysis of the exposure distribution in the female working population showed that about 16% of the women are highly exposed (0.20 μT). However, only 5% would be classified as such if the job-exposure matrix for men (Floderus, Persson & Stenlund, 1996) was used (Table 21). Furthermore, only 20% of the women with high exposure would be correctly classified as highly exposed by the job-exposure matrix for men. Using the job-exposure matrix for men in an epidemiological study that involves women would hence cause not only loss of power but could also dilute any effects through misclassification of the exposure.

Table 21. Distribution of exposure in the population of women gainfully employed in Stockholm County 1980 by using job-exposure matrices (JEM)

	Pecentage of women exposed	
Geometric mean of time-weighted average (μT)	**JEM for women [a]**	**JEM for men [b]**
≤ 0.10	21.4	7.2
0.11–0.20	48.3	47.4
0.21–0.30	13.7	4.4
> 0.30	3.0	1.0
Missing	13.6	40.0

[a] Source: Forssén et al., 2004.

[b] Source: Floderus, Persson & Stenlund, 1996.

Despite the improvements in exposure assessment, the ability to explain exposure variability in complex occupational environments remains poor. Job titles alone explain only a small proportion of exposure variability. A consideration of the work environment and of the tasks undertaken by workers in a specific occupation leads to a more precise estimate (Kelsh, Kheifets & Smith, 2000). Harrington et al. (2001) have taken this approach one stage further by combining job information with historical information not only on the environment in general but on specific power stations and substations. The within-worker and between-worker variability which account for most of the variation are not captured using these assessments.

In addition to the need for correct classification of jobs, the quality of occupational exposure assessment depends on the details of work history available to the investigators. The crudest assessments are based on a single job (e.g. as mentioned on a death certificate). This assessment can be improved by identifying the job held for the longest period, or even better, by obtaining a complete job history which would allow for the calculation of the

subject's cumulative exposure over his professional career, often expressed in μT–years.

2.3.8 Assessing exposure to electric fields

Assessment of exposure to electric fields is generally more difficult and less well developed than the assessment of exposure to magnetic fields. All of the difficulties encountered in assessment of exposure to magnetic fields discussed above also apply to electric fields. In addition, electric fields are easily perturbed by any conducting object, including the human body.Although most studies that have assessed electric fields have attempted to assess the unperturbed field, the very presence of subjects in an environment means that they are not being exposed to an "unperturbed field".

Because electric fields are perturbed by the body, the concept of personal exposure is difficult to define, and readings taken with a meter attached to the body are likely to be dominated by local perturbations affected by the precise location of the meter on the body.

A number of electric and magnetic field exposure studies have included measurements of electric fields within homes. Some of these consisted of wearing personal exposure meters for periods of 24 or 48 hours, while others consisted of spot measurements within specific rooms. The majority of studies were epidemiological studies, although one compared homes near to a power line to homes at a considerable distance from any power lines.

In each of the studies data are presented for controls as well as for the cases. A comparison has been made between the measurements for the controls in different studies. Green et al. (1999a) performed continuous monitoring and reported that the average electric field exposure at home for controls was below 16 V m^{-1} for 90% of the group. London et al. (1991) and Savitz et al. (1988) performed spot measurements in the centre of the controls' sitting rooms. London et al. reported a mean of 7.98 V m^{-1} and Savitz et al. reported a median below 9 V m^{-1}. A number of other studies involved monitoring of electric fields over a 24 or 48 hour period. McBride et al. (1999) carried out 48-h personal exposure monitoring, reporting a median exposure for controls of 12.2 V m^{-1}. However no distinction was made between exposure at home and away from home. Studies by Dockerty et al. (1998) and Kaune et al. (1987) performed 24-h monitoring within specific rooms of the home. Both monitored electric field within the sitting room, while the Dockerty et al. study also monitored electric field levels within the bedroom. The study by Dockerty et al. reported arithmetic means less than 10.75 V m^{-1} in at least 60% of the homes, regardless of the room, while Kaune et al. reported a mean value of 33 V m^{-1} across the homes investigated. Kaune et al. reported higher levels that other studies reported to date. Levallois et al. (1995) carried out 24-h monitoring of the electric fields in homes both near to a 735 kV line, and distant to any overhead lines. For those homes distant to power lines, a geometric mean electric field of 14 V

m^{-1} was reported. Finally, Skinner et al. (2002) made measurements in several locations in the home with geometric means around 10 V m^{-1}.

2.3.9 Exposure assessment: conclusions

Electric and magnetic fields exist wherever electricity is generated, transmitted or distributed in power lines or cables, or used in electrical appliances. Since the use of electricity is an integral part of our modern lifestyle, these fields are ubiquitous in our environment.

Residential exposure to power frequency magnetic fields does not vary dramatically across the world. The geometric mean magnetic field in homes ranges between 0.025 and 0.07 μT in Europe and 0.055 and 0.11 μT in the USA. The mean values of electric field in the home are in the range of several tens of volts per metre. In the vicinity of certain appliances, the instantaneous magnetic-field values can be as much as a few hundred microtesla. Near power lines, magnetic fields reach approximately 20 μT and electric fields up to several thousand volts per metre.

Few children have time-averaged exposures to residential 50 or 60 Hz magnetic fields in excess of the levels associated with an increased incidence of childhood leukaemia. Approximately 1% to 4 % have mean exposures above 0.3 μT and only 1% to 2% have median exposures in excess of 0.4 μT.

Occupational exposure, although predominantly to power-frequency fields, may also include contributions from other frequencies. The average magnetic field exposures in the workplace have been found to be higher in “electrical occupations” than in other occupations such as office work, ranging from 0.4–0.6 μT for electricians and electrical engineers to approximately 1.0 μT for power line workers, with the highest exposures for welders, railway engine drivers and sewing machine operators (above 3 μT). The maximum magnetic field exposures in the workplace can reach up to approximately 10 mT and this is invariably associated with the presence of conductors carrying high currents. In the electrical supply industry, workers may be exposed to electric fields up to 30 kV m^{-1}.

3 ELECTRIC AND MAGNETIC FIELDS INSIDE THE BODY

3.1 Introduction

Chapter 2 describes the fields to which people are exposed. Exposure to these fields in turn induces fields and currents inside the body. This chapter describes and quantifies the relationship between external fields and contact currents with the current density and electric fields induced within the body. Only the induced electric field and resultant current density in tissues and cells are considered, as the internal magnetic field in tissues and cells is the same as the external field. The chapter first considers calculations on a macroscopic scale referring to dimensions much greater than those of cells or cell assemblies, and then on a microscopic scale when dimensions considered are comparable to, or smaller than a cell.

At extremely low frequencies, exposure is characterized by the electric field strength (E) or the electric flux density (also called the displacement) vector (D), and the magnetic field strength (H) or the magnetic flux density (also called the magnetic induction) (B). All these parameters are vectors; vectors are denoted in italics in this Monograph (see also paragraph 2.1.1). The flux densities are related to the field strengths by the properties of the medium in a given location r as:

$$D(r) = \hat{\varepsilon}\, E(r)$$
$$B(r) = \hat{\mu}\, H(r)$$

where $\hat{\varepsilon}$ is the complex permittivity and $\hat{\mu}$ is the permeability. For biological media $\hat{\mu} \cong \mu_0$ where μ_0 is the permeability of free space (air). The electric and magnetic fields are effectively decoupled, since quasi-static conditions can be assumed (Olsen, 1994). To determine exposure in a given location, both the electric and magnetic field have to be computed or measured separately. Similarly, the internal induced fields are also evaluated separately. For simultaneous exposure to electric and magnetic fields, the internal measures can be obtained by superposition. Exposures to either electric or magnetic fields result in the induction of electric fields and associated current density in conductive tissue. The magnitudes and spatial patterns of these fields depend on the type of the exposure field (electric vs. magnetic), their characteristics (frequency, magnitude, orientation, etc.), and the size, shape, and electrical properties of the exposed body (human, animal). A biological body significantly perturbs an external electric field, and the exposure also results in an electric charge on the body surface. The external electric field is also strongly perturbed by metallic or other conductive objects.

The primary dosimetric measure is the local induced electric field. This measure is selected because thresholds of the excitable tissue stimulation are defined by the electric field and its spatial variation. However, current density is used in some exposure guidelines (ICNIRP, 1998a). Among the measurements often reported are the average, root mean square (rms) and maximum induced electric field and current density values (Stuchly & Daw-

son, 2000). Additional measurements more recently introduced are the 50th, 95th, and 99th percentiles, which indicate values not exceeded in the given volume of tissue, e.g. the 99th percentile shows the dosimetric measure exceeded in 1% of a given tissue volume (Kavet et al., 2001). Some exposure guidelines (ICNIRP, 1998a) specify dosimetry limit values as current density averaged over 1 cm^2 of tissue. The electric field in tissue is typically expressed in V m^{-1} or mV m^{-1} and the current density in A m^{-2} or mA m^{-2}.

The internal (induced) electric field (E) and conduction current density (J) are related through Ohm's law:

$$J = \sigma E$$

where σ is the bulk tissue conductivity, and may be a tensor in anisotropic tissues (e.g. muscle).

Early dosimetry modeled a human body as homogeneous ellipsoids or other overly simplified shapes. In addition, limited measurements of currents through the whole body and body parts have been performed. During the last few years, a few research laboratories have performed extensive computations of the induced electric field and current density in heterogeneous models of the human body in uniform and non-uniform electric or magnetic fields at 50 or 60 Hz. There is convergence of the results obtained by various groups and agreement with earlier measurements, where such measurements are available (Caputa et al., 2002; Stuchly & Gandhi, 2000). Microscopic dosimetry data remain very limited.

3.2 Models of human and animal bodies

Currently, a number of laboratories have developed heterogeneous models of the human body with realistic anatomy and numerous tissues identified. Most of these models have been developed by computer segmentation of data from magnetic resonance imaging (MRI) and allocation of proper tissue type (Dawson, 1997; Dawson, Moerloose & Stuchly, 1996; Dimbylow, 1997; Dimbylow, 2005; Gandhi, 1995; Gandhi & Chen, 1992; Zubal, 1994). Special care has been taken to make these models anatomically realistic. Table 22 summarizes essential characteristics of some of these models.

Typically, over 30 distinct organs and tissues are identified and represented by cubic cells (voxels) of 1 to 10 mm on a side. Voxels are assigned a conductivity value based on measured values for various organs and tissues (Gabriel, Gabriel & Corthout, 1996). A human body model constructed from several geometrical bodies of revolution has also been used (Baraton, Cahouet & Hutzler, 1993; Hutzler et al., 1994). The model is symmetric and is divided into about 100000 tetrahedral elements, which represent only the major organs. This can be contrasted with over eight million of tissue voxels used in the hybrid method with resolution of 3.6 mm (Dawson, Caputa & Stuchly, 1998). In the hybrid method, the FDTD part of the modeling requires that the body model is enclosed in a parallelpiped. To illustrate the

quality of such models Figure 1 shows the external view, the skeleton and skin, and the main internal organs.

Table 22. Main characteristics of the MRI-derived models of the human body

Model	NRPB [a]	University of Utah [b]	University of Victoria [c]
Height and mass	1.76 m, 73 kg	1.76 m, 64 kg scaled to 71 kg	1.77 m, 76 kg
Original voxels	2.077 x 2.077 x 2.021 mm	2 x 2 x 3 mm	3.6 x 3.6 x 3.6 mm
Posture	upright, hands at sides	upright, hands at sides	upright, hands in front

[a] Source: Dimbylow, 1997.

[b] Source: Gandhi & Chen, 1992.

[c] Source: Dawson, 1997.

Figure 1. Volume rendered images of a female voxel phantom (NAOMI). In the image on the left the opacity of the skin has been hardened and the image is illuminated to display the outside surface. In the middle image the opacity of the skin has been reduced to enable the internal skeleton to be seen. The image on the right shows the skeleton and internal organs. The skin, fat, muscle and breasts have been removed. (Dimbylow, 2005)

A few animal models, namely rats, mice and monkeys have also been developed. The quality of the models varies.

3.3 Electric field dosimetry

3.3.1 Basic interaction mechanisms

As mentioned earlier the human (or animal) body significantly perturbs a low-frequency electric field. In most practical cases of human exposure, the field is vertical (with respect to the ground). At low frequencies, the body is a good conductor, and the electric field is nearly normal to its surface. The electric field inside the body is many orders of magnitude smaller than the external field. Non-uniform charges are induced on the surface of the body and the current direction inside the body is mostly vertical. Figure 2 illustrates the electric fields in air around the human body and body surface charge density for the model in free space and on perfect ground.

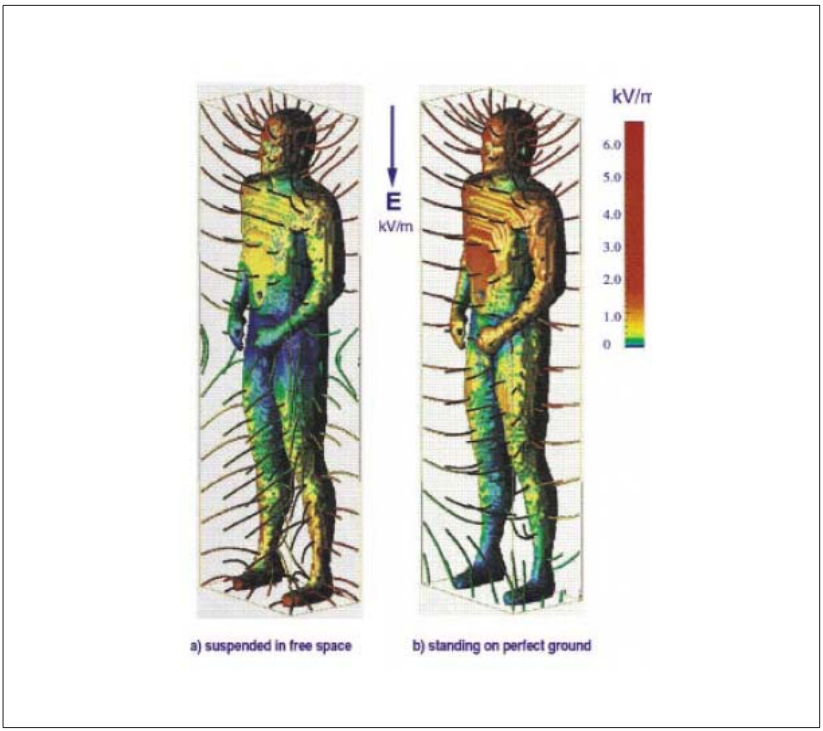

Figure 2. Human body in a uniform electric field of 1 kV m^{-1} at 60 Hz showing the external electric field and surface charge density on the body surface: (a) in free space, and (b) in contact with perfect ground (Stuchly & Dawson, 2000).

The electric field in the body strongly depends also on the contact between the body and the electric ground, where the highest fields are found when the body is in perfect contact with ground through both feet (Deno & Zaffanella, 1982). The further away from the ground the body is located, the

lower the electric fields in tissues. For the same field, the maximum ratio of internal fields for grounded to free space models is about two.

3.3.2 Measurements

Kaune & Forsythe (1985) performed measurements of currents in models consisting of manikins standing in a vertical electric field with both feet grounded. The model was filled with saline solution whose conductivity is equal to that of the average human tissues. The results of the measurements are shown in Figure 3.

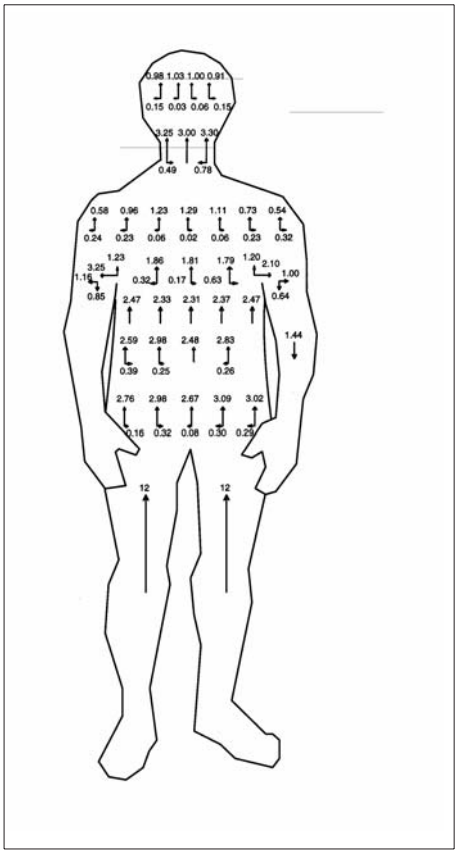

Figure 3. Measured current density (mA m^{-2}) in a saline filled homogeneous phantom grounded through both feet. The electric field strength is 10 kV m^{-1}, the field vector is directed along the long axis of the body, and the frequency is 60 Hz (Kaune & Forsythe, 1985).

3.3.3 Computations

Early dosimetry computations represented the human (or animal) body as a homogeneous body of revolution with a single conductivity value.

Examples of analytic solutions in homogeneous geometric shapes for electric field exposure are available in Shiau & Valentino (1981), Kaune and McCreary (1985), Tenforde & Kaune (1987), Spiegel (1977), Foster and Schwan (1989) and Hart (1992). Measurements of currents within the body have also been performed (Deno & Zaffanella, 1982; Kaune & Forsythe, 1985; Kaune, Kistler & Miller, 1987). As an intermediate development, highly simplified body-like shapes have been evaluated by numerical methods (Chen, Chuang & Lin, 1986; Chiba et al., 1984; Dimbylow, 1987; Spiegel, 1981).

Various computational methods have been used to evaluate induced electric fields in high-resolution models. Computations of exposure to electric fields are generally more difficult than for the magnetic field exposure, since the human body significantly perturbs the exposure field. Suitable numerical methods are limited by the highly heterogeneous electrical properties of the human body and equally complex external and organ shapes. The methods that have been successfully used so far for high-resolution dosimetry are the finite difference (FD) method in frequency domain and time domain (FDTD) and the finite element method (FEM). Each method and its implementation offer some advantages and have limitations, as reviewed by Stuchly and Dawson (2000). Some of the methods and computer codes have undergone extensive verification by comparison with analytic solutions (Dawson & Stuchly, 1996; Stuchly et al., 1998). An extensive valuation of accuracy of various dosimetric measures is also available (Dawson, Potter & Stuchly, 2001).

Several numerical computations of the electric field and current density induced in various organs and tissues have been performed (Dawson, Caputa & Stuchly, 1998; Dimbylow, 2000; Furse & Gandhi, 1998; Hirata et al., 2001). In a more recent publication (Dimbylow, 2000), the maximum current density is averaged over 1 cm^2 for excitable tissues. The latter computation is clearly aimed at compliance with the most recent ICNIRP guideline (ICNIRP, 1998a and a later published clarification on tissue-related applicability of the limit (ICNRIP, 1998b).

Effects of two sets of conductivity have been examined in high-resolution models (Dawson, Caputa & Stuchly, 1998). The difference between calculation with either set is negligible on short-circuit current and very small on the average and maximum electric field and current density values in horizontal slices of the body. This conclusion is in agreement with the basic physical laws as explained by Dawson, Caputa & Stuchly (1998). The average and maximum electric fields vary, but less than the induced current density values for the same organ for the two different sets of conductivity. It is also apparent that not only the conductivity of a given organ determines its current density, but also the conductivity of other tissues. In general, lower induced electric fields (higher current density) are associated with higher conductivity of tissue. The exceptions are locations in the body associated with the concave curvature, e.g. tissue surrounding the armpits, where the electric field is enhanced. For the whole-body the averages are within 2%.

The maximum values of the electric field differ by up to 20% for the two sets of conductivity.

Model resolution influences how accurately the induced quantities are evaluated in various organs. Organs small in any dimension are poorly represented by large voxels. The maximum induced quantities are consistently higher as the voxel dimension decreases. The differences are typically of the order of 30–50% for voxels of 3.6 compared with 7.2 mm (Dawson, Caputa & Stuchly, 1998).

The main features of dosimetry for exposures to the ELF electric field can be summarized as follows.

- Magnitudes of the induced electric fields are typically 10^{-4} to 10^{-7} of the magnitude of external unperturbed field.
- Since the exposure is mostly to the vertical field, the predominant direction of the induced fields is also vertical.
- In the same exposure field, the strongest induced fields are for the human body in contact through the feet with a perfectly conducting ground plane, and the weakest induced fields are for the body in free space, i.e. infinitely far from the ground plane.
- The global dosimetric measure of short-circuit current for a body in contact with perfect ground is determined by the body size and shape (including posture) rather than tissue conductivity.
- The induced electric field values are to a lesser degree influenced by the conductivity of various organs and tissues than are the values of the induced current density.

Figure 4 shows vertical current computed in models of an adult and a child exposed to the vertical electric field in free space and in contact with perfect ground.

Table 23 gives various dosimetric measures for the human body model in a vertical field of 1 kV/m at 60 Hz (Dawson, Caputa & Stuchly, 1998; Kavet et al., 2001). Equivalent data for 50 Hz is shown in Table 24 (Dimbylow, 2005). In these calculations the body is in contact with perfectly conducting ground through both feet, the body height is 1.76 m for NORMAN and 1.63 m for NAOMI and weight is 73 kg for NORMAN and 60 kg for NAOMI. Table 25 gives dosimetric measures for a simplified model of a 5-year old child of 1.10 m and 18.7 kg (Hirata et al., 2001). The voxel maximum values in these models are significantly overestimated, thus 99^{th} percentiles are more representative (Dawson, Potter & Stuchly, 2001).

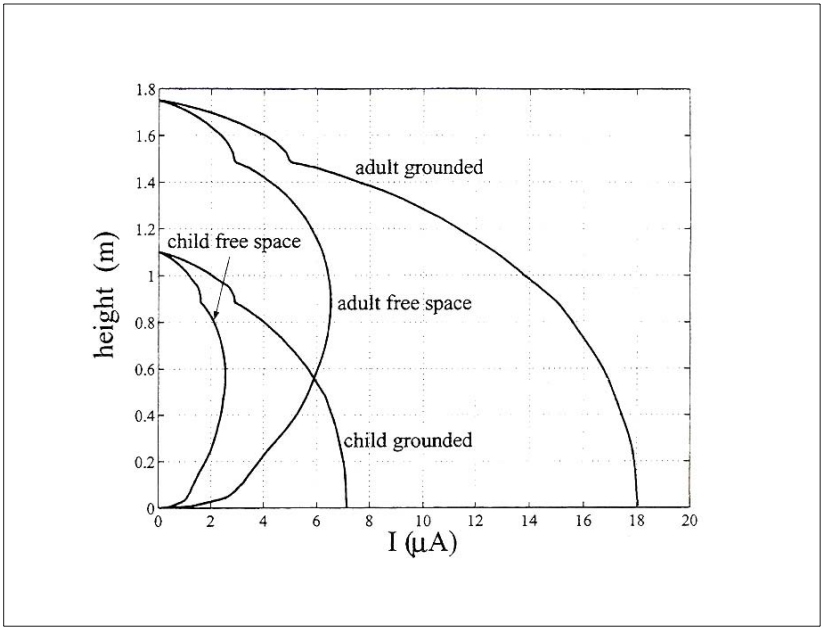

Figure 4. Current in body cross-sections for a human body model in contact with perfect ground at 1 kV m^{-1} and 60 Hz (Hirata et al., 2001).

Table 23. Induced electric fields (mV m^{-1}) of a grounded human body model in a vertical uniform electric field of 1 kV m^{-1} and 60 Hz[a] or 50 Hz[b]

Tissue/Organ	Mean		99th percentile		Maximum	
	50 Hz	60 Hz	50 Hz	60 Hz	50 Hz	60 Hz
Bone	5.72	3.55	49.4	34.4	88.8	40.8
Tendon	9.03		37.9		55.1	
Skin	2.74		33.1		67.3	
Fat	2.31		25.2		84.4	
Trabecular bone	2.80	3.55	15.1	34.4	56.5	40.8
Muscle	1.65	1.57	8.14	10.1	24.1	32.1
Bladder	1.86		6.49		8.58	
Prostate		1.68		2.81		3.05
Heart muscle	1.29	1.42	3.98	2.83	5.83	3.63
Spinal cord	1.16		2.92		4.88	
Liver	1.63		2.88		5.05	
Pancreas	1.09		2.76		6.03	
Lung	1.09	1.38	2.54	2.42	5.69	3.57

Table 23. Continued.

Spleen	1.33	1.79	2.49	2.61	5.07	3.22
Vagina	1.46		2.34		3.23	
Uterus	1.14		2.13		3.01	
Thyroid	1.16		2.03		3.29	
White matter	0.781	0.86	2.02	1.95	6.13	3.70
Kidney	1.29	1.44	1.86	3.12	4.10	4.47
Stomach	0.739		1.86		3.29	
Adrenals	1.35		1.83		2.32	
Ovaries	0.802		1.69		2.03	
Blood	0.690	1.43	1.66	8.91	3.06	23.8
Grey matter	0.474	0.86	1.62	1.95	4.85	3.70
Oesophagus	0.995		1.61		4.16	
Duodenum	0.765		1.60		2.92	
Lower LI	0.897		1.53		3.79	
Breast	0.705		1.46		2.68	
Gall bladder	0.439		1.36		2.03	
Small intestine	0.709		1.20		4.29	
CSF	0.271	0.35	1.15	1.02	2.38	1.58
Thymus	0.719		1.09		1.70	
Cartilage nose	0.598		1.03		1.40	
Upper LI	0.557		0.989		3.57	
Testes		0.48		1.19		1.63
Bile	0.352		0.805		1.26	
Urine	0.295		0.700		1.29	
Lunch	0.370		0.621		1.14	
Sclera	0.292		0.567		0.623	
Retina	0.314		0.552		0.582	
Humour	0.188		0.276		0.321	
Lens	0.211		0.268		0.268	

[a] Source: Dawson, Caputa & Stuchly, 1998; Kavet et al., 2001.

[b] Source: Dimbylow, 2005.

Table 24. Induced electric field for 99th percentile voxel value at 50 Hz for an applied electric field in a female phantom (NAOMI) and a male phantom (NORMAN). The external field is that required to produce a maximum induced electric field in the brain, spinal cord (sc) or retina of 100 mV m^1 [a]

Geometry	Electric field mV m^{-1} per kV m^{-1} for 99th percentile				External field (kV m^{-1})
	Brain	Spinal cord	Retina	Largest	
NAOMI, GRO [b]	2.02	2.92	0.552	2.92 sc	34.2
NORMAN, GRO	1.62	3.42	0.514	3.42 sc	29.2
NAOMI, ISO	1.22	1.40	0.336	1.40 sc	71.4
NORMAN, ISO	0.811	1.63	0.262	1.63 sc	61.3

[a] Source: Dimbylow, 2005.

[b] GRO: grounded; ISO: isolated.

Table 25. Induced electric fields (mV m^{-1}) of a grounded child body model in a vertical uniform electric field of 60 Hz, 1 kV m^{-1} [a]

Tissue/Organ	Mean	99th percentile	Maximum
Blood	1.52	9.18	18.06
Bone marrow	3.70	32.85	41.87
Brain	0.70	1.58	3.07
CSF	0.28	0.87	1.37
Heart	1.60	3.07	3.69
Lungs	1.55	2.63	3.69
Muscle	1.65	9.97	30.56

[a] Source: Hirata et al., 2001.

The current density averaged over 1 cm^2, which is the basic exposure unit in the ICNIRP guidelines (ICNIRP, 1998a), is illustrated in Figure 5.

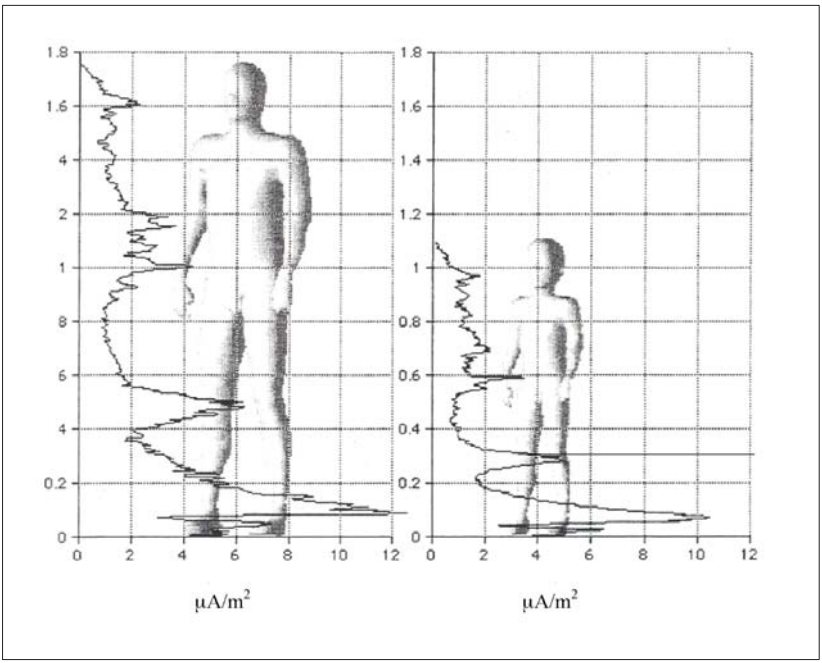

Figure 5. Maximum current density in µA m^{-2} averaged over 1 cm^2 in vertical body layers for grounded models exposed to a vertical electric field of 1 kV m^{-1} and 60 Hz (Hirata et al., 2001).

With certain exposures in occupational situations, e.g. in a substation, when the human body is close to a conductor at high potential, higher electric fields are induced in some organs (e.g. the brain) than calculated using the measured field 1.5 m above ground (Potter, Okoniewski & Stuchly, 2000). This is to be expected, as the external field increases above the ground.

3.3.4 Comparison of computations with measurements

Computed (Gandhi & Chen, 1992) and measured (Deno, 1977) current distributions for ungrounded and grounded human of 1.77 m height standing in a vertical homogeneous electric field are illustrated in Figure 6.

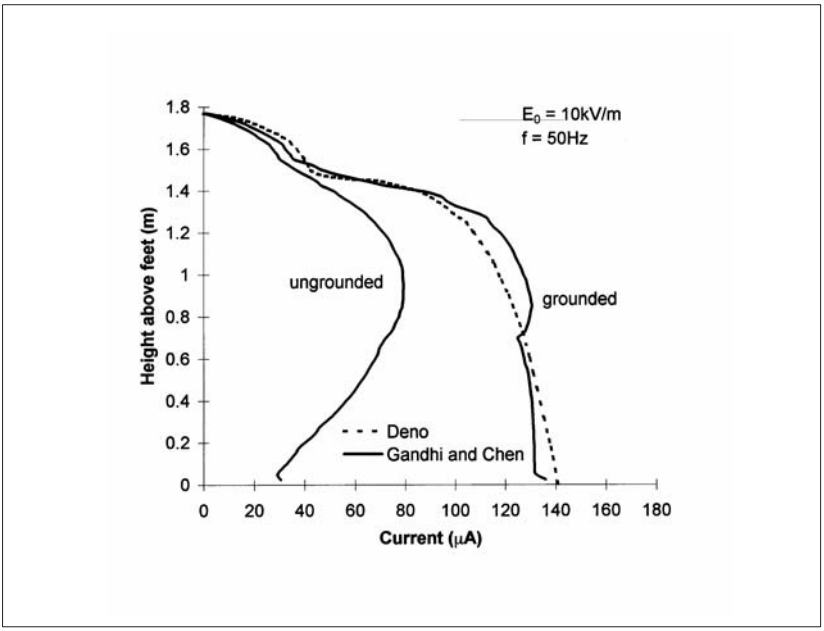

Figure 6. Computed (Gandhi & Chen, 1992) and measured (Deno, 1977) current distribution for an ungrounded and grounded human of 1.77 m in height standing in a vertical homogeneous electric field of 10 kV m^{-1} at 50 Hz.

Table 26 shows a comparison of the computed (Dawson, Caputa & Stuchly, 1998) vertical current across a few cross-sections of the human body with the measurements (Tenforde & Kaune, 1987). Given the modelling differences among the laboratories, the agreement can be considered very acceptable.

Table 26. Induced vertical current (μA) in a human body model in a vertical uniform electric field of 60 Hz and 1 kV m^{-1}

Body position	Grounded		Elevated above ground		Free space	
	Computed[a]	Measured[b]	Computed[a]	Measured[b]	Computed[a]	Measured[b]
Neck	4.9	5.4	3.7	4.0	2.9	3.1
Chest	9.8	13.5	7.0	8.7	5.3	5.4
Abdomen	13.8	14.6	9.1	9.3	6.6	5.7
Thigh	16.6	15.6	9.7	9.4	6.1	5.6
Ankle	17.6	17.0	7.3	8.0	3.0	3.0

[a] Source: Dawson, Caputa & Stuchly, 1998.

[b] Source: Tenforde & Kaune, 1987.

3.4 Magnetic field dosimetry

3.4.1 Basic interaction mechanisms

Human and animal bodies do not perturb the magnetic field, and the field in tissue is the same as the external field, since the magnetic permeability of tissues is the same as that of air. The quantities of magnetic material that are present in some tissues are so minute that they can be neglected in macroscopic dosimetry. The main interaction of a magnetic field with the body is the Faraday induction of an electric field and associated current in conductive tissue. In a homogeneous tissue the lines of electric flux (and current density) are solenoidal. In the case of heterogeneous tissues, consisting of regions of different conductivities, currents are flowing also at the interfaces between the regions. In the simplest model of an equivalent circular loop corresponding to a given body contour the induced electric field is

$$E = \pi \, \mathrm{f} \, \mathrm{r} \, B$$

and the current density is

$$J = \pi \mathrm{f} \sigma \mathrm{r} B$$

where f is the frequency, r is the loop radius and B is the magnetic flux density vector normal to the current loop. Similarly, ellipsoidal loops can be considered to better fit into the body shape.

Electric fields and currents induced in the human body cannot be measured easily. Measurements in animals have been performed, but data are limited, and the accuracy of measurements is relatively poor.

3.4.2 Computations – uniform field

Heterogeneous models of the human body similar to those used for electric field exposures have been numerically analyzed using the impedance method (IM) (Gandhi et al., 2001; Gandhi & Chen, 1992; Gandhi & DeFord, 1988), and the scalar potential finite difference (SPFD) technique (Dawson & Stuchly, 1996; Dimbylow, 1998). Even more extensive data than for the electric field are available for the magnetic field. The influence on the induced quantities of the model resolution, tissue properties in general and muscle anisotropy specifically, field orientation with respect to the body, and to a certain extent body anatomy have been investigated (Dawson, Caputa & Stuchly, 1997b; Dawson & Stuchly, 1998; Dimbylow, 1998; Stuchly & Dawson, 2000). In the past, the maximum current density in a body part has often been calculated using the largest loop of current that can be incorporated in it. Dawson, Caputa & Stuchly (1999b) have shown that induced parameters should be calculated for organs in situ instead of for isolated ones, since there is a significant influence of surrounding structures.

The main features of dosimetry for exposures to the uniform ELF magnetic field can be summarized as follows.

- The electric fields induced in the body depend on the orientation of the magnetic field with respect to the body.
- For most organs and tissues, as expected, the magnetic field orientation normal to the torso (front-to-back) gives maximum induced quantities.
- In the brain, cerebrospinal fluid, blood, heart, bladder, eyes and spinal cord, the highest quantities are induced by the magnetic field oriented side-to-side.
- Consistently lowest induced fields are for the magnetic field oriented along the vertical body axis.
- For a given field strength and orientation, greater electric fields are induced in a body of a larger size.
- The induced electric field values are to the lesser degree influenced by the conductivity of various organs and tissues than the values of the induced current density.

Table 27 presents electric field induced in several organs and tissues at 60 Hz, 1 μT magnetic field oriented front-to-back (Dawson, Caputa & Stuchly, 1997b; Dawson & Stuchly, 1998; Kavet et al., 2001). Comparable data at 50 Hz and normalized to 1 mT are shown in Table 28 (Dimbylow, 2005). An example of the current distribution in the body compared to the body anatomy is illustrated in Figure 7. The layer averaged electric field and current density for two sets of tissue conductivity are shown in Figure 8.

Table 27. Induced electric fields (mV m^{-1}) in the human body model in a uniform magnetic field of 1 mT and 60 Hz or 50 Hz oriented front-to-back [a]

Tissue/organ	Mean		99th percentile		Maximum	
	50 Hz	60 Hz	50 Hz	60 Hz	50 Hz	60 Hz
Bone	11.6	16	50.9	23	166	83
Tendon	2.81		9.35		14.9	
Skin	13.5		36.0		65.6	
Fat	13.7		33.5		129	
Trabecular bone	6.40	16	24.3	23	48.5	83
Muscle	8.44	15	23.0	51	67.6	147
Bladder	11.8		45.8		64.7	
Heart muscle	9.62	14	28.0	38	42.0	49
Spinal	8.90		27.0		53.0	
Liver	13.2		38.2		73.1	
Pancreas	3.52		13.6		24.9	
Lung	8.22	21	24.4	49	93.3	86
Spleen	8.16	41	18.4	72	27.2	92
Vagina	3.76		12.0		19.4	

Table 27. Continued.

Uterus	3.81		9.44		17.0	
Prostate		17		36		52
Thyroid	12.6		21.8		37.9	
White matter	10.1	11	31.4	31	82.5	74
Kidney	10.8	25	22.5	53	39.2	71
Stomach	4.52		15.0		26.8	
Adrenals	9.91		19.2		24.5	
Ovaries	2.40		5.30		7.87	
Blood	5.99	6.9	17.5	23	30.9	83
Grey matter	8.04	11	30.2	31	74.8	74
Oesophagus	4.86		10.0		14.1	
Duodenum	5.22		14.1		22.1	
Lower LI	4.30		12.2		27.4	
Testes		15		41		73
Breast	18.1		31.0		51.6	
Gall bladder	3.41		9.64		14.8	
Small intestine	3.98		10.4		24.8	
CSF	5.25	5.2	14.8	17	33.3	25
Thymus	12.2		19.6		30.7	
Cartilage nose	13.4		31.5		38.3	
Upper LI	5.85		12.7		21.1	
Bile	2.56		6.63		9.56	
Urine	2.16		4.71		7.55	
Lunch	2.31		6.47		7.58	
Sclera	7.78		16.3		18.2	
Retina	6.69		13.5		15.1	
Humour	4.51		7.41		9.20	
Lens	5.22		6.70		6.70	

[a] Sources: Dawson & Stuchly, 1998 (60 Hz), Dimbylow, 2005 (50 Hz).

Table 28. Induced electric field for 99th percentile voxel value at 50 Hz for an applied magnetic field in a female phantom (NAOMI) and a male phantom (NORMAN). The external field (in terms of magnetic flux density) is that required to produce a maximum induced electric field in the brain (br), spinal cord (sc) or retina of 100 mV m^{1} [a]

Geometry	Induced electric field mV m^{-1} per mT for 99th percentile				External field (mT)
	Brain	Spinal cord	Retina	Largest	
NAOMI, AP [b]	25.7	17.7	6.98	25.7 br	3.89
NORMAN, AP	30.7	29.7	7.05	30.7 br	3.26
NAOMI, LAT	31.4	27.0	13.5	31.4 br	3.18
NORMAN, LAT	33.0	48.6	14.6	48.6 sc	2.06
NAOMI, TOP	25.1	8.60	6.90	25.1 br	3.98
NORMAN, TOP	22.1	23.0	10.2	23.0 sc	4.35

[a] Source: Dimbylow, 2005.

[b] AP: front-to-back; LAT: side-to-side; TOP: head-to-feet.

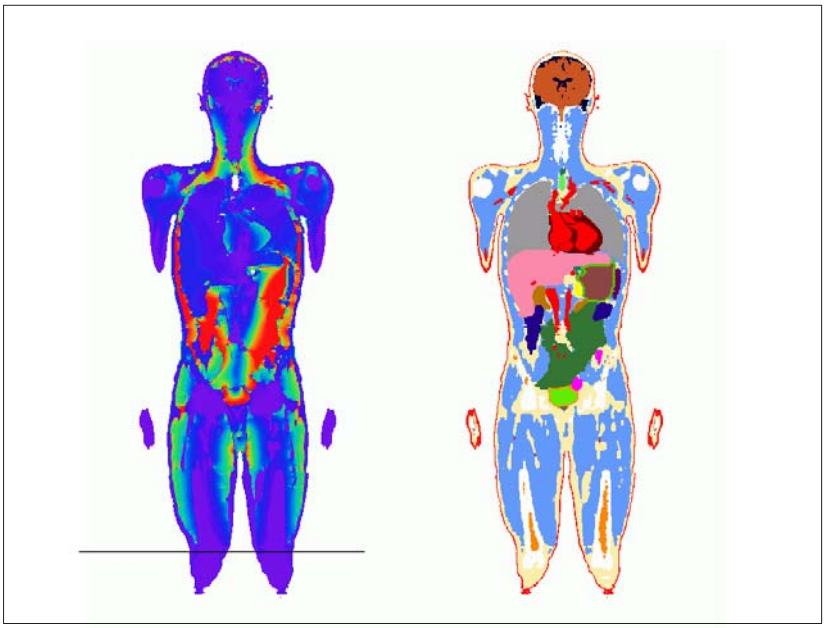

Figure 7. Distribution of the current density (left) induced by a uniform magnetic field of 50 Hz perpendicular to the frontal plane, calculated for an anatomically shaped heterogeneous model of the human body (right) (Dimbylow, 1998). The colour map of the current density (left) is a spectrum, the highest values in red and the lowest values in violet, and is only intended to give a general view of current density patterns.

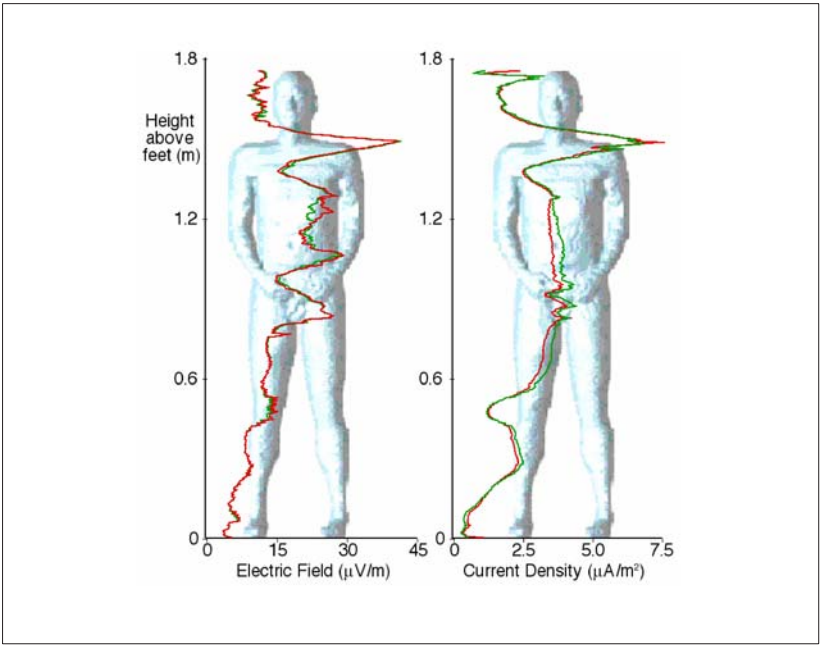

Figure 8. Layer-averaged magnitude of the electric field in V m^{-1} and current density in A m^{-2} for exposure to a uniform magnetic flux density of 1 μT and 60 Hz oriented front-to-back. The two curves on each graph correspond to two sets of conductivity (Dawson & Stuchly, 1998).

3.4.3 Computations – non-uniform fields

Human exposure to relatively high magnetic flux density values most often occurs in occupational settings. Numerical modeling has been considered mostly for workers exposed to high-voltage transmission lines (Baraton & Hutzler, 1995; Dawson, Caputa & Stuchly, 1999a; Dawson, Caputa & Stuchly, 1999c; Stuchly & Zhao, 1996). In those cases, current-carrying conductors can be represented as infinite straight-line sources. However, some of the exposures occur in more complex scenarios, two of which have been analyzed, a more-realistic representation of the source conductors based on finite line segments has been used (Dawson, Caputa & Stuchly, 1999d). Table 29 gives dosimetry for two representative exposure scenarios illustrated in Figure 9 (Dawson, Caputa & Stuchly, 1999c). Current in each conductor is 250 A for a total of 1000 A in a four-conductor bundle.

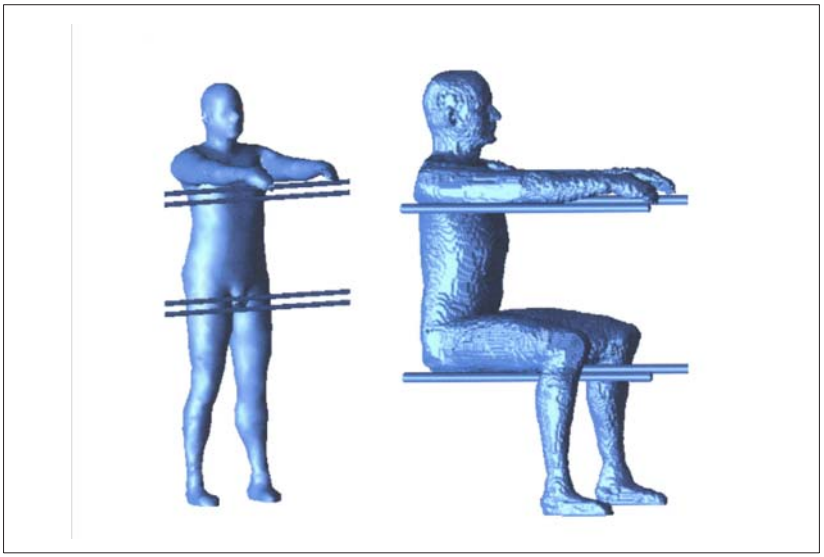

Figure 9. Two exposure scenarios used in calculations for workers exposed to high-voltage transmission lines (Dawson, Caputa & Stuchly, 1999c).

Table 29. Calculated electric fields (mV m^{-1}) induced in a model of an adult human for the occupational exposure scenarios shown in Figure 9 (total current in conductors: 1000 A; 60 Hz) [a]

Tissue/organ	Scenario A		Scenario B	
	E_{max}	E_{rms}	E_{max}	E_{rms}
Blood	20	3.7	15	2.4
Bone	90	11	58	7.2
Brain	22	4.6	28	5.9
Cerebrospinal fluid	9.2	2.3	14	3.7
Heart	27	11	9.0	3.2
Kidneys	22	7.9	2.8	0.9
Lungs	31	10	9.9	2.9
Muscle	59	6.9	33	5.5
Prostate	5.5	1.9	2.6	1.2
Testes	18	5.5	2.7	1.2

[a] Source: Stuchly & Dawson, 2000.

3.4.4 Computations – inter-laboratory comparison and model effects

To assess the reliability of data obtained by using anatomy based body models and numerical methods, an interlaboratory comparison was per-

formed (Caputa et al., 2002). Two groups in the UK and Canada used the 3.6 mm and 2 mm resolution models of average size. Each group applied its own, independently developed, field solver based on the Scalar Potential Finite Difference (SPFD) method. For a great majority of tissues, the difference in calculated parameters between the two groups was 1% or less. Only in a few cases it reaches 2–3 %. Differences of the order of 1–2 % are typically expected on the basis of the accuracy analysis (Dawson, Potter & Stuchly, 2001).

In addition, a larger size model was used to investigate effects of body size and anatomy (Caputa et al., 2002). The size of the body model and its shape (including anatomy and resolution) influenced the average (E_{avg}), voxel maximum and 99 percentile values of the induced electric field (E_{99}). The large size model mass was about 40% greater than that of the two average size models. Correspondingly, the whole-body-average electric fields were also about 40% greater, while 99 percentile electric fields were 41% and 34% greater. Such simple mass-based scaling did not apply even approximately to specific organs and tissues. The actual anatomy of persons represented by the models, as well as the accuracy of the models, both influenced differences in the two dosimetric measures for organs that are computed accurately, namely E_{avg} and E_{99}. The two models of similar size showed typically differences by about 10% or less in the average and 99 percentile values, e.g. E_{avg} in blood, brain, heart, kidney, muscle, and E_{99} in blood, brain, muscle, for the same model resolution. Relatively small organs, such as the testes, or thin organs, such as the spinal cord, indicated larger differences in induced electric field strengths that could be directly ascribed to the differences in the shape and size of these organs in the models.

3.5 Contact current

Contact currents produce electric fields in tissue that are similar to and often much greater than those induced by external electric and magnetic fields. Contact currents occur when a person touches conductive surfaces at different potentials and completes a path for current flow through the body. Typically, the current pathway is hand-to-hand and/or from a hand to one or both feet. Contact current sources may include the appliance chassis that, because of typical residential wiring practices (in North America), carry a small potential above a home ground. Also, large conductive objects situated in an electric field, such as a vehicle parked under a transmission line, serve as a source of contact current. The possible role of contact currents as a factor responsible for the reported association of magnetic fields with childhood leukaemia was first introduced by Kavet et al. (2000) in a scenario that involved contact with appliances. In subsequent papers, a more plausible exposure scenario has been developed that entails contact currents to children with low contact resistance while bathing and touching the water fixtures (Kavet et al., 2004; Kavet, 2005; Kavet & Zaffanella, 2002).

Recently, electric fields have been computed in an adult and a child model with electrodes on hands and feet simulating contact current (Dawson et al., 2001). Three scenarios are considered based on the combinations of

electrodes. In all scenarios contact is through one hand. In scenario A the opposite hand and both feet are grounded. In scenario B only the opposite hand is grounded. This scenario represents touching a charged object with one hand and grounded object with another hand. Scenario C has both feet grounded. This is perhaps the most common and represents touching an ungrounded object while both feet are grounded. Dosimetric measures can be scaled linearly for other contact current values. These in turn can be obtained for a given contact resistance (or impedance) for a known open-circuit voltage. Table 30 gives representative measures for the electric field in bone marrow, which do not vary significantly, for the three scenarios. The measures in the bone marrow are of interest in view of the reports by Kavet and colleagues cited above. It should be noted that the electric fields in the brain are negligibly small in the case of contact currents.

Table 30. Calculated electric field (mV m^{-1}) induced by a contact current of 60 Hz, 1 µA in voxels of bone marrow of a child [a]

Body part	E_{avg}	E_{99}
Lower arm	5.1	14.9
Upper arm	0.9	1.4
Whole body	0.4	3.3

[a] Source: Dawson et al., 2001.

Examination of data in Table 30 indicates that, averaged across the body, electric fields of the order of 1 mV m^{-1} are produced in bone marrow of children from a contact current of 1 µA. However, much higher values occur in the marrow of the lower contacting arm: 5 mV m^{-1} per µA averaged across this anatomical site and an upper 5th percentile of 13 mV m^{-1} per µA in this tissue. As discussed in section 4.6.2, 50 µA may result from the upper 4% of contact voltages measured between the water fixture and the drain (the site of exposure) in one US measurement study (Kavet et al., 2004); such a voltage would produce bone marrow doses of about 650 mV m^{-1} (see section 4.6.2). In contrast, current resulting from contact with an appliance would be very limited owing to the resistance of structural materials, shoes, and dry skin (Kavet et al., 2000). Contact with vehicle-sized objects in an electric field would produce currents in excess of roughly 5 µA per kV m^{-1} (Dawson et al., 2001), and would depend on the grounding of the vehicle relative to the contacting person's grounding.

3.6 Comparison of various exposures

It is interesting to compare different electric and magnetic field exposures that produce equivalent internal electric fields in different organs. Such comparisons are given in Table 31 based on published data (Dawson, Caputa & Stuchly, 1997a; Dimbylow, 2005; Stuchly & Dawson, 2002).

Table 31. Electric (grounded model) or magnetic field (front-to-back) source levels at 50 or 60 Hz needed to induce mean and maximum electric field of 1 mV m^{-1}, calculated from data of tables 23 and 27

Organ	Electric field (kV m^{-1})			
	Mean		99th percentile	
	50 Hz	60 Hz	50 Hz	60 Hz
Blood	1.45	0.70	0.60	0.11
Bone	0.17	0.28	0.020	0.029
Brain	1.28	1.16	0.50	0.51
CSF	3.69	2.86	0.87	0.98
Heart	0.78	0.70	0.25	0.35
Kidneys	0.78	0.69	0.54	0.32
Liver	0.61		0.35	
Lungs	0.92	0.72	0.39	0.41
Muscle	0.61	0.64	0.12	0.099
Prostate		0.60		0.36
Testes		2.08		0.84
Organ	**Magnetic field (μT)**			
	Mean		**99th percentile**	
	50 Hz	**60 Hz**	**50 Hz**	**60 Hz**
Blood	166.9	144.9	57.1	43.5
Bone	86.2	62.5	19.6	43.5
Brain	99.0	90.9	31.8	32.3
CSF	190.5	192.3	67.6	58.8
Heart	104.0	71.5	35.7	26.3
Kidneys	92.6	40.0	44.4	18.9
Liver	75.8		26.2	
Lungs	121.7	47.6	41.0	20.4
Muscle	118.5	66.7	43.5	19.6
Prostate		58.8		27.8
Testes		66.7		24.4

3.7 Microscopic dosimetry

Macroscopic dosimetry that gives induced electric fields in various organs and tissues can be extended to more spatially refined models of subcellular structures to quantitatively predict and understand biophysical interactions. The simplest subcellular modeling that considers linear systems requires evaluation of induced fields in various parts of a cell. Such models, for instance, have been developed to understand neural stimulation (Abdeen & Stuchly, 1994; Basser & Roth, 1991; Malmivuo & Plonsey, 1995; Plonsey

& Barr, 1988; Reilly, 1992). Also, in the past, simplified models of cells consisting of a membrane, cytoplasm and nucleus, and suspended in conductive medium have been considered (Foster & Schwan, 1989). The membrane potential has been computed for spherical (Foster & Schwan, 1996), ellipsoidal (Bernhardt & Pauly, 1973) and spheroidal cells (Jerry, Popel & Brownell, 1996) suspended in a lossy medium. Computations are available as a function of the applied electric field and its frequency. Because cell membranes have high resistivity and capacitance (nearly constant for all mammalian cells and equal to 1 F cm^{-2}), at sufficiently low frequencies high fields are produced at the two faces of the membrane. The field is nearly zero inside the cell, as long as the frequency of the applied field is below the membrane relaxation frequency. This specific relaxation frequency depends on the total membrane resistance and capacitance. The larger the cell, the higher the induced membrane potential for the same applied field. However, the larger the cell, the lower the membrane relaxation frequency.

Gap junctions connect most cells. A gap junction is an aqueous pore or channel through which neighboring cell membranes are connected. Thus, cells can exchange ions, for example, providing local intercellular communication (Holder, Elmore & Barrett, 1993). Certain cancer promoters inhibit gap communication and allow the cells to multiply uncontrollably. It has been hypothesized with support from some suggestive experimental results, that low-frequency electric and magnetic fields may affect intercellular communication. Gap-connected cells have previously been modeled as long cables (Cooper, 1984). Also, very simplified models have been used, in which gap-connected cells are represented by large cells of the size of the gap-connected cell-assemblies (Polk, 1992). With such models relatively large induced membrane potentials have been estimated, even for moderate applied fields.

A numerical analysis has been performed to compute membrane potentials in more realistic models (Fear & Stuchly, 1998a; 1998b; 1998c). Various assemblies of cells connected by gap-junctions have been modeled with cell and gap-junction dimensions and conductivity values representative of mammalian cells. These simulations have indicated that simplified models can only be used for some specific situations. However, even in those cases, equivalent cells have to be constructed in which cytoplasm properties are modified to account for the properties of gap-junctions. These models predict reasonably well the results for very small assemblies of cells of certain shapes and at very low frequencies (Fear & Stuchly, 1998b). On the other hand, numerical analysis can predict correctly the induced membrane potential as well as the relaxation frequency (Fear & Stuchly, 1998a; 1998c). It has been shown that, as the size of the cell-assembly increases, the membrane potential even at DC does not increase linearly with dimensions, as it does for very short elongated assemblies. There is a characteristic length for elongated assemblies beyond which the membrane potential does not increase significantly. There is also a limit of increase for the membrane potential for assemblies of other shapes. Even more importantly, as the assembly size

(volume) increases, the relaxation frequency decreases (at the relaxation frequency the induced membrane potential is half of that at DC).

From this linear model of gap-connected cells, it is concluded that at 50 or 60 Hz the induced membrane potential in any organ of the human body exposed to a uniform magnetic flux density of up to 1 mT or to an electric field of approximately 10 kV m^{-1} or less, does not exceed 0.1 mV. This is small in comparison to the endogenous resting membrane potential in the range 20-100 mV.

3.8 Conclusions

Exposure to external electric and magnetic fields at extremely low frequencies induces electric fields and currents inside the body. Dosimetry describes the relationship between the external fields and the induced electric field and current density in the body, or other parameters associated with exposure to these fields. The local induced electric field and current density are of particular interest because they relate to the stimulation of excitable tissue such as nerve and muscle.

The bodies of humans and animals significantly perturb the spatial distribution of an ELF electric field. At low frequencies the body is a good conductor and the perturbed field lines outside the the body are nearly normal to the body surface. Oscillating charges are induced on the surface of the exposed body and these induce currents inside the body. The key features of dosimetry for the exposure of humans to ELF electric fields are as follows:

- The electric field inside the body is normally five to six orders of magnitude smaller than the external electric field.
- When exposure is mostly to the vertical field, the predominant direction of the induced fields is also vertical.
- For a given external electric field, the strongest induced fields are for the human body in perfect contact through the feet with the ground (electrically grounded) and the weakest induced fields are for the body insulated from the ground (in “free space”).
- The total current flowing in a body in perfect contact with ground is determined by the body size and shape (including posture) rather than tissue conductivity.
- The distribution of induced currents across the various organs and tissues is determined by the conductivity of those tissues.
- The distribution of an induced electric field is also influenced by the conductivities, but less so than the induced current.
- There is also a separate phenomenon in which the current in the body is produced by means of contact with a conductive object located in an electric field.

For magnetic fields, the permeability of tissues is the same as that of air, so the field in tissue is the same as the external field. The bodies of

humans and animals do not significantly perturb the field. The main interaction of magnetic fields with the body is the Faraday induction of electric fields and associated current densities in the conductive tissues. The key features of dosimetry for the exposure to ELF magnetic fields are as follows:

- The induced electric field and current depend on the orientation of the external field. Induced fields in the body as a whole are greatest when the fields are aligned from the front or back of the body, but for some individual organs the highest values are induced for the field aligned from side-to-side.
- The consistently lowest induced electric fields are found when the external magnetic field is oriented along the vertical body axis.
- For a given magnetic field strength and orientation, higher electric fields are induced in a body of a larger size.
- The distribution of the induced electric field values is affected by the conductivity of various organs and tissues. These have a limited effect on the distribution of the induced current density.

4 BIOPHYSICAL MECHANISMS

4.1 Introduction

This chapter considers the biophysical plausibility of various proposed interaction mechanisms for ELF electric and magnetic fields; in particular whether a "signal" generated in a biological process by exposure to ELF fields can be discriminated from inherent random noise. It covers both direct mechanisms (the field interacts directly with sites in the body) and indirect mechanisms (the field affects or is related to another environmental factor, which in turn affects the body).

For exposure to ELF electric and magnetic fields to cause adverse health effects, the following sequence of events must occur. First, the field must interact with a fundamental component of the matter from which the person is made up – an atom or molecule or a characteristic of atoms or molecules such as a dipole moment. This interaction must then produce an effect at the cellular level that ultimately produces biological changes in the person that are regarded as detrimental to health.

Note that if it can be demonstrated that electric or magnetic field exposure, even at very low levels, can adversely affect health, then it follows that a mechanism of interaction must exist, even if this appears biophysically implausible. [An analogy comes from particle physics, where parity conservation was regarded as a fundamental law. However, when a convincing experimental demonstration of parity violation was made (Wu et al., 1957), it was recognised that this "law" was no longer tenable.] The converse, that if a plausible interaction mechanism cannot exist then there can be no health effects from such exposure, cannot be proven. Nevertheless, repeated failure to identify a plausible interaction mechanism might suggest, in the absence of contrary information, that such health effects are unlikely.

This chapter considers the first of the events outlined above, the biophysical interaction mechanism. It first considers the principles on which to assess whether a proposed biophysical interaction mechanism is physically plausible or not. It then surveys the various mechanisms that have been suggested and assesses their plausibility according to the criteria established.

4.2 The concept of plausibility

In the context of this document, the degree of plausibility of a mechanism relates to the extent to which it challenges scientific principles and current scientific knowledge. The degree of plausibility for a mechanism to play a role is strongly linked to the exposure level under consideration. Nevertheless, even the lack of identified plausible mechanisms would not exclude the possibility of a health effect existing even at very low field levels.

For any given mechanism of direct interaction, the magnitude of the response at a molecular level can be calculated from the physical laws involved. However, in order for the mechanism of interaction to count as biophysically plausible, it will have to produce a significant change to some

biological parameter (e.g. the transmembrane voltage) that conveys information about the external field through some signalling mechanism, such as an intracellular or neural signalling pathway. However, the parameter in question will itself be subject to random variation that conveys nothing of biological significance. For example, any voltage has a noise level caused by thermal agitation. The effect produced by the field can be of biological significance only if it can be distinguished from random fluctuations.

A convenient way of expressing this concept is in terms of a signal-to-noise ratio. In this context, the "signal" is the effect on a given parameter produced by the field, and the "noise" is the level of random fluctuations that occur in that parameter. If the signal-to-noise ratio is less than one, there will be no "detectable" change in the parameter that can be attributed to the field and no possibility of subsequent biological effects that are similarly attributable. If the signal-to-noise ratio is one or greater, then there could be a change in the parameter that is attributable to the field, and there is a possibility of subsequent events producing an effect in the organism.

Random fluctuations in biological systems typically extend across a wide range of frequencies. If the biological "transducer", the cellular component that responds to an external signal such as an applied ELF field, is itself sensitive to a wide range of frequencies, then the comparison should be made with the amplitude of the noise over its whole frequency range. However, if the transducer concerned is sensitive only to a narrow range of frequencies, then the applied signal should be compared only to that component of the noise over the frequency range of sensitivity. Vision and hearing are two such phenomena where sensitivity is highly frequency-dependent.

Other factors that could increase the signal-to-noise ratio are amplification mechanisms for the signal. They include enhancement of the signal due to cell geometry or signal processing by large electrically coupled cell aggregates. Those mechanisms are discussed in detail in the following sections.

With indirect effects the principle still applies that the agent (for example chemicals, ions etc.) influenced by or occurring in concert with the fields must be sufficiently large to produce a detectable change in the biological system.

In summary therefore, a proposed biophysical mechanism can only constitute a plausible mechanism for fields to interact with living tissue as to be potentially capable of causing disease if it causes a variation in some parameter that is larger than the background noise. The mechanism will be more plausible if this variation is either substantially larger than the random noise, or if the organism has developed frequency-specific sensitivity.

4.3 Stochastic effects, thresholds and dose-response relationships

The nature of the various possible interaction mechanisms discussed below affects the way in which health effects might be induced. At a fundamental level, stochastic interactions, such as random genotoxic damage

to DNA by, for example, reactive oxygen species, increase the probability of inducing a mutation and hence the risk of initiating cancer. Deterministic effects, on the other hand, occur when some threshold is passed, for example when applied electric fields cause sufficient sodium ion channels in a nerve membrane to have opened so that nerve excitation becomes self-sustaining. Such thresholds usually show a distribution of sensitivity within populations (of cells and of people), and so the induction of an effect will vary over this range within the population.

The way in which a subsequent health effect might vary with exposure can be estimated from the biophysical nature of the interaction alone, although this will tend to neglect the contribution made by the intervening chain of biological responses at the cellular and whole organism level, and so can only be suggestive. For example, the ability to reverse acute physiological changes such as ion fluxes, and to repair for example potentially long term effects like oxidative damage, will affect the overall health outcome.

With regard to alternating fields, if the effect of an interaction depends on the size of the field and not its spatial direction, then the magnitude of the effect depends simply on the size of the field. However, any effect that depends on the direction of the field as well as its size will, to a first order, average to zero over time; as one half cycle increases an effect, the other decreases it by the same amount.

Non-linearities in the interaction mechanism mean that these effects do not average out exactly to zero. (It is worth noting here that any subsequent biological responses are almost certain to be non-linear.) The effect produced, which is the difference between two first-order or linear effects, is a second-order effect, proportional to the field squared (or to an even higher power) rather then the field. Subsequent stages in the mechanism may modify this further, but are unlikely to restore any component proportional to the field itself.

Mathematically, the effect of the field can be expressed as a Taylor expansion. For any effect proportional to the field B, the first order term of the Taylor expansion averages to zero and the lowest order non-zero term is the second power of field (Adair, 1994). However, for an effect proportional to the modulus of B, the first order term can be non-zero as well.

The practical consequence of this is that if the mechanism is proportional to the square of the field or a higher power, the effects will be produced more by short exposures to high fields than by long exposures to low fields. In particular, high fields are experienced predominantly from domestic appliances, so a mechanism proportional to a higher power of field would be expected to show effects related to appliance use more clearly than effects related to background fields in homes. However, this might depend to some extent on the way in which the initial interaction was subsequently modified by biological processes.

4.4 Induced currents and fields

4.4.1 Currents induced by fields

Power-frequency fields, both electric and magnetic, induce electric fields and hence currents in the body. An external electric field is attenuated greatly inside the body, but the internal field then drives a current in the body. A magnetic field induces an electric field, which will in turn drive a current in the conducting body. This is discussed in detail in Chapter 3, where results from numerical modelling are presented.

4.4.2 Comparison with noise

The observation of several cellular and membrane responses to weak ELF fields has raised the question of how the magnitudes of these signals compare with the intrinsic electrical noise present in cell membranes. The three major sources of electrical noise in biological membranes are (Leuchtag, 1990): (1) Johnson-Nyquist thermally-generated electrical noise, which produces a 3-μV transmembrane voltage shift at physiological temperatures; (2) "shot" noise, which results from the discrete nature of ionic charge carriers and can be a major source of membrane electrical noise; and (3) 1/f noise associated with ion current flows through membrane channels, which typically produces a 10-μV transmembrane voltage shift.

Any material (including but not confined to biological material) has fluctuating electric fields and corresponding currents within it, due to the random movement of the charged components of matter. From basic physical consideration, an expression can be derived for a lower limit to the thermal noise voltage or field that appears between two points across any element of material. This thermal noise field depends on the resistance of the element (and hence for a given material its size), the temperature (which for the present purposes can always be taken as the body temperature), and the frequency range. (Strictly speaking, it is the noise in a given frequency band that depends on the resistance; the total noise across all frequencies is independent of the resistance and depends instead on the capacitance.)

There are other sources of noise as well, which in some instances may be much larger than the thermal noise, but the thermal noise always constitutes a lower limit on the noise. One particular other source of noise, shot noise, is considered separately in the next section.

In regard to shot noise, when a process depends on discrete particles, and some property produced by the process depends on the average number of particles fulfilling some condition, there will be a random variation in the number of particles involved, which can be regarded as a noise level superimposed on the average number. This is known as "shot" noise. This can be applied to passage of ions or molecules through a voltage-gated channel in a cell membrane. The number of ions passing through such a channel in the absence of a field depends on the maximum possible flux of ions, a property of the cell membrane, and how often the gates or channels are open, a function of the transmembrane potential, the noise energy den-

sity, the cell gating charge, and the exposure time. The signal-to-noise ratio will be maximised by considering either a long cell parallel to the in situ electric field with the channels confined to the ends (so as to minimise the number of channels which are not affected by the applied field), or by a large spherical cell (so as to maximise the cell's area). For a cylindrical cell 1 mm long and radius 25 μm, or for a spherical cell radius 100 μm, and for typical values of the other parameters, the value of the in situ electric field for a signal-to-noise ratio of one is around 100 mV m^{-1} (Weaver & Vaughan, 1998). By optimising the noise level and the transmembrane potential, the threshold field can be improved, to around 10 mV m^{-1}, corresponding to external fields of 5 kV m^{-1} and 300 μT.

The shot noise considered above is mostly in relation to the spontaneous opening and closing of voltage-gated channels. The arrival of neurotransmitters (synaptic events) also causes voltage fluctuations in nerve and muscle cells. In an experimental study by Jacobson et al. (2005) it was shown that voltage noise in neurons fluctuated with a standard deviation up to 0.5 mV, and that these fluctuations were dominated by synaptic events in the 5–100 Hz range. Shot noise associated with these neurotransmitter events may thus be much more relevant in estimating excitation thresholds in the retinac (Jacobson et al., 2005).

Despite the presence of thermal and shot noise, it appears that 1/f noise is the dominant source of noise on the membrane and represents a reasonable baseline for signal-to-noise considerations, and for the estimation of equivalent external field values. External field values required to produce a signal discernable from noise depend on the specific characteristics of the biological system in question. However, at least for small isolated cells in the human body, the range of external fields would be of the order of 10 mT and 100 kV m^{-1}.

4.4.3 Myelinated nerve fibre stimulation thresholds

The electrical excitability of neurons (nerve cells) results from the presence of voltage-gated ion channels, principally sodium, potassium, calcium and chloride, in the cell membrane (e.g. McCormick, 1998). Sodium, calcium and chloride ions exist in higher concentrations on the outside of each neuron, and potassium and membrane-impermeant anions are concentrated on the inside. The net result is that the interior of the cell is negatively charged compared to the exterior; generally, inactive mammalian neurons exhibit a "resting" membrane potential of –60 to –75 mV. An externally applied electric field will stimulate the peripheral nerve cell axon resulting in one or more action potentials if the induced membrane depolarisation is above a threshold value sufficient for the opening of the voltage gated sodium channels to become self-sustaining. For many nerve axons, the action potential threshold is around –50 mV to –55 mV, some 10–15 mV above the "resting" potential.

Electrical stimulation of myelinated nerve fibres can be modelled using electrical cable theory applied to the membrane conductance changes

originally described by Hodgkin and Huxley (1952) and Frankenhaeuser and Huxley (1964). Reilly, Freeman & Larkin (1985) proposed a spatially extended nonlinear nodal (SENN) model for myelinated nerve fibres that has been used to derive thresholds for various applied electrical fields and currents. Minimum, orientation-dependent stimulus thresholds for large diameter myelinated nerve axons were estimated to lie around 6 V m^{-1} (Reilly, 1998b), which equates to a current density of about 1.2 A m^{-2} assuming a tissue conductivity of 0.2 S m^{-1}. Electric field thresholds were estimated to be larger for smaller diameter neurons. Note however that passive cable theory does not apply to neuronal dendrites in the CNS (e.g. Takagi, 2000).

4.4.4 Neural networks and signal detection

The previous section described estimates of thresholds for stimulating individual nerve fibres. The nervous system itself, however, comprises a network of interacting nerve cells, communicating with each other principally via chemical "junctions" or synapses in which neurotransmitter released by the pre-synaptic terminal binds to specific receptor molecules on the post-synaptic cell, usually in a one-way process. The activation of receptors by the neurotransmitter may then cause a variety of post-synaptic responses, many of which result in an alteration of the probability that a particular type of ion channel will open. Such neural networks are thought to have complex non-linear dynamics that can be very sensitive to small voltages applied diffusely across the elements of the network (e.g. Saunders, 2003). The sensitivity of N interacting neuronal units increases theoretically in proportion to $\sqrt{N}$ (Barnes, 1992). Essentially, the signal-to-noise ratio improves if the noise is added randomly, but the signals are added coherently.

The theoretical basis for neural network sensitivity has been explored by Adair, Astumian & Weaver (1998) and Adair (2001), considering the detection of weak electric fields by sharks, and other elasmobranchs. These fish are known to be able to respond behaviorally to electric fields in seawater as low as 0.5 μV m^{-1} that generate small electrical potentials, of the order of 200 nV, in the "detector" cells of the ampullae of Lorenzini. Adair (2001) suggests that such a weak signal would generate a signal-to-noise ratio greater than 1 within 100 ms with the convergence of approximately 5000 sensory detector cells onto a secondary neuron that exhibits coincidence detection, a property of certain types of neurotransmitter receptor (Hille, 2001).

Such convergence is a common property of sensory systems; evolutionary pressure exists to maximise the sensitivity with which environmental stimuli can be detected. In the peripherey of the mammalian retina, for example, up to 1000 rods converge on one ganglion (retinal output) cell (Taylor & Smith, 2004). In addition, brain function depends on the collective activity of very large numbers of interacting neurons. EMF effects on nervous system function and behaviour are described in Chapter 5. However, a lower limit on neural network sensitivity in humans has been estimated to lie around 1 mV m^{-1} (Adair, Astumian & Weaver, 1998); a similar value of a lower limit was agreed at an ICNIRP/WHO workshop on weak electric field sensitivity

held in 2003 (McKinlay & Repacholi, 2003). Modelling of the human phosphene response and neurphysiological studies of brain tissue function suggest such thresholds are more likely to lie in the 10–100 mV m^{-1} region (see section 5.2.3).

4.4.5 Transients

The current induced by both electric and magnetic fields is directly proportional to the frequency. Thus, a higher frequency could result in an improved signal-to-noise ratio. Induced current effects are plausible from continuous high-frequency signals. Fields produced by power systems have no significant continuous higher frequency component. They can, however, contain transients, that is, short-lasting components of higher frequency. Because they are short-lasting rather than continuous, different considerations apply. Adair (1991) analysed the effect of short-term pulses from a consideration of momentum transfer to various entities. The external pulse is modelled as the sum of exponential rise and fall terms and this is used to calculate the frequency and amplitude components of the corresponding internal pulse. The momentum transferred by the pulse is compared with the thermal momentum for representative ions, molecules, and cells. For an external electric-field pulse of 100 kV m^{-1} the effect of the pulse is small compared to thermal motion.

4.4.6 Heating effects of induced currents

The current induced by an electric or magnetic field produces heating in the tissues through which it passes. From a knowledge of the resistivities of the various components of tissue and of cells it is possible to calculate the heat produced. Combined with knowledge of tissue thermal conductivities and of the effect of circulation, it is then possible to calculate the temperature rise.

Kotnik & Miklavcic (2000) calculated power dissipation in various portions of cells, including the membrane. They do not calculate corresponding temperature rises, which are expected to be small.

4.4.7 Summary on induced currents

Comparisons have been made between the signal produced by external fields and various noise levels or levels of established effects, as shown in Table 32.

Essentially, the effects of weak fields on synapses can only be detected as a biologically meaningful signal through some sort of neural network showing convergence. This characterizes sensory systems like the ampullae of Lorenzini of the sharks, and the periphery of the retina, which have evolved to detect weak signals.

Complex neural circuits exist within the rest of the brain (see Shepherd & Koch, 1998 for a review); the extent to which these might show sensitivity to electric fields induced by EMF exposure is discussed in Chapter 5.

Table 32. Comparison between the signal produced by external fields and various of in situ electric field noise levels or nervous system effect thresholds

Comparison		In situ electric field (mV m^{-1})	Corresponding external electric field (V m^{-1}) [a]	Corresponding external magnetic field [b]
Thermal noise	Volume of cell	20	10^4	600 µT
	Complete membrane	200	10^5	5 mT
	Element of membrane	1000	10^9	40 T
Shot noise	Typical cell	100	$5x10^4$	3 mT
	Optimised cell	10	5000	300 µT
1/f noise			$1x10^5$	10 mT
Myelinated nerve stimulation threshold (SENN)		5000		
Phosphene threshold (dosimetric calculation)		10–100		
Estimated lower limit for neural network threshold		1		

[a] Source: Dimbylow, 2000.

[b] Source: Dimbylow, 1998.

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4.5 Other direct effects of fields

4.5.1 Ionization and breaking of bonds

The bonds that hold molecules together can be broken by delivering sufficient energy to them. Electromagnetic radiation is quantised, and the energy of each quantum is given by Plank's constant, h, multiplied by the frequency. The energy required to break various bonds that are found in biological systems has been quantified, e.g. by Valberg, Kavet & Rafferty (1997). Typical covalent bonds require 1–10 electronvolt (eV), and typical hydrogen bonds require 0.1 eV. The quantum energy of 50 Hz radiation is

10^{-12} eV. Thus a single quantum of 50 or 60-Hz radiation clearly does not have adequate energy to break bonds. The quantum energy becomes comparable to the energy of covalent bonds at around the frequencies of visible light.

Vistnes & Gjotterud (2001) have pointed out that the wavelength at 50 Hz, 6000 km, is so much larger than the distance scales of the interactions being considered in the body that it is inappropriate to consider single-quantum events. They calculate that in the human body in a 10 kV m^{-1} field, far from a situation of single photons, there are in fact of order 10^{34} "overlapping" photons present within the volume that a single photon can be said to occupy. It is still correct to say that chemical bonds cannot be broken by absorption of a single photon, but it would not be correct to use that to rule out any other possible effects of EMFs.

As an alternative to transfer of energy to a bond by quantum energy, fields might transfer sufficient energy to break a bond by accelerating a charged particle and thereby imparting energy to it. The "noise" here is the thermal kinetic energy of the particle, determined from fundamental thermodynamics, and is about 0.04 eV for room or body temperature. If the maximum distance over which a particle can be accelerated is assumed to be limited to 20 μm, the dimension of a typical cell, the fields required to impart equal energy to this thermal energy are of order 10^9 V m^{-1} and 1 μT. In practice the maximum distance would be even shorter and hence the required field even higher.

4.5.2 Forces on charged particles

Both electric and magnetic fields exert forces on charged particles. The force exerted by an electric field on a charge q is F=qE, directed in the same direction as the field. The force exerted by a magnetic field appears only on a moving charge and is F=vq$B$, directed perpendicularly to both velocity v and field B.

These forces can be compared to those required to produce various effects in biological systems (Valberg, Kavet & Rafferty, 1997). These range (to the nearest order of magnitude) from 1 picoNewton (pN) to activate a single hair cell in the inner ear, through 10 pN to open a mechanoreceptor transmembrane ion channel, to 100 pN which equals the force binding a ligand molecule to a protein receptor.

To produce 1 pN would require an external electric field (in air) in the order of 10^{10} V m^{-1} (assuming a molecule with 10 charges located in a cell membrane); or a field of 10 μT (the Lorentz force acting on the same molecule moving with average thermal velocity is less than the force due to the induced electric field).

4.5.3 Forces on magnetic particles

A magnetic field will exert a turning force (a moment or torque) on any entity that has a magnetic moment. If ferromagnetic crystals existed in

the body, they could have a magnetic moment, and hence the field could exert an oscillating moment on them and cause them to vibrate.

The size of the turning force is determined by the size of the field and the size of the magnetic moment. One magnetic material which is known to exist in some biological systems is magnetite. If it is assumed that a particle of magnetite exists where all its individual magnetic domains are aligned, the magnetic moment of the particle is the saturation magnetization of magnetite multiplied by the volume. Thus the maximum turning force exerted on the particle is proportional to its volume. If the magnetic field were a static field, the particle would rotate until either restoring forces equalled the turning force, or it was aligned with the field. With an alternating field, however, the amplitude of oscillation is determined by the viscosity of the surrounding medium as well.

In this instance, the "signal" produced by the field, an amplitude of oscillation at the power frequency, has to be compared to the "noise", the amplitude of oscillation of the same particle produced randomly by thermal noise (i.e. Brownian motion). Adair (1994) has calculated that, for a single-domain magnetite particle of diameter 0.2 μm, and a viscosity of the surrounding medium of seven times water, both of which are regarded as extreme assumptions, the "signal" becomes equal to the "noise" for a field of 5 μT. If alternative assumptions are made, equivalent field values can be calculated, given that the effect is proportional to the diameter of the particle cubed and to the field squared. More plausible choices of the particle size and viscosity lead to an equivalence between noise and signal levels at higher fields.

It is known that some animals use magnetite to detect small changes in the earth's static magnetic field, for navigation purposes (ICNIRP, 2003). For example, certain bee species have been shown to detect a change in static field of 26 nT (Kirschvink & Kirschvink, 1991; Walker & Bitterman, 1985). This appears to be achieved by means of magnetite particles, in air, attached to large numbers of sensory hairs. Signal discrimination by the nervous system dramatically improves the signal-to-noise ratio, and such sensitivity is plausible without requiring a signal-to-noise ratio more than one.

Kirschvink et al. (1992) describe the existence of trace levels of magnetite in the human brain and other tissues, and postulate that such crystals might act as transducers, opening mechanically sensitive transmembrane ion channels in hypothesised "receptor" neurons within the central nervous system. Such a "detector" would be subject to the constraints described above. However, attempts to confirm that humans can use the geomagnetic field for orientation and direction-finding have so far failed (ICNIRP, 2003). These authors concluded that the presence of magnetite crystals in the human brain does not confer an ability to detect the weak geomagnetic field, although some mechanisms of magnetic sensitivity remain to be explored (Kirschvink, 1997). Interestingly, Scaiano, Monahan & Renaud (2006) note that magnetite particles can dramatically effect the way in which external magnetic fields affect radical pair interactions.

4.5.4 Free radicals

The radical pair mechanism is the only generally accepted way in which static and ELF magnetic fields can affect the chemistry of individual molecules (e.g. see Brocklehurst & McLauchlan, 1996; Eveson et al., 2000; Grissom, 1995; Hore, 2005; McLauchlan, 1992; Steiner & Ulrich, 1989). This involves a specific type of chemical reaction: the recombination of a pair of short-lived, reactive free radicals generated either from a single molecule or from two molecules by intermolecular electron or hydrogen atom transfer. The effect of an applied magnetic field depends upon its interaction with the spin of unpaired electrons of the radicals. Importantly, this effect may constitute a mechanism for the biological effects of very weak fields (Adair, 1999; Timmel et al., 1998). Field-sensitivity occurs over the period of radical pair formation and recombination, typically tens of nanoseconds in normal solutions, but possibly extended to a few microseconds in micelles (Eveson et al., 2000) or other biological structures. Power frequency magnetic fields are essentially static over these short time intervals, an equivalence that was confirmed experimentally by Scaiano et al. (1994) and that may extend up to frequencies of a few MHz (Adair, 1999).

Free radicals are a chemical species formed during many metabolic processes and thought to contribute to various disease states such as neurodegenerative disease (see Chapter 7). During normal metabolism, for example, oxygen is reduced to H_2O in mitochondria during energy production by oxidative phosphorylation. This involves the sequential addition of four electrons, producing intermediate reactive oxygen species such as the superoxide anion radical ($O_2^{\cdot -}$), hydrogen peroxide (H_2O_2) and the hydroxyl radical ($OH^{\cdot}$). Most cells contain a variety of radical scavengers such as glutathione peroxidase that provide anti-oxidant defence mechanisms. If these are depleted, for example from exposure to an agent such as long wavelength ultraviolet radiation (UVA) that generates excess reactive oxygen species, tissue damage may ensue (AGNIR, 2002).

Free radicals can also be formed by the homolytic scission of a covalent bond. Most biological molecules exist in a low energy, singlet state in which the angular momentum of a molecule containing pairs of electrons is zero because the spins of electron pairs are antiparallel (reviewed by e.g. Brocklehurst & McLauchlan, 1996; Eveson et al., 2000; McLauchlan, 1992; Timmel et al., 1998). The scission of a covalent bond in such a molecule can result in the formation of two geminate radicals, each bearing an unpaired electron with a spin anti-parallel to the other. The energy released by the reaction causes the free radicals to separate rapidly so that relatively little instantaneous reaction ensues. Subsequently, the magnetic interactions (hyperfine couplings) of the electron spins with the nuclei of nearby hydrogen and nitrogen atoms modify the spin state of the radical pair, giving it some triplet character (Zeeman effect). For applied magnetic fields typically greater than 1–2 mT, the probability of reaction during a re-encounter of the radicals is increased, with a concomitant decrease in the number of free radicals that escape recombination and diffuse into the surrounding medium.

Conversely, in magnetic fields of less than ~1 mT, the free radical concentration is increased with possibly harmful effects. Experimental evidence for such effects in biochemical systems has been recently reported by Hore, McLauchlan and colleagues (e.g. Eveson et al., 2000; Liu et al., 2005). In contrast, effects on the recombination of randomly diffusing radicals with uncorrelated spins that encounter by chance are thought to be negligible (Brocklehurst & McLauchlan, 1996).

Hore (2005) notes that more than 60 enzymes use radicals or other paramagnetic molecules as reaction intermediates, although most do not involve radical pairs with correlated electron spins. The maximum size of an effect of a field of less than ~1 mT on a wide variety of geminate radical pairs has been calculated by Timmel et al. (1998). It was found that a weak field, even one comparable to the geomagnetic field, could alter the yield of any free radical recombination by 15–30%. This depended however, on the radical pair existing in close proximity for a sufficiently long time for the applied field to have an effect. Durations of the order of 100–1000 ns have been suggested as necessary (e.g. Brocklehurst & McLauchlan, 1996; Timmel et al., 1998) but these might only exist where some form of physical constraint applied, such as within a membrane for example, or bound to an enzyme. In addition, theoretical calculation and experimental investigation indicate that variation of the magnitude of these effects with magnetic field intensity is highly non-linear (Brocklehurst & McLauchlan, 1996; Grissom, 1995; Hore, 2005; Timmel et al., 1998).

The biological significance of these types of effects is not clear at present. They have been suggested (Cintolesi et al., 2003; Ritz, Adem & Schulten, 2000; Schulten, 1982) as a mechanism by which animals, particularly birds, may use the Earth's magnetic field as a source of navigational information during migration and there is some experimental support for this view (Ritz et al., 2004). The Earth's magnetic field is ~50 μT, varying from about 30 μT near the equator to about 60 μT at the poles. Apart from this rather specialised instance however, since static and ELF magnetic fields are equivalent in their interactions, Scaiano et al. (1994) and Adair (1999) suggest that power frequency fields of much less than around 50 μT are unlikely to be of much biological significance. Several specific requirements have to be fulfilled for small, but significant modifications to the recombination rate at 50 μT and these conditions are sufficiently special to be considered unlikely (Adair, 1999). Liu et al. (2005) note that, given the efficiency of homeostatic buffering processes such as the radical scavenging mechanisms described above, there does not appear to be a strong likelihood of physiologically significant changes in cellular functions or of long term mutagenic effects resulting from low magnetic field-induced variations in free radical concentrations or fluxes. In addition, processes such as modulation of anisotropic magnetic interactions by radical tumbling may set a lower bound on the detection of this low field effect.

4.5.5 *Effects with narrow bandwidths*

When comparing the signal to the noise, the comparison must be with the noise over the correct frequency range. If a postulated mechanism is sensitive only to a narrow range of frequencies, the noise must be assessed over that same range, which will in general be less than over a wider range of frequencies. A number of mechanisms have been proposed which achieve this narrow bandwidth, usually by some form of resonance condition involving the static field.

4.5.5.1 *Cyclotron resonance*

A moving charged particle in a magnetic field will perform circular orbits (if left undisturbed for sufficiently long) with a frequency determined by the charge q, the field B and the mass m, the frequency being Bq/m. An AC field at the same frequency could then interact in a resonant fashion. However, to produce cyclotron resonance of a biologically relevant particle such as a calcium ion at power frequencies requires unconstrained orbits of order 1 m diameter lasting several cycles, whereas molecular collisions (i.e. damping) occur which would destroy the orbit and the resonance on timescales of 10^{-12} s.

4.5.5.2 *Larmor precession*

A charged particle vibrating in a magnetic field will have its direction of vibration rotated about the field at the Larmor frequency, which is half the cyclotron frequency. If the field itself is modulated at this frequency, the particle will vibrate for longer in certain directions than others, with the potential for altering reaction probabilities (Edmonds, 1993). This mechanism again requires the vibration to continue unperturbed by other factors for an implausible length of time.

4.5.5.3 *Quantum mechanical resonance phenomena*

A number of quantum mechanical phenomena have been suggested to explain biological observations involving low levels of exposure. Among these, one particular phenomenon has been investigated in some detail, ion parametric resonance, whereby the DC field creates various sublevels of a vibrating ion, and the AC field then causes transitions between them. It predicts effects at the cyclotron resonance frequency and integral fractions of it (Blanchard & Blackman, 1994; Lednev, 1991; Lednev, 1993; Lednev, 1994).

The mechanism has been extensively investigated, with the conclusion that it is not plausible. It requires unfeasibly narrow vibrational energy levels, a fixed phase relationship between the vibrational states and the externally applied field, and implausible symmetry of the binding of the ion (Adair, 1992; 1998).

4.5.6 Stochastic resonance

Stochastic resonance is the phenomenon whereby random noise, added to an oscillating, non-linear system, can produce responses which are not seen in the absence of the noise. Under some circumstances it is possible for the addition of noise to a system to produce a dramatic change in the response. However, this applies primarily to the addition of small amounts of noise to a larger signal. It is relevant, for example, when considering the exact threshold for shot noise, and is included in those calculations; but it cannot explain a response to small signals in the presence of a larger noise (Adair, 1996; Weaver & Vaughan, 1998).

4.6 Indirect effects of fields

4.6.1 Surface charge and microshocks

In a power-frequency electric field, a charge is induced on the surface of a body. If the field is large enough (see section 5.2.1) this can be perceived through the vibration of hairs.

In an electric field, different objects acquire different potentials, depending on whether they are grounded or not. A person touching a conducting object, where one is grounded and the other is not, experiences a microshock or small spark discharge (see section 5.2.1). This can be painful and can lead to burns to the skin in extreme circumstances.

4.6.2 Contact currents

When a person simultaneously contacts two conductive objects that are at different electrical potential, that person will conduct a contact current whose magnitude is inversely proportional to the electrical resistance between those two points. A fraction of the pathway's resistance is that which exists between the object's points of contact and the subdermal layers. This fraction is high for a dry fingertip contact and much lower for a wet full-handed grip (large surface area shorted by the moisture across the outer dermal layer). Body resistance exclusive of the skin contact points is much less variable, but depends on body dimensions, fat-to-muscle content, etc.

Kavet and colleagues have identified a child in a bathtub as the most likely scenario for exposure to contact current and have suggested that the electric field induced in the bone marrow of children so exposed might offer a plausible interaction mechanism underlying the increased risk of childhood leukaemia (see section 11.4.2) associated with magnetic field exposure (Kavet et al., 2004; Kavet, 2005; Kavet & Zaffanella, 2002). When bathing, young children frequently engage in exploratory behaviours that include contact with the faucet handle, the spout, or the water stream itself. In residential electrical systems in which a home's water line is connected to the electrical service neutral, a small voltage (usually less than a volt) can appear between the water line, and thus the water fixtures, and earth. If the tub's drain is conductive and sunk into the earth, a child can complete the circuit by touching the water fixtures or water stream. Because both ends of the contact are wet, body resistance is minimised (to perhaps 1–2 kiloohm [kΩ]).

The voltage on the water line may arise from either return current in the grounding system producing an ohmic voltage difference between the water line and earth, or as a result of Faraday induction on the neutral/grounding system, or from both. Measurement studies in the USA indicated that the closed circuit voltage (i.e., with a 1 kΩ resistor replacing a person) from the water line to the drain may exceed 100 mV in a small percentage of homes (~ 4%) (Kavet et al., 2004). Under such conditions roughly 50 μA could enter a child's hand. Dosimetric modelling by Dawson, Potter & Stuchly (2001) estimated that a 50 μA exposure would produce about 650 mV m^{-1} or more in 5% of the marrow in the lower arm of an 18 kg child (normal weight for a 4-year old). Smaller (i.e. younger) children would experience larger internal fields. Chiu & Stuchly (2005) computed that a local field of 1 V m^{-1} could produce 0.2 mV across the gap junctional apparatus connecting two bone marrow stromal cells; these are the cells that orchestrate hematopoiesis that includes lymphocyte precursor cellular proliferation (LeBien, 2000). For the scenario described above, Chiu & Stuchly's (2005) values would scale to 0.13 mV across the gap junction. Bulk tissue fields and transmembrane potentials of these magnitudes constitute signals that exceed competing noise.

There is at present, however, no biological evidence indicating that such fields and currents within bone marrow are either carcinogenic or stimulate the proliferation of initiated cells. Nor is there any epidemiological evidence linking contact current in children to the risk of childhood leukaemia. However, measurement studies (Kavet et al., 2004; Kavet & Zaffanella, 2002) together with computer modelling of typical US neighborhoods (Kavet, 2005) indicate that, across a geographic region characteristic of a population-based epidemiology study, residential magnetic fields are very likely to be positively associated with the source voltage for contact current exposure. These results offer support to this proposed hypothesis.

To date engineering research concerning contact currents has focused largely on electrical systems characteristic of the USA. Some countries in which ELF epidemiology has been conducted have electrical systems with multiple ground points (e.g. the UK; see Rauch et al., 1992) that include the water supply. Others without explicit connections may very well have inadvertent water-line-to-earth voltages, primarily via the water heater connection.

4.6.3 Deflection of cosmic rays

Cosmic rays are produced by the sun, in space, and in the atmosphere, and are known to be able to cause harm to humans through energy deposition in biological tissue. Hopwood (1992) suggested that both electric and magnetic fields from power lines could deflect cosmic rays which pass close to the power lines in such a way as to produce a focussing effect close to the power line. Hopwood reported measuring a doubling of sky particle count a few metres to the side of a power line, though subsequent more sophisticated measurements have failed to show any increase (Burgess & Clark, 1994). Simple analytical calculations suggest the deflections are likely

to be of the order of only centimetres, and then only for those particles which pass very close to the conductors. Skedsmo & Vistnes (2000) have performed sophisticated numerical modelling, and showed that even for low energy electrons (the particles most susceptible to deflection) the difference in particle flux density under and to the sides of the line is less than 0.15%, and for all particles combined it is less than 0.01%. Such differences are too small to be relevant for health effects.

4.6.4 Effects on airborne pollutants

A category of mechanisms has been suggested (Fews et al., 1999b; Fews et al., 1999a; Fews et al., 2002; Henshaw et al., 1996a; Henshaw et al., 1996b) where the electric fields produced by overhead power lines interact with airborne pollutant particles in such a way as to increase the harmful effects of these particles on the body.

Airborne particles having the greatest effects on health include tobacco smoke, radon decay products, chemical pollutants, spores, bacteria and viruses (AGNIR, 2004). If inhaled, some become deposited in the airways of the respiratory system. Others can be deposited on the skin. Since charged particles are more likely than uncharged particles to be deposited when close to the walls of the respiratory airways or to the skin, an increase in the proportion of particles that are charged could lead to an increase in adverse health effects. Fews et al. (1999b) suggested that such an increase could arise from the generation of corona ions by power lines. These positive or negative ions arise when electrical potentials of a few thousand volts or greater cause electrical breakdown of the air by corona discharges. A further increase in the deposition of charged particles could arise due to an increase in the probability of their impact with surfaces of the skin and respiratory airways in the presence of electric fields (Henshaw et al., 1996b).

4.6.4.1 Production of corona ions

As a consequence of corona discharges, high voltage AC power lines may produce clouds of negative or positive ions that are readily blown downwind (AGNIR, 2004). Negative ions are more often produced, especially in fog or misty conditions. Although high voltage AC transmission lines are designed to operate without generating corona discharges, small local intensifications of the conductor surface electric field can occur at dust and dirt accumulations, or at water drops, sometimes causing corona discharges to occur. In addition, some high voltage lines are operated above their original design voltage and can be more prone to corona discharge in adverse weather conditions. An increase of charge density downwind of power lines can often be observed at distances up to several kilometres (Fews et al., 1999a; Fews et al., 2002; Swanson & Jeffers, 1999; Swanson & Jeffers, personal communication in AGNIR, 2004). However, recently, Bracken Senior & Bailey (2005) have reported measurements carried out over two years of DC electric fields and ion concentrations upwind and downwind of 230-kV and 345-kV transmission lines at two sites. They found some evidence of an excess downwind, but the downwind values only

exceeded the range of upwind (ambient) values for a small percentage of the time under most conditions.

The ion clouds charge particles that pass through them. These particles will already carry some charge because of the naturally occurring ions that exist in the atmosphere, but it seems likely that in some regions this will be increased even at ground level as a result of corona discharge. Calculating this increase as a function of particle size is possible but only if a number of simplifying assumptions are made. The effects indoors, where the majority of people spend most of their time, are likely to be less than outdoors, for example because of deposition of corona ions on the surfaces of small apertures through which some air enters buildings.

4.6.4.2 Inhalation of pollutant particles

People may be exposed to these more highly charged pollutant particles and the possibility that electrostatic charge could increase their respiratory tract deposition has been recognised for some time (AGNIR, 2004). In principle, the effect could be significant and AGNIR (2004) estimated that in the size range of about 0.1–1 μm, where lung deposition is normally low (about 10%) there is potential to increase lung deposition by up to a theoretical maximum factor of about 3–10, depending on particle size. The actual increase will depend on the number of charges and particle size, though neither experimental results nor theory currently allow reliable predictions. Nevertheless, experimental and theoretical studies indicate that increased deposition should be very small for particles larger than about 0.3 μm because of the high charge per particle needed to produce a significant effect. For smaller particles, the effect of charge on deposition of a pollutant within the lungs will be appreciably less than the theoretical maximum for various reasons. Indeed, for the smallest (less than about 10 nm diameter) particles, charge may even decrease the probability of deposition in the lungs since a higher proportion will be deposited in the upper airways.

The effect of exposure on individuals will be lower still because of their "occupancy" factor: the fraction of the time to which they are exposed to particles charged by corona ions. One estimate, Henshaw and Fews (personal communication in AGNIR, 2004), is that people downwind of power lines in corona might have 20–60% more particles deposited in their lungs than those upwind. This estimate is for people exposed out of doors to pollutant particles which originate out of doors. When outdoor air enters houses, many of the pollutant particles will be carried with it (Liu & Nazaroff, 2003), so a similar but smaller effect would be expected indoors due to the deposition of some of the pollutant particles on the surfaces of small apertures. The effects of corona ions on lung deposition of particles which originate indoors will be substantially less. There are substantial difficulties in the way of modelling such effects, making all such estimates very uncertain. Furthermore, since wind directions vary, the excess for any one group of people would be lower, but more groups will be affected, than if the wind direction was constant.

4.6.4.3 *Deposition under power lines*

Particles which are electrically charged oscillate with a frequency of 50 Hz along the electric fields produced by the power lines. The distance over which a particle oscillates depends on its charge and inertia, and the strength of the field which is usually greatest immediately underneath the line. However field directions and strengths can be altered by objects in the field and are, for example, normally perpendicular to a conducting object such as a human body. Field strengths are particularly high around pointed conductors. If the oscillation of a particle makes it hit a surface, it will generally stick.

The oscillation of particles in the electric field causes people underneath or near power lines in the open air to have increased numbers of such particles deposited on their clothing and skin compared with the numbers deposited away from the line. Because buildings and other objects screen out the electric field, power lines do not cause increased deposition indoors. Henshaw et al. (1996a; 1996b) considered whether such electric fields could cause increased deposition within the respiratory tract. They calculated that the field is a factor of 10^4 lower inside the body than outside, but nevertheless suggested that this might have an effect on unattached radon decay products. Stather et al. (1996) pointed out that the unattached decay products mainly deposit in the upper airways, so any increase in internal deposition would probably reduce lung deposition.

With regard to deposition of airborne particles on the skin, AGNIR (2004) concluded that it is likely that there will be a small increase downwind of power lines caused by corona discharge. The increase will be mainly of small particles and so any adverse health effects are likely to come from increased surface activity from radon decay products rather than surface effects from chemical pollutants. The change in surface deposition of radon decay products on skin is also very sensitive to the electrostatic charge on the skin and the wind speed over it. It seems likely that even downwind of power lines, these last two variations will be much larger than the increases from corona ions.

There is experimental evidence supported by theoretical analysis (Fews et al., 1999a) that the deposition of particles of sizes associated both with radon decay products and chemical pollutants are somewhat larger directly underneath power lines. The reported increase is ~ 2.4 for radon decay products and ~ 1.2 for chemical pollutants. The increased deposition is attributable to the increase in impact rate and therefore deposition rate of the naturally charged particles in the oscillating electric fields. The oscillation amplitude decreases rapidly with the mass of the particle. Since the mass of chemical pollutants is mostly associated with larger particles, the increased deposition of these would be insignificant in still air. Fews et al. (Fews et al., 1999a) calculate, however, that this is not the case when the air flow is turbulent.

Swanson & Jeffers (personal communication in AGNIR, 2004) agreed that increased deposition of radon decay products will occur under power lines. However they attribute the increased deposition observed of larger particles, and therefore the likely increased deposition of chemical pollutants, to the design of the experiments. They also attribute the theoretically predicted increased deposition of larger particles to the specific parametric values and analytical expressions used by Fews et al. (1999a).

The extent of skin deposition under power lines cannot be determined without further experimental measurements. It is possible that the differences in the theoretical analysis might be reduced by further work. However the physical situation is very complicated and it seems unlikely that it can be modelled with sufficient accuracy to provide reliable information in the foreseeable future.

4.6.4.4 Implications for health

The main health hazards of airborne particulate pollutants are cardio-respiratory disease and lung cancer (AGNIR, 2004). There is strong evidence that the risk of cardio-respiratory disease is increased by inhalation of particles generated outdoors, mainly from motor vehicle exhaust, and of environmental tobacco smoke produced within buildings. The risk of lung cancer is increased by particulate pollution in outdoor air, and by radon decay products and environmental tobacco smoke in buildings. Any health risks from the deposition of environmental particulate air pollutants on the skin appear to be negligible.

In their recent review, AGNIR (2004) conclude that the potential impact of corona ions on health will depend on the extent to which they increase the dose of relevant pollutants to target tissues in the body. It was not possible to estimate the impact precisely, because of uncertainties about: a) the extent to which corona effects increase the charge on particles of different sizes, particularly within buildings; b) the exact impact of this charging on the deposition of particles in the lungs and other parts of the respiratory tract; and c) the dose-response relation for adverse health outcomes in relation to different size fractions of particle. However, it seemed unlikely that corona ions would have more than a small effect on the long-term health risks associated with particulate air pollutants, even in the individuals who are most affected. In public health terms, AGNIR conclude that the proportionate impact will be even lower because only a small fraction of the general population live or work close to sources of corona ions.

4.7 Conclusions

Various proposed direct and indirect interaction mechanisms for ELF electric and magnetic fields are examined for plausibility, in particular whether a “signal” generated in a biological process by exposure to electric or magnetic fields can be discriminated from inherent random noise and whether the mechanism challenges scientific principles and current scientific knowledge. Many mechanisms become plausible only at fields above a cer-

tain strength. Nevertheless, the lack of identified plausible mechanisms does not rule out the possibility of health effects existing even at very low field levels providing the basic scientific principles are adhered to.

Of the numerous suggested mechanisms proposed for the direct interaction of fields with the human body, three stand out as potentially operating at lower field levels than the others: induced electric fields in neural networks, radical pairs, and magnetite.

Electric fields induced in tissue by exposure to ELF electric and magnetic fields will directly stimulate myelinated nerve fibres in a biophysically plausible manner when the internal electric field strength exceeds a few volts per metre. Much weaker fields can affect synaptic transmission in neural networks as opposed to single cells. Such signal processing by nervous systems is commonly used by multicellular organisms to discriminate weak environmental signals. A lower bound of 1 mV m^{-1} on neural network discrimination was suggested, but based on current evidence threshold values around 10-100 mV m^{-1} seem more likely.

The radical pair mechanism is an accepted way in which magnetic fields can affect specific types of chemical reactions, generally increasing reactive free radical concentration in low fields and decreasing them in high fields. These increases have been seen at less than 1 mT. There is some evidence linking this mechanism to navigation during bird migration. Both on theoretical grounds, and because the changes produced by ELF and static magnetic fields are similar, it is suggested that power frequency fields of much less than the geomagnetic field of around 50 μT are unlikely to be of much biological significance.

Magnetite crystals, small ferromagnetic crystals of various forms of iron oxide are found in animal and human tissues, although in trace amounts. Like free radicals, they have been linked to orientation and navigation in migratory animals, although the presence of trace quantities of magnetite in the human brain does not confer an ability to detect the weak geomagnetic field. Calculations based on extreme assumptions suggest a lower bound for the effects on magnetite crystals of ELF fields of 5 μT.

Other direct biophysical interactions of fields, such as the breaking of chemical bonds, forces on charged particles and the various narrow bandwidth “resonance” mechanisms, are not considered to provide plausible explanations for the interactions at field levels encountered in public and occupational environments.

With regard to indirect effects, the surface electric charge induced by exposure to ELF electric fields can be perceived and it can result in painful microshocks when touching a conductive object. Contact currents can occur when young children touch, for example, a tap in a bathtub in some homes. This produces small electric fields, possibly above background noise levels, in bone marrow. However, whether these present a risk to health is unknown.

High voltage power lines produce clouds of electrically charged ions as a consequence of corona discharge. It is suggested that they could increase the deposition of airborne pollutants on the skin and on airways inside the body, possibly adversely affecting health. However, it seems unlikely that corona ions will have more than a small effect, if any, on long-term health risks, even in the individuals who are most exposed.

None of the three direct mechanisms considered above seem plausible causes of increased disease incidence at the exposure levels generally encountered by people. In fact they only become plausible at levels orders of magnitude higher and indirect mechanisms have not yet been sufficiently investigated. This absence of an identified plausible mechanism does not rule out the possibility of adverse health effects, but it does increase the need for stronger evidence from biology and epidemiology.

5 NEUROBEHAVIOUR

Neurobehavioural studies encompass the effects of exposure to ELF electromagnetic fields on the nervous system and its responses at different levels of organization. These include the direct stimulation of peripheral and central nerve tissue, perceptual effects resulting from sensory stimulation, and effects on central nervous system function. Effects on the latter can be assessed both electrophysiologically by recording the electrical activity of the brain, and by tests of cognition, assessment of mood, and other studies.

The nervous system also has a central role in the control of other body systems, particularly the cardiovascular system, through direct nervous control, and the endocrine system, through neural input into the pineal and pituitary glands. These glands in turn influence reproduction and development, and in a more general way, physiology and well-being.

The brain and nervous systems function by using electrical signals, and may therefore be considered particularly vulnerable to low frequency EMFs and the resultant induced electric fields and currents. Substantial numbers of laboratory experiments with volunteers and animals have investigated the possible consequences of exposure to weak EMFs on various aspects of nervous system function, including cognitive, behavioural and neuroendocrine responses. In addition, epidemiological studies have been carried out on the relationship between EMF exposure and both suicide and depression.

These studies have been reviewed by NRC (1997), NIEHS (1998), IARC (2002), ICNIRP (2003) and McKinlay et al. (2004). In particular, ICNIRP (2003) reviewed in detail some of the evidence summarized here.

In general, there are few effects for which the evidence is strong, and even the more robust field-induced responses seen in the laboratory studies tend to be small in magnitude, subtle and transitory in nature (Crasson et al., 1999; Sienkiewicz et al., 1993).

5.1 Electrophysiological considerations

An examination of the electrophysiological properties of the nervous system, particularly the central nervous system (CNS: brain and spinal cord) gives an indication of its likely susceptibility to the electric fields induced in the body by EMF exposure. Ion channels in cell membranes allow passage of particular ionic species across the cell membrane in response to the opening of a “gate” which is sensitive to the transmembrane voltage (Catterall, 1995; Hille & Anderson, 2001; Mathie, Kennard & Veale, 2003). It is well established that electric fields induced in the body either by direct contact with external electrodes, or by exposure to low frequency magnetic fields, will, if of sufficient magnitude, excite nerve tissue through their interaction with these voltage-gated ion channels. Sensitivity is therefore primarily to the transmembrane electric field and varies widely between different ion channels (Hille & Anderson, 2001; Mathie, Kennard & Veale, 2003; Saunders & Jefferys, 2002). Many voltage-gated ion channels are associated with electrical excitability and electrical signalling. Such electrically excit-

able cells not only comprise neurons, glial and muscle cells, but also endocrine cells of the anterior pituitary, adrenal medulla and pancreas, gametes and, with reservations, endothelial cells (Hille & Anderson, 2001).

All these cells generally express voltage-gated sodium and calcium channels. Both of these ion channels are involved in electrical signaling and calcium ions activate a number of crucial cellular processes including neurotransmitter release, excitation-contraction coupling in muscle cells and gene expression (Catterall, 2000; Hille & Anderson, 2001). Some ion channels, for example voltage-gated potassium and chloride ion channels, also exist in other, non-excitable tissues such as those in the kidney and liver and show slow electric potential changes but their voltage sensitivity is likely to be lower (Begenisich & Melvin, 1998; Cahalan, Wulff & Chandy, 2001; Catterall, 2000; Jan & Jan, 1989; Nilius & Droogmans, 2001). Since voltage-gated ion channels in excitable cells are steeply sensitive to the transmembrane electric potential, electric field strength in tissue is a more relevant parameter to relate to electrically excitable cell thresholds than current density (Bailey et al., 1997; Blakemore & Trombley, 2003; Reilly, 2005; Sheppard, Kavet & Renew, 2002). In fact, the relevant parameter in determining the transmembrane current and hence the excitability is the linear gradient in electric field (Tranchina & Nicholson, 1986), which in turn relates to geometric parameters of the neuron, including the degree of bending of the axon.

Peripheral nerves comprise neurons whose cell bodies are located within the CNS with extended processes (axons) that lie outside the CNS. They conduct action potentials (impulses) towards (sensory nerves) or from (motor nerves) the spinal cord and nerve stimulation shows an all-or-nothing threshold behaviour. Excitation results from a membrane depolarisation of between 10–20 mV, corresponding to an electric field in tissue of 5–25 V m^{-1} (McKinlay et al., 2004). Pulsed magnetic fields, where the rate of change of field induces large localised electric fields, can directly stimulate peripheral nerves and nerve fibres located within the brain (see below).

Cells of the central nervous system are considered to be sensitive to electric fields induced in the body by exposure to ELF magnetic fields at levels that are below threshold for impulse initiation in nerve axons (Jefferys, 1995; Jefferys et al., 2003; Saunders, 2003; Saunders & Jefferys, 2002). Such weak electric field interactions have been shown in experimental studies mostly using isolated animal brain tissue to have physiological relevance. These interactions result from the extracellular voltage gradients generated by the synchronous activity of a number of neurons, or from those generated by applying pulsed or alternating currents directly through electrodes placed on either side of the tissue. Jefferys and colleagues (Jefferys, 1995; Jefferys et al., 2003) identified in vitro electric field thresholds of around 4–5 V m^{-1}. Essentially, the extracellular gradient alters the potential difference across the neuronal membrane with opposite polarities at either end of the neuron; a time-constant of a few tens (15–60) of milliseconds results from the capacitance of the neuronal membrane (Jefferys et al., 2003) and indicates a limited frequency response. Similar arguments concerning the limited frequency

response of weak electric field effects due to the long time-constants (25 ms) arising from cell membrane capacitance have been given by Reilly (2002) regarding phosphene data.

The CNS in vivo is likely to be more sensitive to induced low frequency electric fields and currents than are in vitro preparations (Saunders & Jefferys, 2002). Spontaneous activity is higher, and interacting groups or networks of nerve cells exposed to weak electrical signals would be expected, on theoretical grounds, to show increased sensitivity through improved signal-to-noise ratios compared with the response of individual cells (Adair, 2001; Stering, 1998; Valberg, Kavet & Rafferty, 1997). Much of normal cognitive function of the brain depends on the collective activity of very large numbers of neurons; neural networks are thought to have complex non-linear dynamics that can be very sensitive to small voltages applied diffusely across the elements of the network (Adair, 2001; ICNIRP, 2003; Jefferys et al., 2003). Gluckman et al. (2001) placed the detection limit for network modulation in hippocampal slices by electric fields at around 100 mV m^{-1} . Recent experimental work by Francis, Gluckman & Schiff (2003) confirms a neural network threshold of around 140 mV m^{-1}, which the authors found was lower than single neuron thresholds, based on a limited number of measurements. A lower limit on neural network sensitivity to physiologically weak induced electric fields has elsewhere been considered on theoretical grounds to be around 1 mV m^{-1} (Adair, Astumian & Weaver, 1998; Veyret, 2003). The time-course of the opening of the fastest voltage-gated ion channels can be less than 1 ms (Hille & Anderson, 2001), suggesting that effects at frequencies up to a few kilohertz should not be ruled out. Accommodation to a slowly changing stimulus resulting from slow inactivation of the sodium channels will raise thresholds at frequencies less than around 10 Hz.

Other electrically excitable tissues with the potential to show network behaviour include glial cells located within the CNS (e.g. Parpura et al., 1994), and the autonomic and enteric nervous systems (see Sukkar, El-Munshid & Ardawi, 2000), which comprise interconnected non-myelinated nerve cells and are distributed throughout the body and gut, respectively. These systems are involved in regulating the visceral or "housekeeping" functions of the body; for example, the autonomic nervous system is involved in the maintenance of blood pressure. Muscle cells also show electrical excitability; only cardiac muscle tissue has electrically interconnected cells. However, Cooper, Garny & Kohl et al. (2003), in a review of cardiac ion channel activity, conclude that weak internal electric fields much below the excitation threshold are unlikely to have any significant effect on cardiac physiology. EMF effects on the heart could theoretically result from indirect effects mediated via the autonomic nervous system and CNS (Sienkiewicz, 2003). Effects on the endocrine system could potentially also be mediated this way, although the evidence from volunteer experiments indicates that acute ELF magnetic field exposure up to 20 μT does not influence the circadian variation in circulating levels of the hormone melatonin (Warman et al., 2003b), nor other plasma hormone levels (ICNIRP, 2003).

5.2 Volunteer studies

An electric charge is induced on the surface of a human (or other living organism) exposed to a low frequency electric field that alternates in amplitude with the frequency of the applied field. The alternation of the surface charge with time induces an electric field and therefore current flow within the body; in addition, exposure to a low frequency magnetic field induces circulating eddy currents and associated electric fields. If of sufficient magnitude, these induced electric fields and currents can interact with electrically excitable nerve and muscle tissue. Generally, however, the surface charge effects of exposure to low frequency electric fields become prohibitive long before the internal electric fields become large enough to elicit a response in the tissue.

5.2.1 Surface electric charge

The surface electric charge can be perceived directly through the induced vibration of body hair and tingling sensations in areas of the body, particularly the arms, in contact with clothing, and indirectly through spark discharges between a person and a conducting object within the field. In several studies carried out in the 1970's and 1980's (summarized by Reilly, 1998a; 1999), the threshold for direct perception has shown wide individual variation; 10% of the exposed subjects had detection thresholds of around 2–5 kV m^{-1} at 60 Hz, whereas 50% could detect fields of 7–20 kV m^{-1}. These effects were considered annoying by 5% of the test subjects exposed under laboratory conditions above electric field strengths of about 15–20 kV m^{-1}. In addition to showing a wide variation in individual sensitivity, these responses also vary with environmental conditions, particularly humidity; the studies referred to above, however, included both wet and dry exposure conditions.

It has been estimated that spark discharges would be painful to 7% of subjects who are well-insulated and who touch a grounded object within a 5 kV m^{-1} field (Reilly, 1998a; Reilly, 1999) whereas they would be painful to about 50% in a 10 kV m^{-1} field. Unpleasant spark discharges can also occur when a grounded person touches a large conductive object such as a large vehicle that is "well-insulated" from ground and is situated within a strong electric field. Here, the threshold field strength required to induce such an effect varies inversely with the size of the conductive object. In both cases, the presence in the well-insulated person or object of a conductive pathway to ground would tend to mitigate the intensity of any effect (Reilly, 1998a; Reilly, 1999), as would the impedance to earth of the grounded object or person.

People can perceive electric currents directly applied to the body through touching, for example, a conductive loop in which current is induced by exposure to environmental electromagnetic fields. Thresholds for directly applied currents have also been characterised. At 50 to 60 Hz, the male median threshold for perception was between 0.36 mA (finger contact) and 1.1 mA (grip contact), while pain occurred at 1.8 mA (finger contact).

Median thresholds for women were generally found to be two thirds of the male thresholds, while children were assumed to have median thresholds half of male threshold values (WHO, 1993). There is also a wide variety in the individual's ability to detect currents, there is, for example, about one order of magnitude difference in the perception threshold at the 0.5 percentile and the 99.5 percentile at 50/60 Hz (Kornberg & Sagan, 1979). Generally, the ability to detect fields or currents decreases with increasing frequency. This has been characterised for the perception of currents; the threshold is increasing by about two orders of magnitude at higher frequencies: 0.36 mA at 50/60 Hz, 4 mA at 10 kHz and 40 mA at 100 kHz (WHO, 1993).

A series of extensive studies on 50 Hz population thresholds in more than 1000 people from all ages have recently been carried out by Leitgeb and colleagues. Leitgeb & Schröttner (2002) examined perception thresholds in 700 people aged between 16 and 60 years, approximately half of them women. This study was recently extended to include 240 children aged 9–16 years, and about 20 people aged 61 years or more (Leitgeb, Schroettner & Cech, 2005). In both studies, electric current was applied to the forearm using pre-gelled electrodes, and considerable care was taken to rule out subjective bias.

A summary of the studies on perception of electric currents directly applied to the body is given in Table 33.

Table 33. 50 Hz electric current perception values (I_w) for different perception probabilities (p) for men, women and the general population [a]

	I_w (μA)			
p (%)	**Men**	**Women**	**Children**	**Population**
90	602	506	453	553
50	313	242	252	268
10	137	93	112	111
5	106	68	78	78
0.5	53	24	35	32

[a] Source: Leitgeb & Schroettner, 2002; Leitgeb, Schroettner & Cech, 2005.

Leitgeb, Schroettner & Cech (2005) note that the median perception threshold for the population is 268 μA, almost 50% lower than the present limit of 500 μA recommended by the IEC (1994). They also note that whilst the median threshold for women is approximately two thirds of the male threshold values, children aged between 9 and 16 do not exhibit as a high a sensitivity as had been assumed.

An issue with perception levels is that they really depend on the site of application of the current (cheek and inner forearm being very sensitive)

and the area of application of the current (i.e. current density). The latter makes the comparison of current values difficult (Reilly, 1998a).

5.2.2 Nerve stimulation

Large, rapidly changing, pulsed magnetic fields used in various specialised medical applications such as magnetic resonance imaging (MRI) and transcranial magnetic stimulation (TMS) can induce electric fields large enough to stimulate nervous tissue in humans. Minimum, orientation-dependent stimulus thresholds for large diameter (20 μm) myelinated nerve axons have been estimated to be approximately 6 V m^{-1} at frequencies up to about 1–3 kHz (Reilly, 1998a; Reilly, 1999). In addition, accommodation to a slowly changing stimulus resulting from slow inactivation of sodium channels will raise thresholds at low frequencies. In MRI, nerve stimulation is an unwanted side effect of a procedure used to derive cross-sectional images of the body for clinical diagnosis (see Shellock, 2001). Threshold rates of change of the switched gradient magnetic fields used in MRI for perception, discomfort and pain resulting from peripheral nerve stimulation are extensively reviewed by Nyenhuis et al. (2001). Generally, median, minimum threshold rates of change of magnetic field (during periods of < 1 ms) for perception were 15–25 μT s^{-1} depending on orientation and showed considerable individual variation (Bourland, Nyenhuis & Schaefer, 1999). These values were somewhat lower than previously estimated by Reilly (1998a; 1999), possibly due to the constriction of eddy current flow by high impedance tissue such as bone (Nyenhuis et al., 2001). Thresholds rose as the pulse width of the current induced by the switched gradient field decreased; the median pulse width (the chronaxie) corresponding to a doubling of the minimum threshold (the rheobase) ranged between 360 and 380 μs but again showing considerable individual variation (Bourland, Nyenhuis & Schaefer, 1999). Numerical calculations of the electric field induced by pulses in the 84 subjects tested by Nyenhuis et al. (2001) have been used to estimate the median threshold for peripheral nerve stimulation at 60 Hz as 48 mT (Bailey & Nyenhuis, 2005). Furthermore, Nyenhuis et al. (2001) using data from measurements on human volunteers estimated a rheobase electric field of 2.2 V m^{-1} in tissue.

In TMS, parts of the brain are deliberately stimulated in order to produce a transient, functional impairment for use in the study of cognitive processes (see Reilly, 1998a; Ueno, 1999; Walsh, Ashbridge & Cowey, 1998). Furthermore, in TMS, brief, localised, suprathreshold stimuli are given, typically by discharging a capacitor through a coil situated over the surface of the head, in order to stimulate neurons in a small volume (a few cubic centimetres) of underlying cortical tissue (Reilly, 1998a). The induced current causes the neurons within that volume to depolarise synchronously, followed by a period of inhibition (Fitzpatrick & Rothman, 2000). When the pulsed field is applied to a part of the brain thought to be necessary for the performance of a cognitive task, the resulting depolarisation interferes with the ability to perform the task. In principle then, TMS provides cognitive neuroscientists with the capability to induce highly specific, temporally and

spatially precise interruptions in cognitive processing – sometimes known as "virtual lesions". Reilly (1998a) noted induced electric field thresholds to be of the order of 20 V m^{-1}. However, Walsh & Cowey (1998) cited typical rates of change of magnetic field of 30 kT s^{-1} over a 100 μs period transiently inducing an electric field of 500 V m^{-1} in brain tissue.

People are likely to show variations in sensitivity to induced electric fields. In particular, epileptic syndromes are characterised by increased neuronal excitability and synchronicity (Engelborghs, D'Hooge & De Deyn, 2000); seizures arise from an excessively synchronous and sustained discharge of a group of neurons (Engelborghs, D'Hooge & De Deyn, 2000; Jefferys, 1994). TMS is widely used, apparently without adverse effects. However, repetitive TMS has been observed to trigger epileptic seizure in some susceptible subjects (Fitzpatrick & Rothman, 2000; Wassermann, 1998). These authors also reported short- to medium-term memory impairments and noted the possibility of long-term cognitive effects from altered synaptic activity or neurotransmitter balance. Contraindications for TMS use agreed at an international workshop on repetitive TMS safety (Wassermann, 1998) include epilepsy, a family history of seizure, the use of tricyclic antidepressants, neuroleptic agents and other drugs that lower seizure threshold. Serious heart disease and increased intracranial pressure have also been suggested as contraindications due to the potential complications that would be introduced by seizure.

5.2.3 Retinal function

The effects of exposure to weak low frequency magnetic fields on human retinal function are well established. Exposure of the head to magnetic flux densities above about 5 mT at 20 Hz, rising to about 15 mT at 50 Hz, will reliably induce faint flickering visual sensations called magnetic phosphenes (Attwell, 2003; Sienkiewicz, Saunders & Kowalczuk, 1991; Taki, Suzuki & Wake, 2003). It is generally agreed that these phosphenes result from the interaction of the induced electric current with electrically sensitive cells in the retina. Several lines of evidence suggest the production of phosphenes by a weak induced electric field does not involve the initial transduction of light into an electrical signal. Firstly, the amplification of the initial signal generated by the absorption of light takes place primarily through an intracellular "second-messenger cascade" of metabolic reactions prior to any change in ion channel conductivity (Hille & Anderson, 2001). Secondly, the phosphene threshold appears unaffected by "dark" adaptation to low light levels (Carpenter, 1972). In addition, phosphenes have been induced in a patient with retinitis pigmentosa, a degenerative illness primarily affecting the pigment epithelium and photoreceptors (Lövsund et al., 1980).

There is good reason to view retinal circuitry as an appropriate model for induced electric field effects on CNS neuronal circuitry in general (Attwell, 2003). Firstly, the retina displays all the processes present in other CNS areas, such as graded voltage signalling and action potentials, and has a similar biochemistry. Secondly, in contrast to more subtle cognitive effects,

phosphenes represent a direct and reproducible perception of field interaction. A clear distinction can be made in this context between the detection of a normal visual stimulus and the abnormal induction of a visual signal by non-visual means (Saunders, 2003); the latter suggests the possibility of direct effects on cognitive processes elsewhere in the CNS.

Thresholds for electrically induced phosphenes have been estimated to be about 10–14 mA m^{-2} at 20 Hz (Adrian, 1977; Carstensen, 1985). A similar value (10 mA m^{-2} at 20 Hz), based on studies of magnetically induced phosphenes, has been derived by Wake et al. (1998). The equivalent electric field threshold can be estimated as around 100–140 mV m^{-1} using a tissue conductivity for brain tissue of about 0.1 S m^{-1} (Gabriel, Gabriel & Corthout, 1996). More recently, Reilly (2002) has calculated an approximate 20 Hz electric field threshold in the retina of 53 mV m^{-1} for phosphene production. A similar value (60 mV m^{-1}) has been reported elsewhere (see Saunders, 2003). Subsequently, however, Taki et al. (2003) indicated that calculations of phosphene thresholds suggested that electrophosphene thresholds were around 100 mV m^{-1}, whereas magnetophosphene thresholds were around 10 mV m^{-1} at 20 Hz.

More detailed calculation by Attwell (2003) based on neuroanatomical and physiological considerations, suggests that the phosphene electric field threshold in the extracellular fluid of the retina is in the range 10–60 mV m^{-1} at 20 Hz. There is however, considerable uncertainty attached to these values. In addition, the extrapolation of values in the extracellular fluid to those appropriate for whole tissue, as used in most dosimetric models, is complex, depending critically on the extracellular volume and other factors. With regard to the frequency response, Reilly (2002) suggests that the narrow frequency response is the result of relatively long membrane time constants of around 25 ms. However, at present, the exact mechanism underlying phosphene induction is unknown. It is not clear whether the narrow frequency response is due to intrinsic physiological properties of the retinal neurons, as suggested by Reilly (2002) above and by Attwell (2003) considering active amplification process in the retinal neuron synaptic terminals, or is the result of central processing of the visual signal (Saunders, 2003; Saunders & Jefferys, 2002). This issue can only be resolved through further investigation.

5.2.4 Brain electrical activity

Since the first suggestion that occupational exposure to EMFs resulted in clinical changes in the electroencephalogram (EEG) was published in 1966 (Asanova & Rakov, 1966; 1972), various studies have investigated if exposure to magnetic fields can affect the electrical activity of the brain. Such methods can provide useful diagnostic information regarding the functional state of the brain, not only from recordings of the spontaneous activity at rest but also from recording the sensory functions and subsequent cognitive processes evoked in response to specific stimuli (evoked or event-related potentials, ERPs). Nevertheless, neurophysiological studies using magnetic fields need to be performed with much care and attention since

they can be prone to many potential sources of error and artefact (NIEHS, 1998). Changes in arousal and attention of volunteers, in particular, can substantially affect the outcome of these studies.

Various studies have investigated the effects of magnetic fields on brain activity by analysing the spectral power of the main frequency bands of the EEG (Bell et al., 1992; Bell et al., 1991; Bell, Marino & Chesson, 1994a; Bell, Marino & Chesson, 1994b; Gamberale et al., 1989; Heusser, Tellschaft & Thoss, 1997; Lyskov et al., 1993b; Lyskov et al., 1993a; Marino, Bell & Chesson, 1996; Schienle et al., 1996; Silny, 1986). These studies have used a wide variety of experimental designs and exposure conditions, as well as healthy volunteers and patients with neurological conditions, and thus are difficult to compare and evaluate. Despite some scattered field-dependent changes, most notably in the alpha frequency band, and with intermittent exposure perhaps more effective than continuous exposure, these studies have produced inconsistent and sometimes contradictory results.

A difficulty with interpretation of the EEG in individuals at rest is that the intra-individual variability is very high. The variability of ERPs is much lower, resulting in better reproducibility, and other studies have investigated the effects of magnetic fields and combined electric and magnetic fields on these potentials within the EEG waveform. There are some differences between studies, but generally, the early components of the evoked response corresponding to sensory function do not appear affected by exposure (Graham & Cook, 1999; Lyskov et al., 1993b). In contrast, large and sustained changes on a later component of the waveform representing stimulus detection may be engendered by exposure at 60 mT (Silny, 1984; 1985; 1986), with lesser effects occurring using fields of 1.26 mT (Lyskov et al., 1993b), and nothing below 30 μT (Graham & Cook, 1999). Finally, exposure during the performance of some discrimination and attention tasks may affect the late major components of the EEG which are believed to reflect cognitive processes involved with stimulus evaluation and decision making (Cook et al., 1992; Crasson et al., 1999; Graham et al., 1994), although Crasson and Legros (2005) were unable to replicate the effects they reported previously. There also is some evidence that task difficulty and field intermittency may be important experimental variables. However, all these subtle effects are not well defined, and some inconsistencies between studies require additional investigation and explanation.

A summary of studies on changes in brain electrical activity while awake is given in Table 34.

Table 34. Brain electrical activity

Test [a]	Exposure	Response	Comments	Authors
During exposure to magnetic fields up to 10 Hz				
Standard EEG: $C_{3,4}$; $P_{3,4}$; $O_{1,2}$; FFT at 10 Hz, no records during exposure 6 female and 4 male volunteers	10 Hz 100 µT 10 min	Immediately after exposure the spectral power of the brain activity was lower than before exposure and 10 min afterwards, but only at the occipital electrodes was this difference significant.	Data for individual volunteers are not presented, and there is no information concerning the rate of responders.	Bell, Marino & Chesson, 1994b
Standard EEG: $C_{3,4}$; $P_{3,4}$; $O_{1,2}$; FFT at 1.5 Hz or 10 Hz band 13 healthy subjects and 6 patients	5 or 10 Hz 20, 40 µT 2 s on, 5 s off	In each person, the magnetic field altered the brain activity at the frequency of stimulation, but no systematic changes of brain activity.	The strength of the effect was proportional neither to frequency nor to field strength.	Bell, Marino & Chesson, 1994a
Standard EEG: $C_{3,4}$; $P_{3,4}$; $O_{1,2}$; frequency spectrum analysis except for < 2.5 Hz and 9-11 Hz. 13 volunteers, 6 patients	1.5 or 10 Hz 80 µT 2 s on, 5 s off	ICOS (intra-subject comparison of stimulus and non-stimulus state) was altered by ELF exposure in 58% of the subjects.		Marino, Bell & Chesson, 1996
Standard EEG, $O_{1,2}$ spectral analysis of theta (3.5-7.5 Hz), alpha (7.5-12.5 Hz) and beta bands (12.5-25 Hz) 25 female and 36 male volunteers	3 Hz 100 μT_{pp} 20 min one exposure and one control session	Significant changes in theta and beta frequency bands after exposure relative to controls, interpreted as slightly pronounced reduction of alertness during exposure.	Exposure and control sessions on different days, the two session days were not treated as a double blind study.	Heusser, Tellschaft & Thoss, 1997
During exposure to magnetic fields between 45 and 60 Hz				
Standard EEG 26 experienced power utility linemen	50 Hz exposure during workday average exposure 23 µT one day live, one day sham	No changes in alpha EEG, nor evidence of EEG abnormalities.	Intervention study, not laboratory.	Gamberale et al., 1989

Table 34. Continued

Standard EEG (10-20 system): $C_{3,4}$; $P_{3,4}$; $O_{1,2}$; FFT at 1-18.5 Hz in 0.5 Hz steps 3 female, 11 male volunteers	60 Hz 25 or 50 µT 2 s on, 8 s off, first 2 s used as control	No systematic effects for frequency bands and activity-power intensities. In 50 % of volunteers diminished EEG power was observed as a response to the field.		Bell et al., 1991
Standard EEG: $C_{3,4}$; $P_{3,4}$; $O_{1,2}$; FFT at 1-18.5 Hz in 0.5 Hz steps 10 healthy volunteers and 10 neurological patients	60 Hz B_{DC}: 78 µT, B_{AC}: 78 µT, single and combined 2 s on, 5 s off, first 2 s used as control	19 out of 20 persons responded to the fields: overall 35% to B_{DC}; 70% of the patients and 80% of the volunteers to B_{AC}, response to B_{AC} was not different from the responses to the combination B_{AC}+ $B_{DC.}$ Field-induced increase and decrease of brain activity, no systematic changes were observed for the hemispheres or activity loci.	EEG changes were lower in patients than in healthy subjects.	Bell et al., 1992
Standard EEG spectral analysis 6 female and 8 male volunteers	45 Hz 1.26 mT 1s on, 1s off cycle over 15 min, one exposure and one control session	Significant increase of the power values of alpha and beta bands after exposure, no changes in delta- and theta-bands.		Lyskov et al., 1993a
Standard EEG spectral analysis. before and after exposure 11 female and 9 male volunteers	45 Hz 1.26 mT 10 persons: 1 h continuous field, 10 persons: 1s on/off intermittent field for 1 h One exposure and one control session	Several statistically significant changes; increase of alpha activity during intermittent exposure and decrease of delta activity. Increase of beta waves in frontal but not in occipital derivations.	Inhomogeneous results, consistent with increased relaxation. Double blind study.	Lyskov et al., 1993b

Table 34. Continued

During exposure to magnetic fields at higher frequencies				
Standard EEG, $F_{3,4}$,$P_{3,4}$,$O_{1,2,}$ traditional frequency bands 0.1 - 30 Hz, psychological parameters and questionnaires 26 female and 26 male volunteers	Spherics simulation: 10 kHz 500 µs duration, random intervals between 50 and 150 ms 38 A m^{-1} peak value electric field shielded exposure 10 min and control session	Significant reduction of the power only in the alpha frequency band (8-13 Hz) in parietal and occipital derivations, when analysing sub-groups only in 10 - 10.75 Hz. P / O recordings show significant reductions in the voltage power.	Factors such as physical condition and neurotics were considered as mediators of spherics effectiveness.	Schienle et al., 1996
Evoked potentials after exposure to EMF				
Visual evoked potentials 100 subjects	5 – 50 Hz pulsed magnetic field up to 100 mT	Phase reversal of components of the visual evoked potential at 60 mT.	Very intense fields.	Silny, 1984; 1985; 1986
Auditory evoked potentials 6 female and 8 male volunteers	45 Hz 1.26 mT 1s on, 1 s off, 15 min one exposure and one control session	N100 components were shorter, amplitudes were reduced.		Lyskov et al., 1993a
Auditory evoked potentials 11 female and 9 male volunteers	45 Hz 1.26 mT 10 persons: 1 h continuous field 10 persons: 1 h 1 s on/off intermittent field one exposure and one control session	Not affected.		Lyskov et al., 1993b

Table 34. Continued

Auditory, visual and somatosensory evoked potentials before, during and after exposure 36 (male and female) subjects	60 Hz 14.1 or 28.3 μT 45 min	No effect except a reduced amplitude of the somatosensory evoked potential in the lower exposure group.	Double-blind, counterbalanced study.	Graham & Cook, 1999
Event-related potentials after exposure to EMF				
Electrodes C_z, $P_{3,4}$ for event-related potentials (P300), following auditory or visual stimuli in the Oddball task during exposure 30 male volunteers	60 Hz 9 kV m^{-1}, 20 μT 18 exposed and sham-exposed over four 6-h sessions, 12 exposed in all sessions	Amplitude of the auditory P300 was increased. Visual ERPs were not affected.	Effects on auditory ERP components were greatest soon after activation of field and after switching off at the end of the session.	Cook et al., 1992
Event-related brain potentials (N200-P300) following auditory stimuli in the Oddball task during exposure 54 male subjects	3 matched groups of 18 men each, two 6-h sessions, exposure or sham, 60 Hz: a) 6 kV m^{-1}, 10 μT b) 9 kV m^{-1}, 20 μT c) 12 kV m^{-1}, 30 μT	Significant increases of P300 latency in group b), but decrease during sham exposure.	N200-P300 component complex altered in all groups, order of exposure did not affect results. Double blind, counterbalanced study.	Graham et al., 1994
Event-related potentials during performance of the Oddball task, the dichotic listening task and the CNV paradigm after exposure 21 male subjects	50 Hz 100 μT 30 min, continuous or intermittent head only	Differences in ERP amplitudes were seen during the dichotic listening task.	Some effects were inconsistent between trials. Double-blind studies.	Crasson et al., 1999
Event-related potentials during performance of the Oddball task, the dichotic listening task and the CNV paradigm after exposure 18 male subjects	50 Hz 100 μT 30 min, continuous or intermittent head only	No effects in ERP amplitudes were seen during the dichotic listening task or in other measures of performance.	Replication and extension of above study by the same group.	Crasson & Legros, 2005

[a] C, F, O & P represent standard EEG recording electrode positions; FFT = Fast Fourier Transform.

5.2.5 Sleep

Sleep is a complex biological process controlled by the central nervous system and is necessary for general health and well-being. The possibility that EMFs may exert a detrimental effect on sleep has been examined in two studies. Using the EEG to assess sleep parameters, Åkerstedt et al. (1999) reported that continuous exposure of healthy volunteers to 50 Hz at 1 μT at night caused disturbances in sleep. In this study, total sleep time, sleep efficiency, slow-wave sleep (stage III and IV), and slow-wave activity were significantly reduced by exposure, as was subjective depth of sleep. Graham & Cook (1999) reported that intermittent, but not continuous, exposure to 60 Hz, 28 μT magnetic fields at night resulted in less total sleep time, reduced sleep efficiency, increased time in stage II sleep, decreased time in rapid eye movement (REM) sleep and increased latency to first REM period. Consistent with a pattern of poor and broken sleep, volunteers exposed to the intermittent field also reported sleeping less well and feeling less rested in the morning.

A comparison between these two studies is made difficult because of the differences in the exposure levels used, 1 μT (Åkerstedt et al., 1999) vs. 28 μT (Graham & Cook, 1999) and also of other differences in the design. As to the results, in the Åkerstedt study, results were apparently obtained by low-level continuous exposure, whereas the Graham study failed to elicit such results by continuous exposure, but did produce similar results with intermittent exposures. Further studies with similar designs are needed before any conclusions can be drawn.

A summary of studies on brain electrical activity during sleep is given in Table 35.

Table 35. Brain electrical activity during sleep

Test	Exposure	Response	Comments	Authors
Sleep EEGs, conventional recordings 8 female and 10 male healthy volunteers	50 Hz 1 μT one night (23:00-07:00) with field on, one night with field off	Significantly reduced slow wave activity and slow wave sleep. Also tendency for reduced total sleep time, sleep efficiency, REM sleep (not statistically significant).	Absolute values were within the normal variability; the observed changes are far from clinical significance. Blind study, balanced design.	Åkerstedt et al., 1999
Sleep EEG, 3 nights (23:00-07:00), C_z, C_4, O_z 24 male volunteers	60 Hz 28.3 μT, circularly polarised 8 sham-exposed controls, 7 subjects exposed to continuous fields, 9 to intermittent 1 h on, 1 h off, 15 s on/off cycle	Intermittent exposure to magnetic fields produced significant disturbances in nocturnal sleep EEGs in 6 of 9 persons: decreased sleep efficiency, altered sleep architecture, suppression of REM sleep, lower well-feeling of several subjects in the morning.	No effect was seen during continuous field exposure relative to sham-exposed controls. Double-blind, counterbalanced study.	Graham & Cook, 1999

5.2.6 Cognitive effects

Despite the potential importance of field-induced effects on attention, vigilance, memory and other information processing functions, relatively few studies have looked for evidence of changes in cognitive ability during or after exposure to low frequency EMFs. These have been reviewed by NIEHS (1998), Cook, Thomas & Prato (2002), Bailey (2001), Crasson (2003) and ICNIRP (2003). While few field-dependent changes have been observed, it is important to consider that this type of study may be particularly susceptible to various environmental and individual factors which may increase the variance of the experimental endpoint and decrease the power to detect a small effect. This may be particularly important, since any field-dependent effects are likely to be small with fields at environmental levels (Sienkiewicz et al., 1993; Whittington, Podd & Rapley, 1996).

The effects of acute exposure to magnetic fields on simple and choice reaction time have been investigated in several recent studies using a wide range of magnetic flux densities (20 μT – 1.26 mT) and experimental conditions. Some studies did not find any field-dependent effects (Gamberale et al., 1989; Kurokawa et al., 2003b; Lyskov et al., 1993b; Lyskov et al., 1993a; Podd et al., 2002; Podd et al., 1995), although modest effects on speed (Crasson et al., 1999; Graham et al., 1994; Whittington, Podd & Rapley, 1996) and accuracy during task performance (Cook et al., 1992; Kazantzis, Podd & Whittington, 1998; Preece, Wesnes & Iwi, 1998) have been reported. However, Crasson & Legros (2005) were unable to replicate these observations. These data also suggest that effects may depend on the difficulty of the task (Kazantzis, Podd & Whittington, 1998; Whittington, Podd & Rapley, 1996) and that exposure may attenuate the usual improvement seen with practice in reaction time (Lyskov et al., 1993b; Lyskov et al., 1993a; Stollery, 1986)

A few studies have reported subtle field-dependent changes in other cognitive functions, including memory and attention. Using a battery of neuropsychological tests, Preece, Wesnes & Iwi (1998) found that exposure to a 50 Hz magnetic field at 0.6 mT decreased accuracy in the performance of numerical working memory task and decreased sensitivity of the performance in a word recognition task. Similarly Keetley et al. (2001) investigated the effects of exposure to 28 μT, 50 Hz fields using a series of cognitive tests. A significant decrease in performance was seen with one working memory task (the trail-making test, part B) that involves visual-motor tracking and information processing within the prefrontal and parietal areas of the cortex. Podd et al. (2002) reported delayed deficits in the performance of a recognition memory task following exposure to a 50 Hz field at 100 μT. Trimmel & Schweiger (1998) investigated the effects of acute exposure to 50 Hz magnetic fields at 1 mT. The fields were produced using a power transformer, and volunteers were exposed in the presence of a 45 dB sound pressure level noise. Compared with a no-field, no-noise condition and noise alone (generated using a tape recording) significant reductions in visual attention, perception and verbal memory performance were observed during

Table 36. Cognitive effects

Test	Exposure	Response	Comments	Authors
Reaction time, vigilance, memory and perception speed tested before and after each day 26 experienced power utility linemen.	50 Hz exposure during workday average exposure 23 µT one day live, one day sham	No difference in performance between exposed and non-exposed days.	Intervention study, not laboratory.	Gamberale et al., 1989
Reaction time (RT) and target-deletion test (TDT) 6 female and 8 male volunteers	45 Hz 1.26 mT 1 s on, 1 s off cycle, 15 min one exposure and one control session	No significant differences for RT, TDT not affected.		Lyskov et al., 1993a
Reaction time (RT) 11 female and 9 male volunteers	45 Hz 1.26 mT 10 persons: 1 h continuous field 10 persons: 1 hour 1 s on/off intermittent field one exposure and one control session	RT not directly affected.	Learning to perform the RT test (decrease of RT in repeated trials) affected by exposure .	Lyskov et al., 1993b
Reaction time to light flashed at variable intervals during exposure 12 subjects (expt 1) and 24 subjects (expt 2), male and female	Experiment 1: 10.1 or 0.2 Hz 1.1 mT 300 s Experiment 2: 0.2 or 43 Hz 1.8 mT 300 s	No effects found.	Experiment 2 designed to test for possible parametric resonance theory. Double blind studies.	Podd et al., 1995
Reaction time, accuracy and memory recognition	60 Hz 100 µT 1 s on, 1 s off for 11 min	Effect on memory, not on reaction time or accuracy.	Results different from previous studies (Whittington et al., 1996)	Podd et al., 2002

Table 36. Continued

Reaction time, accuracy, time perception and visual perception 12 male and 8 female subjects	50 Hz 22 µT circularly polarised with harmonics and repetitive transients up to 100 µT 55 min	No effects.		Kurokawa et al., 2003b
Reaction time (RT), attention, differential reinforcement of low response rate (DRL) 54 male volunteers	3 matched groups of 18 men each, two 6-h sessions, exposure or sham, 60 Hz: a) 6 kV m^{-1}, 10 µT b) 9 kV m^{-1}, 20 µT c) 12 kV m^{-1}, 30 µT	Slower reaction time in Oddball task and lower accuracy of DRL in group a) only.	No effect on other measures or in other exposure groups. Double blind, counterbalanced study.	Graham et al., 1994
A visual duration-discrimination task with 3 levels of difficulty 100 male and female subjects	50 Hz 100 µT intermittent 9 min	Decreased reaction time for the hardest level of performance.	A relaxed significance level (0.15) was used. Double-blind, counter-balanced study.	Whittington, Podd & Rapley, 1996
Rey Auditory Verbal Learning test (with delayed recall) and Digit Span Task 21 male subjects.	50 Hz 100 µT continuous or intermittent 30 min head only	No effects (reported in discussion).	Double-blind studies.	Crasson et al., 1999
Choice serial reaction time task, time estimation task, interval production task, vigilance task, digit span memory task and Wilkinson Addition task during exposure 54 male subjects	60 Hz 9 kV m^{-1} and 20 µT 2 x 3 h / day for 4 days	Fewer errors in choice reaction time task. No effects on reaction time, memory or vigilance.	Double-blind, counterbalanced study.	Cook et al., 1992

Table 36. Continued

A visual duration-discrimination task with 3 levels of difficulty. 40 male and 59 female subjects	50 Hz 100 μT intermittent 7.9 min	Improved accuracy for the hardest level of performance.	A relaxed significance level (0.3) was used. Double-blind, counter-balanced study.	Kazantzis, Podd & Whittington, 1998
Immediate word recall, reaction time, digit vigilance task, choice reaction time, spatial working memory, numeric working memory, delayed word recall and recognition and picture recognition during exposure. 16 (male and female) subjects	50 Hz or static magnetic fields at 0.6 mT applied to the head. Duration not specified. Current density in head estimated as 2–6 mA m^{-2}	Reduced accuracy of word and number recall and performance of choice reaction time task.	Randomised blind cross-over design.	Preece, Wesnes & Iwi, 1998
Duration Discrimination Task and Stroop Colour Word test. 18 male subjects	50 Hz 100 μT continuous or intermittent 30 min head only	No effect on reaction time and performance accuracy.	Double blind with counter-balanced exposure order.	Crasson & Legros, 2005
Syntactic and semantic verbal reasoning tasks, 5-choise serial reaction time task, and visual search tasks during exposure 76 male subjects	50 Hz current 500 μA directly applied to head and shoulders 5.5 h / day for 2 days	Increased latency in syntactic reasoning task.	Possible differences between groups. Double-blind procedures with cross over design.	Stollery, 1986; 1987
Rey Auditory Verbal Learning test; Digit Span Memory Task; Digit Symbol Substitution test; Speed of Comprehension Test and Trail Making Test 30 subjects, both sexes	50 Hz 28 μT 50 min verbal and written tests administered 20 min from exposure onset	Most results indicated no effect, but data suggestive of detrimental effect on short-term learning and executive functioning.	Double-blind cross-over design.	Keetley et al., 2001
Visual discrimination, perception, verbal memory and mood and symptom checklist 66 (male and female) subjects	50 Hz 1 mT 45dB noise compared to noise alone	Significant reduction in visual attention, perception and verbal memory performance.	Double blind studies.	Trimmel & Schweiger, 1998

field exposure. The presence of the noise during exposure, however, complicates interpretation of this study.

Generally, while electrophysiological considerations suggest that the central nervous system is potentially susceptible to induced electric fields; cognitive studies have not revealed any clear, unambiguous finding. There is a need for a harmonisation of methodological procedures used in different laboratories, and for dose-response relationships to be investigated. The studies on various cognitive effects from ELF field exposure are summarized in Table 36.

5.2.7 Hypersensitivity

It has been suggested that some individuals display increased sensitivity to levels of EMFs well below recommended restrictions on exposure. People self-reporting hypersensitivity may experience a wide range of severe and debilitating symptoms, including sleep disturbances, general fatigue, difficulty in concentrating, dizziness, and eyestrain. In extreme forms, everyday living may become problematical. A number of skin problems such as eczema and sensations of itching and burning have also been reported, especially on the face, and, although there may be no specific symptom profile (see Hillert et al., 2002), increased sensitivity to chemical and other factors often occurs (Levallois et al., 2002). The responses to EMFs are reported to occur at field strengths orders of magnitude below those required for conventional perception of the field (Silny, 1999). These data have been reviewed by Bergqvist & Vogel (1997) and more recently by Levallois (2002), ICNIRP (2003) and Rubin et al. (2005).

In contrast to anecdotal reports, the evidence from double-blind provocation studies (Andersson et al., 1996; Flodin, Seneby & Tegenfeldt, 2000; Lonne-Rahm et al., 2000; Lyskov, Sandström & Hansson Mild, 2001b; Swanbeck & Bleeker, 1989) indicate that neither healthy volunteers nor self-reporting hypersensitive individuals can reliably distinguish field exposure from sham-exposure. In addition, subjective symptoms and circulating levels of stress-related hormones and inflammatory mediators could not be related to field exposure. Similar results were reported in a survey of office workers (Arnetz, 1997). In studies reported by Keisu (1996) and by Toomingas (1996), the outcome of tests on an individual was used therapeutically in the medical handling of the patient. In none of these series was there any reproducible association between exposure and symptoms. Further test series have been performed in Sweden, the UK and in Germany, including an unsuccessful repetition of the Rea et al. (1991) study (see below), but these have not been published in a peer reviewed form. For a review, see Bergqvist & Vogel (1997). These results are consistent with the view that hypersensitivity to EMFs is a psychosomatic syndrome, suggested by Gothe, Odoni & Nilsson (1995).

Not all studies dismiss the possibility of EMF hypersensitivity, however. Two studies have reported weak positive field discrimination (Mueller, Krueger & Schierz, 2002; Rea et al., 1991) and another two studies

reported subtle differences in heart rate, visual evoked potentials, electroretinogram amplitudes and electrodermal activity between normal and hypersensitive volunteers (Lyskov, Sandström & Hansson Mild, 2001a; Sandström et al., 1997). The study by Rea et al. (1991) has, however, been criticised on several methodological grounds (ICNIRP, 2003): the selection of individuals, the exposure situation and whether the test was blind or not. There is some morphological evidence to suggest that the numbers and distribution of mast cells in the dermis of the skin on the face may be increased in individuals displaying hypersensitive reactions (Gangi & Johansson, 2000; Johansson et al., 1994; Johansson, Hilliges & Han, 1996). Increased responsiveness was attributed to changes in the expression of histamine and somatostatin and other inflammatory peptides. Similar effects in the dermis have also been reported following provocation tests to VDU-type fields in normal, healthy volunteers (Johansson et al., 2001).

EMF hypersensitivity was addressed by the World Health Organization (WHO) at a workshop held in Prague in October 2004 (WHO, 2005). It was proposed that this hypersensitivity, which has multiple recurrent symptoms and is associated with diverse environmental factors tolerated by the majority of people, should be termed "idiopathic environmental intolerance (IEI) with attribution to EMF". The workshop concluded that IEI incorporates a number of disorders sharing similar nonspecific symptoms that adversely affect people and cause disruptions in their occupational, social, and personal functioning. These symptoms are not explained by any known medical, psychiatric or psychological disorder, and the term IEI has no medical diagnostic value. IEI individuals cannot detect EMF exposure any more accurately than non-IEI individuals, and well-controlled and conducted double-blind studies have consistently shown that their symptoms are not related to EMF exposure *per se*. A summary of hypersensitivity studies is given in Table 37.

5.2.8 Mood and alertness

The possible impact of EMFs on mood and arousal has also been assessed in double-blind studies in which volunteers completed mood checklists before and after exposure. No field-dependent effects have been reported using a range of field conditions (Cook et al., 1992; Crasson et al., 1999; Crasson & Legros, 2005; Graham et al., 1994). However, in contrast Stollery (1986) reported decreased arousal in one of two participating groups of subjects when mild (500 μA) 50 Hz electric current was passed through the head, upper arms, and feet. This was done to simulate the internal electric fields generated by exposure to an external electric field strength of 36 kV m^{-1}. Also Stevens (2001) reported that exposure to a 20 Hz, 50 μT magnetic field increased positive affective responses displayed to visual stimuli compared with sham-exposure. Arousal, as measured by skin conductance, gave variable results. Table 38 summarizes the studies on effects of ELF field exposure on mood and alertness.

Table 37. Hypersensitivity

Test	Exposure	Response	Comments	Authors
Skin symptoms 30 patients	VDU: static electric field 0,2 and 30 kV m^{-1} ELF magnetic field: 50 and 800 nT dB/dt: 23 and 335 mT s^{-1}	No response related to exposure.	Heat, reddening, itching, stinging, oedema in exposed and sham exposed situations.	Swanbeck & Bleeker, 1989
Perception and symptoms 17 patients	Fields from VDU, pre-tested as causing symptoms in open provocation prior to double blind sessions. In shielded laboratory.	16 individuals failed to detect (guess) presence of the fields, symptoms were related to guesses, not to the fields.		Andersson et al., 1996
Perception and symptoms 15 patients and 26 controls	Fields from VDUs and other objects. Subjects tested in their normal home environment, using a variety of devices.	15 individuals failed to detect presence of the fields, symptoms were not related to the fields.		Flodin, Seneby & Tegenfeldt, 2000
Provocation study of stress hormone levels, skin biopsies and facial skin sensations 24 patients and 12 controls	VDUs: 5 Hz–2 kHz: 12 V m^{-1} 198 nT 2 kHz–400 kHz: 10 V m^{-1} 18 nT 30 min / week for 4 weeks	None of the test parameters differed between exposed and sham exposed conditions, but skin symptoms appeared in the open provocation tests.	Double-blind study.	Lonne-Rahm et al., 2000

Table 37. Continued

EEG, visual evoked potentials, electrodermal activity, ECG and blood pressure. 20 patients and 20 control subjects	60 Hz intermittent 15 sec on/off cycle at 10 T magnetic field exposure and sham exposure applied randomly during a 40 min period	Magnetic field exposure had no effect on any of the parameters examined.	Patients reporting EHS differed from control subjects in baseline values.	Lyskov, Sandström & Hansson Mild, 2001b
General health survey of 133 office employees. Exploratory study of skin disease, office ergonomics and air quality in 3 office workers reporting EMF hypersentitivity compared to 5 controls	VDUs: 5 Hz–2 kHz ~ 10–15 V m^{-1} 100–150 nT	10% (13) of general staff reported EMF hypersensitivity; no differences in skin symptoms between EMF hypersensitives and controls in exploratory study.	The authors were not able to attribute EMF hypersensitivity to any particular environmental factor.	Arnetz, 1997
Perception and symptoms in one female patient 10 double-blind tests	Fields from VDU	The discomfort the patient experienced had no correlation to whether or not the monitor actually was on.	The patient reconsidered her own perception of the illness, and in time the symptoms receded completely.	Keisu, 1996
Perception and symptoms in one patient	50 Hz 34 or 100 µT 1 or 10 s repeated	Positive response when humming of the coils audible, disappeared when “camouflaged” by masking noise.	.	Toomingas, 1996
Symptoms and physiological reactions 100 subjects	Low level magnetic fields (< 1 µT) at varying frequencies (0.1 Hz–5 MHz), in shielded laboratory.	16 out of 100 individuals reacted repeatedly to fields by several parameters (symptoms, pupil diameter changes etc.).	Not sure whether fully blind study.	Rea et al., 1991

Table 37. Continued

EMF perception 49 subjects with EHS and 14 controls	50 Hz 100 V m^{-1} 6 µT randomly presented as 2 min block of exposure / sham exposure	Perception by 7 subjects, but no difference in perception between subjects with or without self-reported EHS.		Mueller, Krueger & Schierz, 2002
Electrocardiogram, visual evoked potentials (VEP) and electroretinograms 10 subjects reporting EMF hypersensivity and 10 controls	Exposure to flickering light at between 25 and 75 flashes per second. No EMF exposure	Higher VEP amplitudes in EMF hypersensitive patients.	Differences between mean age of patients and controls (37 vs 47 year).	Sandström et al., 1997
Self-reported symptoms, blood pressure, heart rate, (skin) electrodermal activity, EEGs and visual evoked potentials 10 subjects reporting hypersensitivity and 10 controls	No EMF exposure	Differences between patients and controls regarding self-reported symptoms, heart rate, electrical activity of the skin, and visual evoked potential amplitudes.		Lyskov, Sandström & Hansson Mild, 2001a
Immuno-fluorescent staining of mast cells from skin biopsies 13 healthy subjects	VDU (TV or PC) exposure for 2 or 4 h	Increase in number of mast cells in papillary and reticular dermis in 5 subjects.		Johansson et al., 2001

Table 38. Mood and alertness

Test	Exposure	Response	Comments	Authors
Mood Adjective Checklist before and after exposure; Stanford Sleepiness Scale before during and after exposure 30 male subjects	60 Hz 9 kV m^{-1} and 20 µT 2 x 3 h / day for 4 days	No effect.	Double-blind, counterbalanced study.	Cook et al., 1992
Alertness Rating Scale, Mood Adjective Checklist before and after exposure 54 male subjects	60 Hz 6 kV m^{-1} and 10 µT 9 kV m^{-1} and 20 µT 12 kV m^{-1} and 30 µT 2 x 3 h / day for 4 days	No effect.	Double-blind, counterbalanced study.	Graham et al., 1994
State-Trait Anxiety Inventory, Profile of Mood States, Visual Analogue Scales of mood and vigilance before and after exposure 21 male subjects	50 Hz 100 µT 30 min, continuous or intermittent Head only exposures	No effect.	Double-blind studies.	Crasson et al., 1999
State-Trait Anxiety Inventory, Profile of Mood States, Visual Analogue Scales of mood 18 subjects	50 Hz 100 µT 30 min, continuous or intermittent Head only exposures.	No effect.	Replicate and extension of Crasson et al., 1999	Crasson & Legros, 2005
Mood checklist before and after exposure 76 male subjects	50 Hz current; 500 µA directly applied to head and shoulders 5.5 h / day for 2 days	Decreased arousal in one of two groups; no effect on mood.	Possible differences between groups. Double-blind procedures with cross-over design.	Stollery, 1986
Skin conductance and self-assessed arousal and affective content 20 male, 9 female subjects	20 Hz 50 µT 5 s with concurrent visual stimulus	No effect on skin conductance and arousal but positive effect of exposure on image content.	Subject blind as to exposure status.	Stevens, 2001

Table 39. Depression

Study base and subject identification	Definition and estimation of exposure	Study design and numbers	RR (95% CI)	Authors
Persons who lived near a 132 kV line and persons who lived 3 miles away Questionnaire asking about depression	Distance between home and overhead line	Cross-sectional 132 near line, 9 with depression 94 away from line, 1 with depression	Strong association of depression to proximity to overhead power line.	Dowson et al., 1988
Persons discharged with depression from hospital (England) and controls from electoral list	Measurements at front doors. Average for case and control groups compared	Case-control 359 persons discharged with diagnosis depressive illness	Average measurement cases: 0.23 μT; controls 0.21 μT.	Perry, Pearl & Binns, 1989
Residents in 8 towns along a transmission line right-of-way (ROW) in the US, 1987. A sample was interviewed. Depressive symptoms obtained by CES-D[a] scale. Cut-off for depression was median of score.	Distance from power-line: near vs far Near: properties abutting ROW or towers visible	Cross-sectional 382 persons interviewed	2.8 (1.6–5.1)	Poole et al., 1993
Male veterans who served in the US army first time 1965-71. Two diagnostic inventories used: the Diagnostic Interview Schedule and the Minnesota Personality Inventory. Life time depression used for this report	Present job identified in interview together with duration Electrical worker	Cross-sectional 183 electrical workers (13 with life-time depression) 3861 non-electrical workers	1.0 (0.5–1.7)	Savitz & Ananth, 1994
Population of neighborhood near a transmission line in Orange County, CA, USA, 1992. A sample of homes near a power line and one block away from the power line. Depressive symptoms identified through questionnaire CES-D* scale	EMDEX measurements at the front door. Average for homes on easement: 0.486 μT and one block away 0.068 μT	Cross-sectional 152 women	0.9 (0.5–1.9)	McMahan, Ericson & Meyer, 1994
Finnish twins who had answered the Beck Depression Inventory (BDI) in 1990	Residential magnetic field estimated from power lines near the homes	Cross-sectional 12063 persons	BDI scores not related to exposure.	Verkasalo et al., 1997

[a] CES-D scale: Centre for Epidemiologic Studies-Depression scale.

5.3 Epidemiological studies

With regard to neurobehavioural effects, epidemiological studies have focussed on depression and suicide. Studies of an association between EMF exposure and neurodegeneration are covered in Chapter 6.

5.3.1 Depression

Two early studies relating ELF EMF exposure to depression (Dowson et al., 1988; Perry, Pearl & Binns, 1989) are difficult to interpret because of methodological limitations to the procedures for selection of study subjects, because they did not use validated scales for identification of depressive symptoms (ICNIRP, 2003). Moreover, Perry, Pearl & Binns (1989) also reported unusually high average EMF levels that remain unexplained.

More recent studies used validated depression scales. One of these studies showed a clear association between proximity to power lines and depression (Poole et al., 1993), whereas three more recent studies (McMahan, Ericson & Meyer, 1994; Savitz & Ananth, 1994; Verkasalo et al., 1997) provided little evidence for such an association. The study by Poole et al. (1993) is well designed: it compares subjects on properties abutting a power line right-of-way to subjects further away, and the results appear internally consistent. The investigators report a relative risk of 2.8 (95% CI: 1.6–5.1). McMahan, Ericson & Meyer (1994) employed a similar design and measurements to confirm that the homes close to the line have considerably higher EMF levels than those further away. This study also appears valid but yields a relative risk of 0.9 (95% CI: 0.5–1.9). McMahan, Ericson & Meyer (1994) offer a number of possible explanations for the lack of consistency between these two studies but none of the explanations is convincing (ICNIRP, 2003).

Overall, ICNIRP (2003) conclude that the literature on depressive symptoms and EMF exposure is difficult to interpret because the findings are not consistent. This complexity cannot easily be resolved by suggesting that one type of result can be confined to a group of studies with methodological problems or some other limitation.

A summary of studies on the effects of ELF field exposure on depression is given in Table 39.

5.3.2 Suicide

An early case control study carried out in England (Perry et al., 1981; Reichmanis et al., 1979) found significantly higher EMFs in case homes than control homes. However, ICNIRP (2003) considers the study methodologically limited both for the way subjects were selected and for the statistical analysis employed. Subsequent studies have used a range of different approaches to assess exposure, varying from crude techniques based on distance between home and power lines, or on job titles, to more sophisticated approaches based on detailed information about cohorts of utility workers (Baris et al., 1996a; Baris et al., 1996b; Baris & Armstrong, 1990; Johansen & Olsen, 1998a; McDowall, 1986; van Wijngaarden et al., 2000). Only the latter study provides some support for the original findings,

although McKinlay et al. (2004) note that the findings were variable. The two more recent occupational study, based on job titles recorded on death certificates, report contradictory results (Järvholm & Stenberg, 2002; van Wijngaarden, 2003). However, the exposure assessments in these studies were not as detailed as in the previous occupational studies listed.

In a review of ICNIRP (2003) it was observed that, despite methodological limitations, particularly relating to the earlier studies, the detailed study by Van Wijngaarden et al. (2000) suggested that an excess risk for suicide might exist.

A summary of the ELF suicide studies is given in Table 40.

Tabel 40. Suicide

Study base and subject identification	Definition and estimation of exposure	Study design and numbers	RR (95% CI)	Authors
Suicide cases and controls in England	Estimates of residential exposure from power lines Measurements at the homes of subjects	Case-control 589 suicide cases	Higher estimated and measured fields at case homes.	Reichmanis et al., 1979 Perry et al., 1981
Male employees in Danish utility companies observed during 1974–-93 Cases: deaths from suicide in mortality registry	Employment records and job exposure matrix estimated average exposure level Medium and high exposure	SMR [a] 21 236 males in cohort; exposed cases	1.4 (non-significant)	Johansen & Olsen, 1998a
Persons resident in the vicinity of transmission facilities, in specified areas in the UK, at the time of 1971 Census	Home within 50 meters from substation or 30 meters from overhead line	SMR [a] 8 cases	0.75 (non-significant)	McDowall, 1986
Deaths in England and Wales during 1970–72 and 1979–83	Job titles on death certificates Electrical workers in aggregate as well as specific jobs	PMR [b] 495 cases in electrical occupations	No increase for electrical workers.	Baris & Armstrong, 1990
Male utility workers, Quebec, Canada, 1970–88 Cases: deaths from suicide in mortality registry Controls: 1% random sample from the cohort	Job exposure matrix based on Positron measurements was created. E- and B-and pulsed fields from average and geometric means and from cumulative and current exposure	Case-control 49 cases 215 controls	No evidence for effects of magnetic fields. Some support for some electric field indices.	Baris et al., 1996a; 1996b

Table 40. Continued

Male electric utility workers	Jobs and indices of cumulative exposure based on measurement survey	Case-control 36 cases 5348 controls	Electrician: 2.18 (1.25–3.80) Line worker: 1.59 (1.18–2.14)	van Wijngaarden et al., 2000
Swedish male electricians in construction industry Swedish death register	Job exposure matrix	Cohort study - 33 719 electricians (0.31 µT) - 72 653 glass and woodworkers (0.27–0.29 µT) - general population	SMR Electricians: 0.58 (0.47–0.71) Glass and woodworkers: 0.81 (0.72–0.91)	Järvholm & Stenberg, 2002
United States death certificate files for the years 1991 and 1992	Occupation code; usual occupation and industry on the death certificates	Case-control 11 707 cases 132 771 controls	1.3 (1.2–1.4)	van Wijngaarden, 2003

[a] SMR: Standardized Mortality Ratio.

[b] PMR: Proportional Mortality Ratio.

5.4 Animal studies

Various animal models have been used to investigate possible field-induced effects on brain function and behaviour. These include effects on neurotransmitter levels, electrical activity, field detection and the performance of learned tasks. Overall, a few field-dependent responses have been tentatively identified but even the most consistent effects appear small in magnitude and transient in nature.

5.4.1 Perception and field detection

It is known that animals can detect the presence of low frequency electric fields, possibly as a result of surface charge effects (Weigel & Lundstrom, 1987). Using appropriate behavioural techniques, a number of studies using rats (Sagan et al., 1987; Stell, Sheppard & Adey, 1993; Stern et al., 1983; Stern & Laties, 1985; reviewed in ICNIRP, 2003; NIEHS, 1998; NRC, 1997) indicate that the threshold for field detection is about 3–13 kV m^{-1}. Detection thresholds are similar in a variety of other species, with thresholds reported at 5–15 kV m^{-1} in baboons (Orr, Rogers & Smith, 1995a), and 30–35 kV m^{-1} in miniature swine (Kaune et al., 1978).

Detection thresholds for magnetic fields in animals are less clear and show greater variability than those for electric fields (ICNIRP, 2003). Using a conditioned suppression paradigm, Smith, Clarke & Justesen (1994)

reported that rats were able to detect ELF magnetic fields as low as 200 μT, although the validity of this result has been questioned by Stern & Justesen (1995).

A summary of studies on perception and detection of fields is given in Table 41.

Table 41. Perception and field detection

Endpoint	Exposure	Response	Comment	Authors
ELF electric fields				
Rats: operant behaviour Electric field acting as cue or discriminative stimulus	60 Hz up to 55 kV m^{-1} brief daily exposures	Threshold of between 3 and 10 kV m^{-1}.		Stern et al., 1983 Stern & Laties, 1985
Rats: operant behaviour Electric field acting as cue	60 Hz up to 27 kV m^{-1} brief daily exposures	Threshold of 8 or 13 kV m^{-1} depending on the test protocol.		Sagan et al., 1987
Rats: effect of air current on operant behaviour Electric field acting as cue	60 Hz up to 25 kV m^{-1} brief daily exposures	Threshold of 7.5 kV m^{-1} unaffected by wind-induced hair movement.	Detection below threshold increased; results difficult to interpret.	Stell, Sheppard & Adey, 1993
Baboons: operant behaviour Electric field acting as cue	60 Hz 4–50 kV m^{-1} brief daily exposures	Average threshold of 12 kV m^{-1}; range of 5–15 kV m^{-1}.		Orr, Rogers & Smith, 1995a
Handford minature swine: drinking behaviour (n=4) Electric fields acts as conditioned stimulus	60 Hz up to 55 kV m^{-1} brief (20 s) repeated exposures	Threshold of 30–35 kV m^{-1}.		Kaune et al., 1978
ELF magnetic fields				
Rats: conditioned suppression of operant behaviour	7, 16, 30, 60 and 65 Hz 200 μT – 1.9 mT 1 h / day, 5 days / week, 5 weeks	All magnetic fields effective as cue for conditioned response suppression.	Temporal rather than magnetic field conditioning?	Smith, Clarke & Justesen, 1994; Stern, 1995

5.4.2 *Arousal and aversion*

Initial exposure to power-frequency electric fields in excess of detection thresholds may cause transient arousal and stress responses in rodents and non-human primates (Coelho, Easley & Rogers, 1991; Easley, Coelho & Rogers, 1991; Rosenberg et al., 1983; Rosenberg, Duffy & Sacher, 1981; reviewed in IARC, 2002; ICNIRP, 2003). These responses appear to habituate quickly following prolonged exposure. There is also some evidence that animals may avoid exposure to intense electric fields (e.g. Hjeresen et al., 1980; 1982), and that such fields can elicit aversive behaviours following exposure to high field strengths in rats (Creim et al., 1984) and in non-human primates (Rogers, Orr & Smith, 1995; Stern & Laties, 1989). The results of the latter study indicated that electric fields at levels of up to 65 kV m^{-1} are not highly aversive to non-human primates.

Exposure of baboons to combined 60 Hz electric and magnetic fields at 6 kV m^{-1} and 50 μT or at 30 kV m^{-1} and 100 μT did not produce significant changes in social behaviour (Coelho, Rogers & Easley, 1995) previously seen to be affected by exposure to electric fields alone (Coelho, Easley & Rogers, 1991; Easley, Coelho & Rogers, 1991). While it is possible that the magnetic field may have modulated the electric field-induced responses, it was considered that some of the animals in the later experiment may have become desensitised by prior subthreshold electric field exposure.

Acute exposure to power frequency magnetic fields at up to 3 mT does not appear to induce aversive behaviour (Lovely et al., 1992). Such results suggest that the arousal responses observed using electric fields are not caused by field-induced internal electric fields, and may be attributed to body-surface interactions. One study reported that long-term, intermittent exposure to 50 Hz at 18 mT reduced behavioural responses ("irritability") induced by tactile and somatosensory stimuli in rats (Trzeciak et al., 1993). Another study reported that exposure to specific combinations of static and low frequency fields affected exploratory behaviour in rats (Zhadin, Deryugina & Pisachenko, 1999). Exposure to conditions corresponding to the putative cyclotron resonance for calcium ions reduced this behaviour, and exposure to conditions for magnesium ions increased it.

Studies on arousal and aversion in experimental animals are summarized in Table 42.

Table 42. Arousal and aversion

Endpoint	Exposure	Response	Comment	Authors
Arousal and activity				
ELF electric fields				
Mice: arousal assessed by activity, oxygen consumption, carbon dioxide production during exposure	60 Hz 10, 25, 35, 50, 75 and 100 kV m^{-1} Four 1 h exposures at 1 h intervals	Increased arousal during the first exposure to fields of 50 kV m^{-1} and above; little effect during subsequent exposures.		Rosenberg et al., 1983; Rosenberg, Duffy & Sacher, 1981
Mice: exploratory activity in open field arena after exposure	15, 30 and 50 Hz 50, 100, 400 V m^{-1} 30 min / day for 5 days	No effect.		Blackwell & Reed, 1985
Baboons: social behaviour in 8 adult males	60 Hz 30 kV m^{-1} 12 h / day, 7 days / week for 6 weeks	Initally, exposed animals showed passive affinity (e.g. huddling), tension and stereotypy (e.g. scratching).	Indicative of stress.	Coelho, Easley & Rogers, 1991
Baboons: social behaviour in 8 adult males	60 Hz 60 kV m^{-1} 12 h / day, 7 days / week for 6 weeks	Increased initial levels of passive affinity, tension and stereotypy.	Repeat of previous study using higher electric field strength.	Easley, Coelho & Rogers, 1991
ELF magnetic fields				
Rats: rearing, ambulatory and grooming behaviour in an open field arena after exposure.	50 Hz 80 µT 4 h at beginning of light (quiet) period or dark (active) period	Increased rearing after exposure in quiet but not active period. No effects on ambulation or grooming.	Effect replicated in 2nd experiment. No sham exposed controls.	Rudolph et al., 1985

Table 42. Continued

Rats: irritability, exploratory (open field) activity and locomotion	50 Hz 18 mT 2 h / day for 20 days	Decrease in irritability, no effects on exploratory activity or locomotion.		Trzeciak et al., 1993
Rats: open field behaviour	DC fields of 50 or 500 μT corresponding AC fields set for cyclotron resonance conditions for several ionic species	Reduced locomotor and exploratory behaviour during calcium ion resonance conditions; opposite effect for magnesium.		Zhadin, Deryugina & Pisachenko, 1999
ELF Electric and Magnetic Fields				
Baboons: social behaviour in 8 adult males	60 Hz 6 kV m[1] and 50 μT 30 kV m[1] and 100 μT 12 h / day, 7 days / week for 6 weeks	No effects on passive affinity, tension and stereotypy.	Results contrast with effects of 50 Hz electric fields alone described above.	Coelho, Rogers & Easley, 1995
Avoidance and aversion				
ELF electric fields				
Rats: avoidance behaviour in a shuttlebox (which has exposed and unexposed ends)	60 Hz 25–105 kV m^{-1} 45 min / week for 4 weeks or once for 23.5 h	Significant preference for shielded region above 90 kV m^{-1} (short exposure) or 75 kV m^{-1} (long exposure).		Hjeresen et al., 1980
Rats: taste aversion to electric field plus flavoured water	60 Hz 50, 101 or 196 kV m^{-1} (unperturbed fields) 20 min	No effect.	Positive control with chemical inducer.	Creim et al., 1984
Rats: avoidance behaviour in a shuttlebox	60 Hz 30 kV m^{-1} 20 h	Significant preference for shielded region.	Follow on to chronic study.	Hjeresen et al., 1982

Table 42. Continued				
Baboons: behavioural aversion through operant responses (lever press) to terminate exposure	60 Hz up to 65 kV m^{-1} during testing	Field perceived but did not act as negative (aversive) re-inforcer.	No support for stress effect.	Rogers, Orr & Smith, 1995
Baboons: behavioural aversion through operant responses (lever press) to terminate exposure	60 Hz 90 or 100 kV m^{-1} brief exposures	Exposure did not induce lever pressing (field termination) behaviour.	Incandescent lamp as positive control.	Stern & Laties, 1989
ELF magnetic fields				
Rats: avoidance behaviour in a shuttlebox	60 Hz 3.03 mT 1 h	No effect.		Lovely et al., 1992

5.4.3 Brain electrical activity

A number of animal studies have investigated if acute exposure to low frequency electric and magnetic fields can affect brain electrical activity demonstrated in the EEG or as evoked potentials following presentation of a sensory stimulus (e.g. Blackwell, 1986; Dowman et al., 1989, reviewed by NIEHS, 1998; Sienkiewicz, Saunders & Kowalczuk, 1991). The results of these studies are somewhat mixed and difficult to interpret, but none suggests any obvious hazard (ICNIRP, 2003). Some of these studies may have been confounded by experimental design: for example, it has long been recognised that recording electrical potentials through electrodes attached to the skull is liable to produce artefacts in the presence of EMFs. Two more recent studies reported significant EEG changes in rabbits during magnetic field exposure (Bell et al., 1992) and in rats following magnetic field exposure (Lyskov et al., 1993c). However, the possibility of an artefact or of false positive results complicates interpretation of both studies (NIEHS, 1998). A summary of studies on brain electrical activity in experimental animals exposed to ELF fields is given in Table 43.

Table 43. Brain electrical activity

Endpoint	Exposure	Response	Comment	Authors
ELF electric fields				
Rats: CNS neuronal activity in anaesthetised animals during exposure	15, 30 and 50 Hz 100 V m^{-1} (peak–peak)	No overall effect on firing rate; some synchrony at 15 and 30 Hz.	Anaesthesia-depressed responsiveness.	Blackwell, 1986
ELF magnetic fields				
Rabbits: EEG recordings during exposure	5 Hz, 100 µT DC + 25 Hz, 64 µT 25 Hz, 1 µT	Increased EEG signal in response to 5 Hz.	Possibility of induction artefact.	Bell et al., 1992
Rats: EEG recordings from Sprague-Dawley rats before and after exposure	45 Hz 126 µT, intermittent 1.26 mT, 24 h exposure twice, 24 h apart	Dose-dependent increase in significant changes to EEG pattern following exposure.	Induced currents possibly increased due to permanent electrodes.	Lyskov et al., 1993c
Electric & magnetic fields				
Macaque monkeys: auditory, visual and somatosensory evoked potentials recorded during “field off” period.	60 Hz 3 kV m^{-1} and 10 µT 10 kV m^{-1} and 30 µT 30 kV m^{-1} and 90 µT 3 weeks	Most measures unaffected. Decreased amplitude of late components of somatosensory evoked potentials.		Dowman et al., 1989

5.4.4 Neurotransmitter function

A number of studies have investigated the potential of ELF fields to affect the levels of different neurotransmitters within various regions of the brain. Neurotransmitters are chemical substances released from nerve cells which enable the transmission of information to adjacent nerve cells equipped with appropriate receptors and may also have more widespread effects when released into the circulation. Different neurotransmitter systems are associated with different functions: the main groups are the cholinergic neurotransmitters such as acetylcholine, the biogenic amines comprising the catecholamines, including dopamine, norepinephrine (noradrenaline), epinephrine (adrenaline), and serotonin, the amino acid neurotransmitters such as glutamate and aspartate, and the peptide neurotransmitters such as the opioids. Most groups have important roles in brain function, the latter two almost exclusively so. Altered transmitter levels can be associated with functional changes but interpretation is usually difficult (NIEHS 1999).

These data have been most recently reviewed by ICNIRP (2003). Early studies (e.g. Vasquez et al., 1988; Zecca et al., 1991) reported effects of both acute and chronic exposure to intense electric fields on catecholamine and amino acid neurotransmitter levels in some parts of the brain, but values often stayed within the normal range. More recently, Margonato et al. (1995) reported that chronic exposure to 50 Hz magnetic fields at 5 μT had no effect on levels of norepinephrine, dopamine and its major metabolites, or 5-hydroxytryptamine or its major metabolite in the striatum, hypothalamus, hippocampus or cerebellum. However, in a companion study, Zecca et al. (1998) reported effects on norepinephrine levels in the pineal gland but not elsewhere in the brain following chronic exposure to combined electric and magnetic fields at either 1 kV m^{-1} and 5 μT or 5 kV m^{-1} and 100 μT. In addition, intensity-dependent changes were reported in the opioid receptor system in the frontal cortex, parietal cortex and hippocampus, but not in other brain areas investigated.

Other studies have also investigated field-dependent changes in opioid-related physiology in molluscs and in mammals. In a series of related experiments, Kavaliers, Prato and colleagues (e.g. Kavaliers & Ossenkopp, 1986a; Kavaliers & Ossenkopp, 1986b; Kavaliers, Ossenkopp & Hirst, 1984; Ossenkopp & Kavaliers, 1987) have indicated that various types of ELF magnetic fields may affect the endogenous opioid systems and modulate the response of both groups of animals to the analgesic effects of injected opiates such as morphine (reviewed by Kavaliers et al., 1994; Kavaliers & Ossenkopp, 1991). These responses are complex, and magnetic fields appear to have a differential effect on the functions of different opioid receptor subtypes. There is evidence that the mechanism for these effects may involve changes in calcium ion channel function in mice (Kavaliers et al., 1998) and in protein kinase C activity, nitric oxide (NO) release and NO synthase activity in the land snail *Cepaea nemoralis* (1998; Kavaliers, Ossenkopp & Tysdale, 1991). Further studies with land snails suggest that the field induced analgesic effects depend on the relative direction of the applied fields (Prato

et al., 1995) as well as the presence of light (1997; Prato, Kavaliers & Carson, 1996; 2000).

In another series of experiments, it was reported that the acute exposure of rats to a 60 Hz magnetic field at 0.75 mT decreased activity in the cholinergic pathways in the frontal cortex and hippocampus (Lai et al., 1993). These effects were blocked by naltrexone, but not by naloxone methiodide, which was taken as evidence that magnetic fields affected endogenous opioids only within the central nervous system. Further studies showed the changes in cholinergic activity appeared to be mediated by activation of endogenous opioids (Lai, Carino & Ushijima, 1998). There also appears to be some interaction between exposure duration and field intensity, such that longer exposures (3 hours) at lower intensity fields (0.05 mT) could induce changes in cholinergic activity similar to those induced by shorter exposure at higher intensity (Lai & Carino, 1999).

Overall, limited changes in neurotransmitter levels in different parts of the rodent brain have been reported. Although of less direct relevance to human health, similar results have been reported in the molluscan nervous system. The biological significance of the changes seen in mammals is difficult to assess without corroborative changes in brain function and behaviour. However, several studies suggest possible EMF effects on the opioid and cholinergic systems which can be modulated by appropriate antagonists and should be studied further. Studies on the effects of ELF fields on neurotransmitters and analgesia are summarized in Table 44.

5.4.5 Cognitive function

Early studies with macaque monkeys reported that exposure to ELF electric fields at well below detection thresholds may affect operant performance (IARC, 2002; ICNIRP, 2003). However, well-conducted studies using baboons found that exposure to 60 Hz electric fields at 30 and 60 kV m^{-1} had no sustained effect on the performance of two operant schedules (Rogers et al., 1995a; 1995b) although initial exposure may contribute towards producing a temporary interruption in responding.

Similarly, studies using 60 Hz electric and magnetic fields (Orr, Rogers & Smith, 1995b) indicated that combined exposure to 6 kV m^{-1} and 50 μT or to 30 kV m^{-1} and 100 μT had no effect on operant performance on a delayed match-to-sample task in baboons. This result is generally consistent with earlier results from other research groups using non-human primates (reviewed by ICNIRP, 2003; NIEHS, 1998; Sienkiewicz, Saunders & Kowalczuk, 1991). However, one study using rats (Salzinger et al., 1990) suggested exposure to 60 Hz fields of 30 kV m^{-1} and 100 μT may exert subtle effects on performance that depend on the time of testing within the light-dark cycle.

Table 44. Neurotransmitters and analgesia

Endpoint	Exposure	Response	Comment	Authors
Neurotransmitters				
ELF electric field				
Rats: biogenic amine levels in striatum, hypothalamus and hippocampus	60 Hz 39 kV m^{-1} 20 h / day, 4 weeks	No effects in hippocampus; some changes in striatum and hypothalamus.		Vasquez et al., 1988
Rats: amino acid levels in striatum	50 Hz 25 and 100 kV m^{-1} 8–22 h / day, 5–7 days/ week for 320, 640, 1240, or 1408 h	General increase after 320 h exposure; decreased levels after longer periods.	Observed values within normal range. Three replicate experiments.	Zecca et al., 1991
ELF magnetic field				
Rats: central cholinergic systems in brain	60 Hz 0.5, 0.75, 1 mT 45 min	Reduced high-affinity choline uptake in frontal cortex and hippocampus.	Effect blocked by central but not peripheral opioid antagonists.	Lai et al., 1993
Rats: biogenic amine levels in 4 regions of the brain	50 Hz 5 µT 22 h / day, 32 weeks	No effect.	Two replicate experiments.	Margonato et al., 1995
ELF Electric and Magnetic Fields				
Rats: neurotransmitter and receptor levels in brain and pineal	50 Hz 5 µT and 1 kV m^{-1} 100 µT and 5 kV m^{-1} 8 h / day, 5 days / week, 8 months	Increase in norepinephrine levels in the pineal gland; changes in the distribution of µ-opioid receptors in the brain.		Zecca et al., 1998

Table 44. Continued

Opioids and analgesia				
ELF magnetic fields				
Land snails: morphine-induced analgesia	60 Hz 100 mT 2 h	Exposure-induced reduction in analgesia.	Effect enhanced by PKC activators.	Kavaliers & Ossenkopp, 1991
Land snails: morphine-induced analgesia	10–240 Hz 0–547 μT with parallel static magnetic field	Non-linear dose-response; frequency response relationships seen in analgesia reduction.	Results suggested direct effect of magnetic field.	Prato et al., 1995
Land snails: morphine-induced analgesia	60 Hz 141 μT 15 min	Exposure-induced reduction in analgesia.	Effects enhanced by NO releasing agent, and reduced by NO synthase inhibitor.	Kavaliers et al., 1998
Land snails: morphine-induced analgesia	ELF magnetic fields consistent with the PRM for Ca^{2+} or K^{+} ions	Effects on morphine-induced analgesia consistent with PRM mechanism.	Effects dependent on the presence of light.	Prato, Kavaliers & Thomas, 2000
Mice: morphine-induced analgesia	0.5 Hz 150 μT – 9 mT in mid-light-phase and mid dark phase 5–10 days	Reduction in the increased night-time latency to respond to hot-plate.	Exposure system comprised motor-driven, rotating horseshoe permanent magnets.	Kavaliers, Ossenkopp & Hirst, 1984
Mice: stress (restraint) induced analgesia and hyperactivity	0.5 Hz 150 μT – 9 mT 30 min in mid-light-phase and mid dark phase	Reduction in the increased night-time latency and day-time activity.	As above; similar effect with opioid antagonist naloxone.	Kavaliers & Ossenkopp, 1986b
Mice: opioid-induced analgesia	0.5 Hz 150 μT – 9 mT 60 min in mid-light-phase	Inhibition of daytime opioid analgesia.	As above; affects actions of mu, delta and kappa but not sigma agonists.	Kavaliers & Ossenkopp, 1986a

Table 44. Continued

Mice: morphine-induced analgesia	60 Hz 50, 100 or 150 μT 1 h	Dose-dependant reduction in analgesia.		Ossenkopp & Kavaliers, 1987
Mice: steroid-induced analgesia	60 Hz 141 μT 30 min	Exposure-induced reduction in analgesia.	Effect blocked by calcium channel antagonists.	Kavaliers, Wiebe & Ossenkopp, 1998
Rat: central cholinergic systems in brain	60 Hz 2 mT 1 h	Reduced high-affinity choline uptake in frontal cortex and hippocampus.	Effect blocked by mu- and delta-opiate antagonists.	Lai, Carino & Ushijima, 1998
Rat: central cholinergic systems in brain	60 Hz 0.5, 1.0, 1.5 or 2.0 mT, 1 h 1.0 mT, 30, 45, 60 or 90 min	High-affinity choline uptake in frontal cortex and hippocampus reduced.	Reduction occurs in intensity and duration-dependent manner.	Lai & Carino, 1999

Several recent studies using the Morris water maze or radial arm maze have investigated the effects of magnetic fields on spatial memory and place learning. These studies provide evidence that exposure of rats, mice or voles to power frequency fields at ~100 μT and above may modulate task performance (Kavaliers & Ossenkopp, 1993 Kavaliers et al., 1996; Lai, 1996; Lai, Carino & Ushijima, 1998; Sienkiewicz et al., 1998; Sienkiewicz, Haylock & Saunders, 1998). Exposure to complex pulsed magnetic fields may also affect performance (McKay & Persinger, 2000; Thomas & Persinger, 1997). In addition, much evidence has accrued over the last decade that effects may also occur using specific combinations of static and time-varying fields (see Sienkiewicz, Haylock & Saunders, 1998). The mechanism for these effects has been partly explored and the changes in behaviour have been attributed to decreases in cholinergic functions caused by field-induced changes in endogenous opioid activity (Lai, 1996; Lai, Carino & Ushijima, 1998; Thomas & Persinger, 1997).

The conditions to produce any of these phenomena are not well defined, and both deficits and enhancements in performance have been observed and one study did not report any field-dependent effects (Sienkiewicz, Haylock & Saunders, 1996). It is feasible that these differences in outcome may depend on experimental or other variables including the timing and duration of exposure relative to learning (McKay & Persinger, 2000; Sienkiewicz et al., 2001). While these results suggest that the neural representations or processes underlying the performance of spatial memory tasks may be vulnerable to the effects of magnetic fields, some part of the observed outcome may be attributable to changes in arousal (IARC, 2002; ICNIRP, 2003) or in motivation (Thomas & Persinger, 1997). Nevertheless, the transient nature and small magnitudes of the responses do not suggest an obvious deleterious effect.

Two studies using rodents have investigated the effects of magnetic fields on recognition memory. Using the field conditions putatively identified as having an acute effect of spatial memory, Sienkiewicz et al. (2001) found no effects on the performance of an object recognition task by mice. Animals were exposed for 45 minutes to a 50 Hz field at 7.5, 75 or 750 μT. However, Mostafa, Mostafa & Ennaceur et al. (2002) reported that discrimination between familiar and novel objects was impaired in rats following chronic exposure at 200 μT for 2 weeks.

Stern et al. (1996) failed to replicate the results of earlier studies (Liboff, McLeod & Smith, 1989; Thomas, Schrot & Liboff, 1986) suggesting exposure to combined static and power frequency magnetic fields, arranged to simulate the cyclotron resonance conditions for lithium ions, significantly impaired operant performance. The earlier positive results were attributed to possible confounding.

A summary of studies on cognitive function in animals is given in Table 45.

Table 45. Cognitive function				
Endpoint	**Exposure**	**Response**	**Comment**	**Authors**
Spatial memory				
ELF magnetic fields				
Meadow voles and deer mice: water maze performance	60 Hz 100 µT 5 min during task acquisition	Enhanced performance opiate-induced reduction abolished by magnetic field exposure in deer mice.	Suggests magnetic field reduces opiate activity.	Kavaliers & Ossenkopp, 1993 Kavaliers et al., 1996
Rats: radial arm maze performance	60 Hz 750 µT 45 min prior to behavioural testing	Performance reduced. Effect abolished by cholinergic antagonist.	Suggests magnetic field reduces cholinergic activity.	Lai, 1996
Mice: radial arm maze performance	50 Hz 5, 50 or 500 µT or 5 mT during behavioural testing (up to 15 min)	No effect.		Sienkiewicz, Haylock & Saunders, 1996
Rats: radial arm maze with operant task at the end of each arm	Pulsed (burst firing pattern for 1 sec every 3 sec) 1–4 µT 5 or 30 min immediately or 30 min after 8 training sessions	Some differences were seen between the exposed and sham exposed animals.	Small number of animals; complex post hoc interpretation of data.	Thomas & Persinger, 1997
Rats: water maze performance	60 Hz 1 mT 1 h prior to behavioural testing	No effect on performance but retention impaired.	Reduced swim speed.	Lai, Carino & Ushijima, 1998
Mice: radial arm maze performance	50 Hz 7.5, 75, or 750 µT or 7.5 mT prior to behavioural testing	No overall effect but transiently reduced acquisition rate.	No effect on movement or motivation.	Sienkiewicz et al., 1998; 1998
Rats: complex radial maze performance	A complex low intensity magnetic field of between 200–500 nT for 1 h of a 2 h period between training and testing	Exposure immediately after training impaired spatial memory and those immediately before testing impaired motivation.		McKay & Persinger, 2000

Table 45. Continued

Mice: spontaneous object recognition task	50 Hz 7.5, 75, or 750 μT between initial testing and re-testing	No significant field-dependent effects.		McKay & Persinger, 2000 Sienkiewicz et al., 2001
Rats: spontaneous object recognition task	50 Hz 200 μT 1 or 2 weeks	Significant decrease in discrimination between familiar and novel objects.	Significant corticosterone elevation in exposed animals.	Mostafa, Mostafa & Ennaceur, 2002
Operant behaviour				
ELF electric fields				
Baboons: multiple FR (fast) and DRL (slow) schedules	60 Hz 30 or 60 kV m^{-1} 6 weeks during behavioural testing	Exposure on day 1 induced temporary work stoppage.		Rogers et al., 1995a
Static and ELF magnetic fields				
Rats: multiple FR (fast) and DRL (slow) schedules	Static field of 26 μT plus 60 Hz field of up to 200 μT 30 min prior to operant testing	DRL response impaired; temporal discrimination reduced.	Cyclotron resonance conditions for lithium.	Thomas, Schrot & Liboff, 1986 Liboff, McLeod & Smith, 1989
Rats: multiple FR (fast) and DRL (slow) schedules	Static field of 26 or 27 μT plus 60 Hz field of 50 or 70 μT 30 min prior to behavioural testing	No effect.	Attempted replication of Thomas et al. 1986,	Stern et al., 1996
ELF electric and magnetic fields				
Rats: multiple random interval (RI) schedule in adult males exposed perinatally followed by extinction and reconditioning	60 Hz 100 μT, 30 kV m^{-1} 20 h / day, 22 days in utero and 8 days postnatally	Reduced performance in exposed rats.	Two replicate studies.	Salzinger et al., 1990
Baboons: delayed match-to-sample procedure (light-flash stimulus)	60 Hz 6 kV m^{-1}, 50 μT 30 kV m^{-1}, 100 μT 6 weeks during behavioural testing	No effect.		Orr, Rogers & Smith, 1995b

5.5 Conclusions

Exposure of volunteers to power frequency electric fields causes well-defined biological responses, ranging from perception to annoyance, through surface electric-charge effects. These responses depend on field strength, ambient environmental conditions, and individual sensitivity. The thresholds for direct perception by 10% of volunteers varied between 2 and 20 kV m^{-1}, while 5% found 15–20 kV m^{-1} annoying. The spark discharge from a person to ground is found to be painful by 7% of volunteers in a field of 5 kV m^{-1}. Thresholds for the discharge from an object through a grounded person depend on the size of the object and therefore require specific assessment.

High field strength, rapidly pulsed magnetic fields can stimulate peripheral or central nerve tissue; such effects can arise during MRI exposure and are used in transcranial magnetic stimulation. Threshold induced electric field strengths for direct nerve stimulation could be as low as a few volts per metre. The threshold is likely to be constant over a frequency range between a few hertz and a few kilohertz. People suffering from or predisposed to epilepsy are likely to be more susceptible to induced ELF electric fields in the CNS. Furthermore, sensitivity to electrical stimulation of the CNS seems likely to be associated with a family history of seizure and the use of tricyclic antidepressants, neuroleptic agents and other drugs that lower the seizure threshold.

The function of the retina, which is part of the CNS, can be affected by exposure to much weaker ELF magnetic fields than those that cause direct nerve stimulation. A flickering light sensation, called magnetic phosphenes or magnetophosphenes, results from the interaction of the induced electric field with electrically excitable cells in the retina. Threshold electric field strengths in the extracellular fluid of the retina have been estimated to lie between about 10–100 mV m^{-1} at 20 Hz. There is, however, considerable uncertainty attached to these values.

The evidence for other neurobehavioural effects in volunteer studies, such as the effects on brain electrical activity, cognition, sleep, hypersensitivity and mood, is less clear. Generally, such studies have been carried out at exposure levels below those required to induce effects described above, and have produced evidence only of subtle and transitory effects at best. The conditions necessary to elicit such responses are not well defined at present. There is some evidence suggesting the existence of field-dependent effects on reaction time and reduced accuracy in the performance of some cognitive tasks, which is supported by the results of studies on the gross electrical activity of the brain. Studies investigating EMF-induced changes in sleep quality have reported inconsistent results. It is possible that these differences may be attributable in part to differences in the design of the studies.

Some people claim to be hypersensitive to EMF. However, the evidence from double blind provocation studies suggests that the reported symptoms are unrelated to EMF exposure.

There is only inconsistent and inconclusive evidence that exposure to ELF electric and magnetic fields causes depressive symptoms or suicide. Thus, the evidence is considered inadequate.

In animals, the possibility that exposure to ELF fields may affect neurobehavioral functions has been explored from a number of perspectives using a range of exposure conditions. Few robust effects have been established. There is convincing evidence that power-frequency electric fields can be detected by animals, most likely as a result of surface charge effects, and may induce transient arousal or mild stress. In rats, the detection range is between 3 and 13 kV m^{-1}. Rodents have been shown to be aversive to field strengths greater than 50 kV m^{-1}. Other possible field-dependent changes are less well-defined and generally laboratory studies have only produced evidence of subtle and transitory effects. There is some evidence that exposure to magnetic fields may modulate the functions of the opioid and cholinergic systems, and this is supported by the results of studies investigating the effects on analgesia and on the acquisition and performance of spatial memory tasks.

6 NEUROENDOCRINE SYSTEM

The pineal and pituitary neuroendocrine glands, both situated in the brain and intimately connected with and controlled by the nervous system, release hormones into the blood stream which exert a profound influence on body metabolism and physiology, particularly during development and reproduction, partly via their influence on the release of hormones from other endocrine glands situated elsewhere in the body. These studies have been reviewed by NIEHS (1998), IARC (2002), McKinlay et al. (2004) and recently by AGNIR (2006).

The hypothesis, first suggested by Stevens (1987), that exposure to EMFs might reduce melatonin secretion and thereby increase the risk of breast cancer has stimulated a number of human laboratory studies and investigations of circulating melatonin levels in people exposed to EMFs in domestic or occupational situations.

6.1 Volunteer studies

The majority of studies have investigated the effects of EMF exposure, mostly to power frequencies, on circulating levels of the pineal hormone melatonin (or on the urinary excretion of a metabolite of melatonin). Fewer studies have been carried out on circulating levels of pituitary hormones or other hormones released from other endocrine glands such as the thyroid gland, adrenal cortex and reproductive organs.

6.1.1 The pineal hormone: melatonin

Melatonin is produced by the pineal gland in the brain in a distinct daily or circadian rhythm which is governed by day length. It is implicated in the control of daily activities such as the sleep/wake cycle and in seasonal rhythms such as those of reproduction in animals that show annual cycles of fertility and infertility. Maximum serum levels occur during the night, and minimum levels during the day, even in nocturnally active animals. Night-time peak values of serum melatonin in humans, however, can vary up to ten-fold between individuals (Graham et al., 1996). It has been suggested that melatonin has a negative impact on human reproductive physiology, but that any changes are slight compared to those seen in experimental animals (Reiter, 1997). However, the overall evidence suggests that human melatonin rhythms are not significantly delayed or suppressed by exposure to magnetic fields (AGNIR, 2001b; IARC 2002; ICNIRP, 2003; NIEHS, 1998; although see Karasek & Lerchl, 2002).

6.1.1.1 Laboratory studies

Several laboratory studies have been carried out in which volunteers, screened for various factors which might have influenced melatonin levels, were exposed or sham exposed overnight to circularly or horizontally polarized intermittent or continuous power-frequency magnetic fields. No significant effects of exposure on night-time serum melatonin levels were found (Crasson et al., 2001; Graham et al., 1996; Graham, Cook & Riffle,

1997; Kurokawa et al., 2003a; Selmaoui, Lambrozo & Touitou, 1996; Warman et al., 2003a). Other studies, using the excretion of the major urinary metabolite of melatonin as a surrogate measures of serum melatonin, also found no effect (Åkerstedt et al., 1999; Crasson et al., 2001; Graham et al., 2001a; Graham et al., 2001b; Selmaoui, Lambrozo & Touitou, 1996). The use of the urinary excretion data complicates interpretation, however, since information regarding any possible phase shift in melatonin production is lost. Griefahn (2001; 2002) found no effect of exposure to 16.7 Hz magnetic fields on hourly saliva melatonin concentration.

Some positive effects have been reported, but these have generally not proved consistent. An initial report (Graham et al., 1996) of a magnetic field-induced reduction of night-time serum melatonin levels in volunteers with low basal melatonin levels was not confirmed using a larger number of volunteers. It is possible that the initial positive findings were due to chance with a relatively small number of subjects. However, the results of a study investigating the effects of night-time exposure to 60 Hz fields for four nights (Graham et al., 2000b) suggested a weak cumulative effect of exposure. Exposed subjects showed more intra-individual variability in the overnight levels of excretion of melatonin or its major metabolite on night 4, although there was no overall effect on levels of melatonin.

Wood et al. (1998) exposed or sham exposed male subjects to an intermittent, circularly-polarised, power-frequency magnetic field at various times during the dusk or night and measured the effect on night-time serum melatonin levels. The results indicated that exposure prior to the night-time rise in serum melatonin may have delayed the onset of the rise by about half an hour and may have reduced peak levels, possibly in a sensitive sub-group of the study population. However, exposure categorisation was made post-hoc (Wood et al., 1998) and the result can only be considered to be exploratory.

6.1.1.2 Residential and occupational studies

Several studies of responses have been carried out in people in residential or occupational situations. These are naturally more realistic than laboratory studies but suffer from diminished control of possible confounding factors, such as differences in lifestyle (Warman et al., 2003b). With regard to domestic exposure, one study (Wilson et al., 1990) has examined the possible effects on volunteers exposed at home to pulsed EMFs generated by mains or DC-powered electric blankets over a 6–10 week period. Overall, no effect of exposure was seen on the urinary excretion of the major urinary metabolite of melatonin (aMT6s). However, transient increases in night-time excretion were seen in the periods following the onset of a period of electric blanket use and following the cessation of the period of electric blanket use in seven of 28 users of one type of electric blanket. This observation may, however, be rather weak given the lack of correspondence of the effect with field condition and the fact that responsiveness was only identified following the separate analysis of the excretion data from each of 42 volunteers, of

which some analyses may have turned out positive by chance (Hong et al., 2001). In contrast, Hong et al. (2001) found no significant field dependent effects on melatonin rhythms in nine men following 11 weeks of night-time exposure. In this study, the urinary excretion of aMT6s was followed in five urine samples collected each day. This study too, however, exercised very little control over possible confounding by environmental and lifestyle factors.

Several more recent studies relating to residential exposure have been carried out. Davis et al. (2001) reported lower nocturnal levels of melatonin, measured as the excretion of aMT6s, in women with a history of breast cancer to be associated with higher bedroom magnetic field levels, once adjustment had been made for hours of daylight, age, body mass index, current alcohol consumption and the use of certain medications. Levallois et al. (2001) found no relation of night-time excretion of aMT6s to proximity of the residence to power lines or to EMF exposure. There were, however, significantly stronger relations to age and obesity (out of five variables for which the authors investigated effect modification) in women who lived close to power lines than in those who lived more distantly. In a general review of all these studies, IARC (2002) concluded that it was difficult to distinguish between the effects of magnetic fields and those of other environmental factors. In a later study, Youngstedt et al. (2002) found no significant associations between several measures of magnetic field exposure in bed (but not elsewhere) and various measures of the urinary excretion of aMT6s in 242 adults, mostly women, aged 50–81.

A number of other studies have examined urinary metabolite excretion in occupationally exposed workers. For railway workers, Pfluger & Minder (1996) reported that early evening aMT6s excretion (taken as an index of daytime serum melatonin levels) but not early morning excretion was decreased in exposed workers. However, the authors noted that the effects of differences in daylight exposure, which suppresses night-time melatonin, could not be excluded. In a study of electric utility workers, Burch et al. (1998; 1999) found no overall effect of exposure on night-time aMT6s excretion (taken as an index of night-time melatonin levels) when considering mean levels of exposure. The authors did find lower levels of night-time excretion in individuals exposed to temporally more stable magnetic fields, raising some questions as to the interpretation of these data. A reduction in melatonin levels was found to be associated with working near 3-phase conductors and not near 1-phase conductors, indicating a possible role of field polarisation (Burch et al., 2000). Burch, Reif & Jost (1999) also found that reduction of aMT6s excretion was associated with high geomagnetic activity. Juutilainen et al. (2000) found that occupational exposure to magnetic fields produced by sewing machines did not affect the ratio of Friday morning/Monday morning levels of aMT6s excretion, suggesting that weekends without workplace exposure did not change melatonin response. Average Thursday night excretion (Friday morning sample) was lower in exposed compared to control workers.

In a study of a further group of male electrical utility workers, Burch et al. (2002) investigated nocturnal excretion of aMT6s in men with high compared with low or medium workplace 60-Hz exposure. After adjusting for light exposure at work, reduced melatonin levels were found within men with high cellular phone use; the effect was not present in those with medium or no such phone use. Touitou et al. (2003) found no effect on serum melatonin levels or the overnight excretion of urinary aMT6s in workers at a high voltage substations chronically exposed to 50 Hz magnetic fields compared to white collar workers from the same company.

A preliminary study by Arnetz & Berg (1996) of daytime serum melatonin levels in visual display units (VDU) workers (sex not given) exposed to ELF and other frequency electromagnetic fields (values not given) reported a slightly larger decrease during VDU work compared to leisure time. The biological significance of this small daytime effect is not at all clear, given that serum melatonin peaks during the night.

In a study by Lonne-Rahm et al. (2000), 24 patients with electromagnetic hypersensitivity and 12 controls were exposed to a combination of stress situations and electric and magnetic fields from a VDU. Blood samples were drawn for circulating levels of stress-related hormones (melatonin, prolactin, adrenocorticotrophic hormone, neuropeptide Y and growth hormone). In double-blind tests, none of these parameters responded to the fields, neither alone nor in combination with stress levels.

Table 46 summarizes the human melatonin studies.

6.1.2 Pituitary and other hormones

Few studies of EMF effects on hormones of the pituitary and other endocrine glands have been carried out. Principal pituitary hormones investigated in EMF studies include several hormones involved in growth and body physiology, particularly thyroid-stimulating hormone (TSH) which controls the function of the thyroid gland and the release of thyroxin; adrenocorticotropic hormone (ACTH), which regulates the function of the adrenal cortex and particularly the release of cortisol; and growth hormone (GH), which affects body growth. Hormones released by the pituitary which have important sexual and reproductive functions have also been studied, particularly follicle stimulating hormone (FSH), luteinising hormone (LH) and prolactin. Both FSH and LH influence the function of the testis and the release of testosterone.

Three laboratory studies have investigated the possible effects of acute exposure to power-frequency magnetic fields and power-frequency electric and magnetic fields on TSH, thyroxin, GH, cortisol, FSH, LH and testosterone in men (Maresh et al., 1988; Selmaoui, Lambrozo & Touitou, 1997) and GH, cortisol and prolactin in men and women (Åkerstedt et al., 1999). Overall, no effects were found.

An occupational study (Gamberale et al., 1989) of linesmen working on “live” or “dead” 400-kV power lines found no effect of combined

Table 46. Human melatonin studies

Endpoint	Exposure	Response	Comment	Authors
ELF magnetic fields				
Laboratory studies				
Night-time serum melatonin levels	60 Hz 1 or 20 μT, intermittent 8 h at night	No effect. Possible effect on low melatonin subjects not replicated in larger study.	Well described and well planned double blind study.	Graham et al., 1996
Night-time serum melatonin levels	60 Hz 20 μT, continuous 8 h at night	No effect.	Well described and well planned double blind study.	Graham, Cook & Riffle, 1997
Night-time serum melatonin levels and excretion of its major urinary metabolite (aMT6s).	50 Hz 10 μT, continuous or intermittent 9 h at night	No effect.	Well described and well planned double blind study.	Selmaoui, Lambrozo & Touitou, 1996
Night-time serum melatonin levels	50 Hz 20 μT, sinusoidal or square wave field, intermittent 1.5–4 h at night	Possible delay and reduction of night-time melatonin levels in sub-group.	Double blind study; incomplete volunteer participation.	Wood et al., 1998
Night-time serum melatonin levels	50 Hz 1 μT during sleep (24.00 to 08.00 h)	No effect.	Double blind study.	Åkerstedt et al., 1999
Night-time serum melatonin levels and excretion of aMT6s.	60 Hz 28.3 μT, continuous 8 h at night	No effect.	Well described and well planned double blind study.	Graham et al., 2000b
Night-time serum melatonin levels and excretion of aMT6s	50 Hz 100 μT, continuous or intermittent 30 min	No effect.	Well described and well planned double blind study.	Crasson et al., 2001

Table 46. Continued

Night-time serum melatonin levels in women	60 Hz 28.3 μT, intermittent 8 h at night	No effect.	Well described and well planned double blind study.	Graham et al., 2001a
Night-time serum melatonin levels and excretion of aMT6s	60 Hz 127 μT, continuous or intermittent 8 h at night	No effect.	Well described and well planned double blind study.	Graham et al., 2001b
Night-time serum melatonin levels and excretion of aMT6s	60 Hz 28.3 μT, continuous 8 h at night	No effect.	Well described and well planned double blind study.	Graham et al., 2001c
Salivary melatonin levels	16.7 Hz 200 μT 6 h at night	No effect.	Well described and well planned double blind study.	Griefahn et al., 2001
Salivary melatonin levels	16.7 Hz 200 μT 6 h at night	No effect.	Well described and well planned double blind study.	Griefahn et al., 2002
Night-time serum melatonin levels	50 Hz 20 μT, linearly polarised 8 h at night	No effect.	Well described and well planned double blind study.	Kurokawa et al., 2003a
Night-time serum melatonin levels	50 Hz 200 or 300 μT 2 h at night across rising phase of melatonin secretion	No effect.	Well described and well planned double blind study.	Warman et al., 2003a
ELF electric and magnetic fields				
Domestic occupational studies				
Early morning excretion of urinary aMT6s	60 Hz EMFs generated by pulsed AC or DC current supply to electric blankets 7–10 weeks at night	No overall effect; transient increases in 7/28 users of one type of blanket.	Realistic, but concomitant lack of control over lifestyle etc.	Wilson et al., 1990

Table 46. Continued

Urinary excretion of aMT6s collected 5 times per day	50 Hz ~1–8 μT, electric 'sheet' over the body 11 weeks at night	No effect.	The only restriction on each subject's usual daily activities were avoiding overeating and strenuous exercise.	Hong et al., 2001
Morning and evening urinary excretion of aMT6s in railway workers.	16.7 Hz approximately 20 μT mean value in engine drivers	Decreased evening 6-aMT6s levels but no effect on morning levels. No dose-response effect.	Subjects acted as own controls; samples collected early autumn; fully described protocol.	Pfluger & Minder, 1996
Night-time and early morning urinary excretion of aMT6s in electric utility workers	60 Hz ~0.1–0.2 μT 24 hr at work, home and during sleep	No overall effect with exposure. Temporally more stable fields at home (using calculated index) associated with reduced nocturnal melatonin.	Well described study; some adjustment for age, month of participation and light exposure.	Burch et al., 1998
Post work urinary excretion of aMT6s electric utility workers	60 Hz occupational exposure over a week	No overall effect. Reduction in aMT6s excretion in workers exposed to more stable fields during work.	Significant interaction with occupational light exposure.	Burch et al., 1999
Night-time urinary excretion of aMT6s in electric utility workers	60 Hz occupational exposure to magnetic fields	Exposure-related reduction in aMT6s excretion in workers exposed in substations or 3 phase environments for > 2 h.	Adjusted for workplace light exposure.	Burch et al., 2000
Night-time urinary excretion of aMT6s in garment workers	50 Hz occupational exposure to magnetic fields	Average aMT6s excretion lower in exposed workers compared to office workers.	No difference in Friday to Monday levels	Juutilainen et al., 2000
Night-time urinary excretion of aMT6s	50 Hz proximity to power lines and/or exposure to domestic EMFs	No overall effect. Significantly stronger association with age and obesity in women living closer to power lines.	Adjusted for confounders.	Levallois et al., 2001

Table 46. Continued

Night-time urinary excretion of aMT6s	60 Hz domestic exposure to magnetic fields	Borderline association with one measure of exposure in a subgroup of women.	Significant association with day length.	Davis et al., 2001
Night-time urinary excretion of aMT6s in electric utility workers	60 Hz occupational exposure to magnetic fields	Exposure-related reduction in aMT6s excretion in highly exposed workers associated with mobile phone use.	Not present in workers with low or medium phone use.	Burch et al., 2002
24 hr urinary excretion of aMT6s	60 Hz domestic exposure to magnetic fields measured in the bedroom only	No significant associations between exposure and excretion.	Potential confounders such as lighting, age and medication taken into account.	Youngstedt et al., 2002
Serum melatonin levels and urinary excretion of aMT6s in high-voltage sub-station workers	Geometric mean fields of 0.1–2.6 μT chronic occupational exposure (1–20 y)	No effect compared to levels in white-collar workers.	Considerable care taken to avoid some confounders, e.g. study participants all non-smokers.	Touitou et al., 2003
ELF and VLF electric and magnetic fields				
Occupational studies				
Morning and afternoon serum melatonin levels in VDU workers during one working and one leisure day.	Exposure details not given	Decrease in serum melatonin during the day was statistically significant at work (-0.9 ng/l) but not leisure (-0.8 ng/l).	Samples collected Oct – Feb. Experimental protocol briefly described. No measured fields; no control over lifestyle etc.	Arnetz & Berg, 1996
Circulating levels of stress-related hormones (melatonin, prolactin, ACTH, neuropeptide Y and growth hormone)	24 patients with electromagnetic hypersensitivity and 12 controls electric and magnetic fields from a VDU	No effect.	Double blind study.	Lonne-Rahm et al., 2000

electric and magnetic field exposure over a working day on daytime levels of serum TSH, cortisol, FSH, prolactin, LH and testosterone. A preliminary study (Arnetz & Berg, 1996) of VDU workers (sex not specified) exposed to ELF electric and magnetic fields (exposure not given) reported elevated ACTH levels at work compared to leisure time; an effect, as the authors note, which is probably attributable to work-related factors other than EMFs.

The studies on the effects of ELF on the human pituitary and endocrine system are summarized in Table 47.

Table 47. Human pituitary and other endocrine studies

Endpoint	Exposure	Response	Comment	Authors
ELF magnetic fields				
Laboratory studies				
Night-time serum levels of TSH, thyroxin, cortisol, FSH and LH in young men	50 Hz 10 μT, continuous or intermittent overnight from 23.00 to 08.00 h	No differences between exposed and sham-exposed.	Well designed, double-blind study.	Selmaoui, Lambrozo & Touitou, 1997
Night-time levels of GH, cortisol and prolactin in men and women	50 Hz 1 μT during sleep (24.00 to 08.00 h)	No effect.	Double blind study.	Åkerstedt et al., 1999
ELF electric and magnetic fields				
Laboratory study				
GH, cortisol and testosterone in young men	60 Hz 9 kV m^{-1} and 20 μT 2 h following 45 min rest	No effect.	Double-blind study.	Maresh et al., 1988
Occupational studies				
Day-time serum TSH, cortisol, FSH, prolactin, LH, and testosterone in linesmen working on “live” and “dead” 400 kV power lines	50 Hz 2.8 kV m^{-1} and 23.3 μT 4.5 h during working day	No effect.	Counterbalanced presentation of “live” and “dead” power lines.	Gamberale et al., 1989
Morning and afternoon serum ACTH levels in VDU workers during one working and one leisure day	Exposure details not given.	Increase in serum ACTH during the day was statistically significant at work (0.6 pmol/l). but not leisure (0.1 pmol/l)	Samples collected Oct – Feb. Experimental protocol briefly described. No measured fields; no control over lifestyle etc.	Arnetz & Berg, 1996

6.2 Animal studies

A large number of studies have been carried out investigating the effects of EMF on circulating melatonin levels in animals, because of the possible links between EMF and breast cancer. The impact of melatonin on reproduction is particularly pronounced in seasonally breeding animals, where the effect varies depending on the length of gestation in order to ensure that the offspring are born in late spring when food is plentiful. Thus, for melatonin, the studies have been subdivided into those on laboratory rodents, which have short gestational periods and seasonally breeding animals and primates, which are more closely related to humans.

6.2.1 Melatonin

As indicated above, Stevens (1987) first suggested that chronic exposure to electric fields may reduce melatonin secretion by the pineal gland and increase the risk of breast cancer. This followed reports particularly by Wilson et al. (1981) of a significant overall reduction in pineal melatonin in rats chronically exposed to 60 Hz electric fields and by Tamarkin et al. (1981) and Shah, Mhatre & Kothari (1984) of increased DMBA-induced mammary carcinogenesis in rats with reduced melatonin levels. However, the significance of these observations for humans is not clearly established.

6.2.1.1 Laboratory rodents

Few studies have been carried out using mice. In a study by Picazo et al. (1998) a significant reduction in the night-time serum melatonin levels of mice exposed up to sexual maturity for four generations to power frequency magnetic fields was observed.

A great many more studies have been carried out using rats. The effects of electric fields were investigated before interest turned predominantly to magnetic fields. Several studies by one group of authors (Reiter et al., 1988; Wilson et al., 1981; Wilson et al., 1983; Wilson, Chess & Anderson, 1986) reported that the exposure to electric fields significantly suppressed pineal melatonin and the activity of the N-acetyl-transferase enzyme (NAT) important in the synthesis of melatonin in the pineal gland. This effect was transient, appearing within three weeks of exposure but recovered within three days following the cessation of exposure. Subsequently, however, the same laboratory (Sasser et al., 1991) reported in an abstract that it was unable to reproduce the E-field-induced reduction in pineal melatonin. Another laboratory (Grota et al., 1994) also reported that exposure to power-frequency electric fields had no effect on pineal melatonin levels or NAT activity, although serum melatonin levels were significantly depressed.

Further work used rats to investigate the effect of exposure to power-frequency magnetic fields. An early study by Martínez-Soriano et al. (1992) was inconclusive because of technical difficulties. A more extensive series of tests has been carried out by Kato et al. (1993; 1994a; 1994b; 1994c; 1994d, summarized in Kato & Shigemitsu, 1997). They studied the effects of exposure to circularly- or linearly-polarised power-frequency mag-

netic fields of up to 250 μT for up to 6 weeks on pineal and serum melatonin levels in male rats. These authors reported that exposure to circularly polarised but not linearly polarised field reduced night-time serum and pineal melatonin levels. However, a major difficulty with the interpretation of many of the studies by this group was that the sham-exposed groups were sometimes treated as a "low dose" exposed groups because they were exposed to stray magnetic fields (of less than 2%) generated by the exposure system. Thus, statistical comparison was sometimes made with historical controls. Such procedures fail to allow for the inter-experimental variability that was reported in replicate studies by Kato & Shigemitsu (1997). Results from four further groups who have investigated magnetic-field effects on serum and pineal melatonin levels in rats (Bakos et al., 1995; Bakos et al., 1997; Bakos et al., 1999; John, Liu & Brown, 1998; Löscher, Mevissen & Lerchl, 1998; Mevissen, Lerchl & Löscher, 1996; Selmaoui & Touitou, 1995; Selmaoui & Touitou, 1999) were inconsistent but mostly negative.

Table 48 summarizes the studies into effects of ELF fields on melatonin in experimental animals.

6.2.1.2 Seasonal breeders

Four different laboratories have investigated the effects of EMF exposure on pineal activity, serum melatonin levels and reproductive development in animals which breed seasonally. A series of studies by Yellon and colleagues (Truong, Smith & Yellon, 1996; Truong & Yellon, 1997; Yellon, 1994; Yellon, 1996; Yellon & Truong, 1998) investigated magnetic field exposure of Djungarian hamsters in which the duration of melatonin secretion during the shortening days of autumn and winter inhibit reproductive activity. These authors reported that a brief exposure to a power-frequency magnetic field 2 h before the onset of darkness reduced and delayed the night-time rise in serum and pineal melatonin. In expanded replicate studies no reduction in melatonin was observed and no effect was seen on reproductive development. In contrast to this work, Niehaus et al. (1997) reported that the chronic exposure of Djungarian hamsters to "rectangular" power-frequency magnetic fields resulted in increased testis cell numbers and night-time levels of serum melatonin. However, the results are not easy to interpret: increased melatonin levels in the Djungarian hamster are usually accompanied by decreased testicular activity. Wilson et al. (1999) investigated the effect of exposure to power-frequency magnetic fields on pineal melatonin levels, serum prolactin levels and testicular and seminal vesicle weights in Djungarian hamsters moved to a "short day" light regime in order to induce sexual regression. Night-time pineal melatonin levels were reduced following acute exposure but this effect diminished with prolonged exposure. In contrast, induced sexual regression, as indicated by the testicular and seminal vesicle weights, seemed to be enhanced rather than diminished by prolonged magnetic field exposure, suggesting a possible stress response.

Table 48. Melatonin studies in laboratory rodents

Endpoint	Exposure	Response	Comment	Authors
ELF electric fields				
Rats				
Night-time pineal melatonin levels and NAT enzyme activity in adult rats	60 Hz 1.7–1.9 kV m^{-1} (not 65 kV m^{-1} due to equipment failure) 20 h per day for 30 days	Reduced pineal melatonin and NAT activity.	Data combined in one experiment because of variability.	Wilson et al., 1981
Night-time pineal melatonin levels and NAT enzyme activity in adult rats	60 Hz 65 kV m^{-1} (39 kV m^{-1} effective) up to 4 weeks	Pineal melatonin and NAT activity reduced within 3 weeks exposure; recovered 3 days after exposure.		Wilson, Chess & Anderson, 1986
Night-time pineal melatonin levels in adult rats	60 Hz 10, 65 or 130 kV m^{-1} during gestation and 23 days postnatally	Night-time peak reduced and delayed in exposed animals.	No simple dose-response relationship.	Reiter et al., 1988
Night-time pineal melatonin levels in adult rats	60 Hz 65 kV m^{-1} 20 h per day for 30 days	No effect on night-time peak pineal melatonin.	Meeting abstract, but included because it attempted to replicate earlier studies from this group.	Sasser et al., 1991
Night-time pineal melatonin and NAT activity and serum melatonin in adult rats	60 Hz 10 or 65 kV m^{-1} 20 h per day for 30 days	No effect on night-time melatonin and NAT; serum melatonin down after 65 kV m^{-1}.	Similar to Wilson et al. 1986.	Grota et al., 1994

Table 48. Continued

ELF magnetic Fields				
Mice				
Serum melatonin levels in 4th gen. male mice	50 Hz 15 μT for 4 generations	Reduced night-time levels.	Experimental procedures not fully described.	Picazo et al., 1998
Rats				
Serum melatonin levels in adult rats	50 Hz 5 mT 30 min during the morning for 1, 3, 7, 15 and 21 days	Serum melatonin reduced on day 15; no values for days 1, 7 or 21.	Technical difficulties; brief description of method.	Martinez et al., 1992
Pineal and serum melatonin levels in adult rats	50 Hz 1, 5, 50 or 250 μT, circularly polarised 6 weeks	Night-time and some daytime reductions in serum and pineal melatonin.	Questionable comparisons to historical controls.	Kato et al., 1993
Serum melatonin levels in adult rats	50 Hz 1 μT, circularly polarised 6 weeks	Night-time melatonin levels reduced, returning to normal within one week.	Comparison to sham exposed.	Kato et al., 1994d
Pineal and serum melatonin levels in adult rats	50 Hz 1 μT, circularly polarised 6 weeks	Night-time pineal and serum levels reduced.	Comparison to sham exposed and historical controls.	Kato et al., 1994c
Serum melatonin levels in adult rats	50 Hz 1 μT, horizontally or vertically polarised 6 weeks	No effect.	Comparison to sham exposed and historical controls.	Kato et al., 1994b

Table 48. Continued

'Antigonadotrophic' effect of melatonin on serum testosterone in adult rats	50 Hz circularly polarised 1, 5, or 50 μT for 6 weeks	No effect.	Comparison with sham exposed.	Kato et al., 1994a
Night-time serum melatonin levels and pineal NAT activity in adult rats	50 Hz 1, 10 or 100 μT 12 h once, or 18 h per day for 30 days	Reduced melatonin and NAT activity after 100 μT (acute) and 10 and 100 μT (chronic).		Selmaoui & Touitou, 1995
Night-time serum melatonin levels and pineal NAT activity in young (9 wks) and aged (23 mos) rats	50 Hz 100 μT 18 h per day for one week	Reduced melatonin and NAT activity in young rats but not old rats.		Selmaoui & Touitou, 1999
Night-time excretion of melatonin urinary metabolite in adult rats	50 Hz 1, 5, 100 or 500 μT 24 h	No significant effects compared to base-line pre-exposure controls.		Bakos et al., 1995; 1997; 1999
Night-time pineal melatonin levels in non-DMBA treated adult rats	50 Hz 10 μT 13 weeks	No effect.	A small part of a larger, well planned mammary tumour study.	Mevissen, Lerchl & Löscher, 1996
Night-time serum melatonin, levels in SD rats	50 Hz 100 μT 1 day, 1, 2, 4, 8 or 13 weeks	No consistent effects on melatonin.	The few positive effects could not be replicated.	Löscher, Mevissen & Lerchl, 1998
Night-time excretion of melatonin urinary metabolite in adult rats	60 Hz 1 mT continuous for 10 days or 6 weeks intermittent for 2 days	No effect.		John, Liu & Brown, 1998

Table 49. Melatonin levels in seasonally breeding animals

Endpoint	Exposure	Response	Comment	Authors
ELF magnetic fields				
Djungarian hamsters				
Night-time pineal and serum melatonin levels	60 Hz 100 µT 15 min, 2 h before dark	Reduced and delayed night-time peak; diminished and absent in 2nd and 3rd replicates.	Considerable variability between replicate studies.	Yellon, 1994
Night-time pineal and serum melatonin levels; adult male reproductive status	60 Hz 100 µT 15 min, 2 h before dark; second study over 3-week period	Reduced and delayed night-time peak; diminished in 2nd replicate study; no effect on melatonin-induced sexual atrophy.	Considerable variability between replicate studies.	Yellon, 1996
Night-time pineal and serum melatonin levels; adult male reproductive status	60 Hz 100 µT 15 min, 2 h before dark for 3 weeks	No effect on pineal or serum melatonin; no effect on melatonin-induced sexual atrophy.	Second part of above paper.	Yellon, 1996
Night-time pineal and serum melatonin levels; male puberty, assessed by testes weight	60 Hz 100 µT 15 min, 2 h before dark from 16–25 days of age	Reduced and delayed night-time peak; absent in 2nd replicate study. No effect on development of puberty.	Considerable variability in melatonin levels between replicate studies.	Truong, Smith & Yellon, 1996
Night-time pineal and serum melatonin levels	60 Hz 10 or 100 µT (continuous) or 100 µT (intermittent) 15 or 60 min before or after onset of dark period	No effect.		Truong & Yellon, 1997
Night-time rise in pineal and serum melatonin levels; testes weight	60 Hz 100 µT 15 min per day, in complete darkness, for up to 21 days	No effect, even in absence of photoperiodic cue.		Yellon & Truong, 1998
Night-time pineal and serum melatonin levels; testis cell numbers	50 Hz 450 µT (peak) sinusoidal or 360 µT (peak) rectangular 56 days	Increased cell number and night-time serum melatonin levels after rectangular field exposure.	Animals on long day schedule; difficult interpretation.	Niehaus et al., 1997

Table 49. Continued				
Night-time pineal melatonin levels, and testis and seminal vesicle weights in short day (regressed) animals	60 Hz 100 or 500 T, continuous and/or intermittent starting 30 min or 2 h before onset of darkness; for up to 3 h up to 42 days	Reduced pineal melatonin after 15 min exposure; reduced gonad weight but not melatonin after 42 day exposure.	Authors suggest a stress-like effect.	Wilson et al., 1999
ELF electric and magnetic fields				
Suffolk sheep				
Night-time serum melatonin levels and female puberty, detected by rise in serum progesterone	60 Hz 6 kV m^{-1} and 4 μT, generated by overhead power lines 10 months	No effect of EMFs; strong seasonal effects.	Two replicate studies; open air conditions.	Lee et al., 1993; 1995

The third set of studies of EMF effects on seasonal breeders concerned Suffolk sheep; these have a long gestational period and become reproductively active in the autumn, as day length shortens. In two replicate studies (Lee et al., 1993; 1995), Suffolk lambs were exposed outdoors to the magnetic fields generated by overhead transmission lines for about 10 months. The authors reported no effect of exposure on serum melatonin levels or on the onset of puberty.

Table 49 summarizes the studies into effects of ELF fields on melatonin in seasonal breeders.

6.2.1.3 Non-human primates

Non-human primates are close, in evolutionary terms, to humans and share many similar characteristics. Rogers et al. (1995b; 1995a) studied responses in male baboons. Generally, no effect on night-time serum melatonin levels was seen (Rogers et al., 1995a). However, a preliminary study (Rogers et al., 1995b), based on data from only two baboons, reported that exposure to an irregular, intermittent sequence of combined electric and magnetic fields in which switching transients were generated, resulted in a marked suppression of the night-time rise in melatonin. These studies are summarized in Table 50.

Table 50. Melatonin levels in non-human primates

Endpoint	Exposure	Response	Comment	Authors
ELF electric and magnetic fields				
Night-time serum melatonin level in baboons	60 Hz 6 kV m^{-1} and 50 μT, 6 weeks 30 kV m^{-1} and 100 μT, 3 weeks	No effect.		Rogers et al., 1995a
Night-time serum melatonin level in baboons	60 Hz 6 kV m^{-1} and 50 μT or 30 kV m^{-1} and 100 μT irregular and intermittent sequence for 3 weeks	Reduced serum melatonin levels.	Preliminary study on two baboons.	Rogers et al., 1995b

6.2.2 The pituitary and other hormones

The pituitary gland, like the pineal gland, is intimately connected to the nervous system. It releases hormones into the blood stream either from specialised neurosecretory cells originating in the hypothalamus region of the brain, or from the cells in the pituitary whose function is under the control of such neurosecretory cells via factors released into a specialised hypothalamic-pituitary portal system. The main pituitary hormones investigated in EMF studies include several involved in growth and body physiology, particularly thyroid-stimulating hormone (TSH), which controls the function of the thyroid gland, adrenocorticotrophic hormone (ACTH), which regulates the function of the adrenal cortex, and growth hormone (GH), which affects body growth, and hormones which have important sexual and reproductive functions, particularly follicle stimulating hormone (FSH), luteinising hormone (LH) and prolactin (or luteotrophic hormone).

6.2.2.1 Pituitary-adrenal effects

The possibility that EMF might act as a stressor has been investigated in a number of studies that have examined possible effects of EMF exposure on the release of hormones involved in stress responses, particularly ACTH and cortisol and/or corticosterone released from the adrenal cortex. For ELF electric fields, Hackman & Graves (1981) reported a transient (minutes) increase in serum corticosterone levels in young rats immediately following the onset of exposure to levels greatly in excess of the electric field perception threshold; however, exposure for longer durations had no effect. A lack of effect of prolonged exposure to ELF fields has been reported by other authors on ACTH levels (Portet & Cabanes, 1988) and on cortisol/corticosterone levels (Burchard et al., 1996; Free et al., 1981; Portet & Cabanes, 1988; Quinlan et al., 1985; Thompson et al., 1995). Two studies, both limited by small numbers of animals, reported positive effects of exposure to power frequency electric (de Bruyn & de Jager, 1994) and magnetic (Picazo et al.,

1996) fields on the diurnal rhythmicity of cortisol/corticosterone levels in mice.

6.2.2.2 Other endocrine studies

Studies of TSH levels and of the thyroid hormones (T3 and T4), which have a major influence on metabolic functions, have been carried out in three studies. No effect on serum TSH levels was found (Free et al., 1981; Portet & Cabanes, 1988; Quinlan et al., 1985); in addition, no effects were reported on serum thyroxin (T3 and T4) levels in rabbits (Portet & Cabanes, 1988), but T3 levels were reduced in rats (Portet and Cabanes, 1988). Growth hormone levels were reported to increase in rats intermittently exposed for 3 h (Quinlan et al., 1985), but were reported to be unaffected following prolonged (3–18 weeks) electric-field exposure at the same level (Free et al., 1981).

Similarly negative or inconsistent data exist concerning possible effects of ELF field exposure on hormones associated with reproduction and sexual development. Prolactin, FSH, LH and testosterone levels in rats were reported unaffected by exposure to power-frequency electric fields (Margonato et al., 1993; Quinlan et al., 1985); similar results for prolactin were reported by Free et al. (1981), but variable effects on FSH levels were seen during development and serum testosterone levels were reported to be decreased in adults. In contrast, an increase in serum prolactin levels was reported in Djungarian hamsters briefly exposed to ELF magnetic fields (Wilson et al., 1999), and an increase in serum progesterone in cattle exposed to combined electric and magnetic fields (Burchard et al., 1996). In a subsequent study, Burchard et al. (2004) found that continuous exposure to an electric field for 4 weeks had no effect on circulating levels of progesterone, prolactin and insulin-like growth factor.

Table 51 summarizes the studies investigating the effects of ELF fields on hormone levels in experimental animals.

6.3 In vitro studies

In vitro studies of exposure to EMFs divide into two types of investigation: effects on the production of melatonin by cells from the pineal gland; and effects on the action of melatonin on cells. Some studies have investigated the effects of static magnetic fields, but these have not been reviewed here.

Table 51. The pituitary and other hormones

Endpoint	Exposure	Response	Comment	Authors
ELF electric fields				
Mice				
Serum levels of corticosterone in adult male mice	60 Hz 10 kV m^{-1} 22 h per day for 6 generations	Elevated daytime but not night-time levels compared to controls.	Small numbers and variable daytime data.	de Bruyn & de Jager, 1994
Rats				
Serum levels of TSH, GH, FSH, prolactin, LH, corticosterone and testosterone in young and adult male rats	60 Hz 100 kV m^{-1} (unadjusted) 20 h per day for 30 and/or 120 days (adults) or from 20–56 days of age (young)	Testosterone levels significantly decreased after 120 days; no other consistent effects in adults; significant changes in FSH levels in young rats.	Variable changes in hormone plasma concentration during development.	Free et al., 1981
Serum corticosterone levels in adult male mice.	60 Hz 25 or 50 kV m^{-1} 5 min per day up to 42 days	Transient increase in serum levels at onset of exposure.	Positive control group; incomplete presentation of data.	Hackman & Graves, 1981
Serum levels of TSH, GH, prolactin and corticosterone in adult male rats	60 Hz 100 kV m^{-1}, continuous or intermittent 1 or 3 h	Increase in GH levels in rats exposed intermittent for 3 h, but not 1 h; no other effects.	Care taken to avoid extraneous confounding factors.	Quinlan et al., 1985
Serum levels of TSH, ACTH, thyroxin ($T_3 + T_4$) and corticosterone in young male rats	50 Hz 50 kV m^{-1} 8 h per day for 28 days	No significant effects except T_3 (but not T_4) reduced.		Portet & Cabanes, 1988
Serum levels of FSH, LH and testosterone in adult male rats	50 Hz 25 or 100 kV m^{-1} 8 h per day for up to 38 weeks	No significant effects.	Variable data.	Margonato et al., 1993
Rabbits				
Serum levels of GH, ACTH, thyroxin ($T_3 + T_4$) and corticosterone (and cortisol) in 6 week old rabbits	50 Hz 50 kV m^{-1} 16 h per day from last 2 weeks of gestation to 6 weeks after birth	No significant effects.		Portet & Cabanes, 1988

Table 51. Continued				
ELF magnetic fields				
Mice				
Serum cortisol levels in adult male mice	50 Hz 15 µT 14 weeks prior to conception, gestation and 10 weeks post gestation	Loss of diurnal rhythmicity; daytime levels fell and night-time levels rose.	Small numbers per group.	Picazo et al., 1996
Djungarian hamsters				
Serum levels of prolactin in adult male Djungarian hamsters on long or short days	60 Hz 100 µT 15 min before dark 100 µT, intermittent / continuous 45 min per day before dark for 16–42 days	Prolactin levels elevated 4 h after dark following acute but not chronic exposure.	Incomplete presentation of prolactin data.	Wilson et al., 1999

6.3.1 Effects on melatonin production in vitro

There are only a few studies that have investigated the effect of magnetic fields on melatonin production in vitro. All used rodents as the source of pineal gland cells but there are marked differences in their methodology. Most used power frequencies (50 or 60 Hz), but the field strength (50 µT–1 mT) and duration (1–12 h) differ between the studies. Direct measures include melatonin content or melatonin release from cells. Indirect measures can be made from the activity of N-acetyltransferase (NAT), an enzyme involved in the synthesis of melatonin, or of hydroxyindole-O-methyltransferase (HIOMT), an enzyme responsible for methylation and hence release of melatonin from the cells. Most of the studies have stimulated pharmacologically the production of melatonin in the isolated glands by the addition of noradrenaline (NA) or isoproterenol.

Lerchl et al. (1991) exposed pineal glands from young rats, removed during the day light period, to a combination of a static field (44 µT) and a low frequency magnetic field (44 µT at 33.7 Hz), the theoretical conditions for cyclotron resonance of the calcium ion. Exposure caused a reduction in NAT activity, melatonin production and melatonin release into the culture medium. Rosen, Barber & Lyle (1998) also used pineal glands from the rat, but this study was different to the other studies in that the pineal gland was separated into individual cells. The overall result was that magnetic field exposure caused a statistically significant 46% reduction in stimulated melatonin release. Chacon (2000) used rat pineal glands to study NAT activity. The enzyme activity decreased by approximately 20% after 1 h exposure to the highest field strength tested (1000 µT) but was not significantly altered by field strengths of 10 or 100 µT. The interpretation of the

result may be complicated by the removal of the pineal gland during the rats' dark period, which may have had an effect on melatonin synthesis and a confounding effect on the result.

A study by Brendel, Niehaus & Lerchl (2000) used pineal glands from the Djungarian hamster. It also differed from the previous studies in that the glands were maintained in a flow-system, so that changes of melatonin released from the glands could be monitored throughout the duration of the experiment. The experimental protocol appears to have been well-designed with random allocation of exposure or sham to identical exposure systems and the experiments run blind. The authors concluded that EMF inhibited melatonin production in both the 50 Hz and 16.67 Hz experiments. However there is only one time point in one of four experiments that the melatonin released is statistically different from the sham exposed. Similarly, a study by Tripp, Warman & Arendt (2003) used a flow system to detect changes of melatonin release during the course of the exposure. The exposure was for 4 h to a circularly polarised magnetic fields at 500 μT, 50 Hz. Samples were taken every 30 min; the process used remote collection to avoid potential artefacts involved in manual collection. The glands were not stimulated pharmacologically and no field-dependent changes in melatonin release were detected.

Lewy, Massot & Touitou (2003) used rat pineal glands isolated in the morning and hence during the 12 h light period. The glands were exposed for 4 h to a 50 Hz magnetic field at 1 mT. The activity of enzymes NAT and HIOMT was measured, as well as the release of melatonin into the incubation liquid. In contrast to many other studies, field exposure given simultaneously with NA or 30 min prior to NA administration caused a significant increase (approximately 50%) in melatonin release. There was no change in melatonin release due to field exposure in glands that had not been stimulated by NA.

6.3.2 Effects on the action of melatonin in vitro

The main interest in this area was caused by the claim that exposure to magnetic fields can block the inhibitory effect of melatonin on growth of breast cancer cells. The original work was reported by Liburdy et al. (1993) in a study using a human oestrogen-responsive breast cancer cell line (MCF-7). They found that the proliferation of MCF-7 cells can be slowed by the addition of physiological concentrations of melatonin (1 nM). However, if the cells are simultaneously exposed to a 60 Hz, 1.2 μT magnetic field, then the effect of melatonin on the rate of proliferation is reduced. The effects are fairly small and can only been seen after 7 days in culture. They suggested that the magnetic field disrupted either the ligand/receptor interaction or the subsequent signalling pathway. The authors found no effect at a magnetic field strength of 0.2 μT and suggested a threshold between 0.2 μT and 1.2 μT. No effect was seen using field exposure alone. A similar effect of a 60 Hz field was reported by Harland & Liburdy (1997) but using tamoxifen (100 nM) rather than melatonin to bring about the initial inhibition. The effect has been reported in other cell lines, namely a second breast cancer

cell line, T47D, (Harland, Levine & Liburdy, 1998) and a human glioma cell line 5F757 (Afzal, Levine & Liburdy, 1998). However, as previously noted (AGNIR, 2001b; NIEHS, 1998), the effect seen in the initial study (Liburdy et al., 1993) was small (10–20 % growth over 7 days) and some concern was noted regarding the robustness of the effect.

Blackman, Benane & House (2001) set out to replicate these findings, using the MCF-7 cells supplied by Liburdy, but with a modified and improved experimental protocol. Melatonin caused a significant 17% inhibition of MCF-7 growth ($p < 0.001$), even though the standard errors of the estimated growth statistics showed considerable overlap. This reported effect was abolished by exposure to a 60 Hz magnetic field at 1.2 μT, confirming the results of Liburdy et al. (1993). In addition, tamoxifen caused a 25% inhibition in cell numbers, which was reduced to a 13% inhibition by exposure to a 60 Hz magnetic field at 1.2 μT. This result confirmed the results reported by Harland & Liburdy (1997), in which a 40% inhibition was reduced to 25% by EMF exposure. A later study by Ishido (2001) exposed MCF-7 cells (supplied by Liburdy) to 0, 1.2 or 100 μT at 50 Hz for 7 days. Melatonin at concentrations of 10^{-9} M or higher induced inhibition of intracellular cyclic AMP which was blocked by exposure to a 50 Hz field at 100 μT. Similarly DNA synthesis, which was inhibited by 10^{-11} M melatonin levels, was partially released by exposure at 1.2 μT.

However, although the MCF-7 cell line has undoubtedly provided a useful model to investigate effects on isolated breast cancer cells it is only one possible model in cells that have been separated from their natural environment and therefore its implication for breast cancer in general is limited. The cell line is rather heterogeneous; different subclones show different growth characteristics (e.g. Luben & Morgan, 1998; Morris et al., 1998) raising the possibility that the effects were specific to individual subclone phenotypes. The effects of stronger magnetic fields were studied by Leman et al. (2001) in three breast cancer cell lines that were reported to have different metastatic capabilities: MDA-MB-435 cells, which were considered to be highly metastatic, MDA-MB-231 cells which were considered to be weakly metastatic, and MCF-7 cells, which were considered as non-metastatic. Only the weakly and non-metastatic cells responded to melatonin and optimum inhibition was achieved at 1mM concentration of melatonin (a million-fold higher than used in the Liburdy study). Exposure for 1 h to a pulsed field at 300 μT repeated for 3 days had no effect on growth in either cell line.

The in vitro studies into the effects of ELF magnetic fields on melatonin are summarized in Table 52.

Table 52. Magnetic field effects on melatonin

Endpoint	Exposure	Response	Comment	Authors
Effects on melatonin production in vitro				
NA stimulation of melatonin production and release from rat pineal gland	Static field and 33.7 Hz, 44 μT 2.5 h	Reduced production and release.	Opposite to expected effect of calcium ions.	Lerchl et al., 1991
NA stimulation of melatonin release from rat pineal cells	60 Hz 50 μT 12 h	Reduced release.		Rosen, Barber & Lyle, 1998
NAT activity in rat pineal glands	50 Hz 10, 100 μT or 1 mT 1 h	Decreased NAT activity at the highest exposure level only.		Chacon, 2000
Isoproterenol stimulation of melatonin production in Djungarian hamster pineal gland	50 Hz or 16.7 Hz 86 μT 8 h	Melatonin production reduced.	Continuous flow system used allowing temporal resolution of any effect.	Brendel, Niehaus & Lerchl, 2000
Melatonin release from rat pineal gland	50 Hz 0.5 mT 4 h	No effect on melatonin release.	Continuous flow system used allowing temporal resolution of any effect.	Tripp, Warman & Arendt, 2003
NA stimulated melatonin release from rat pineal gland.	50 Hz 1 mT 4 h	Melatonin release increase.		Lewy, Massot & Touitou, 2003
Effects on cell responses to melatonin or tamoxifen in vitro				
Melatonin inhibition of MCF-7 cell growth	60 Hz 1.2 μT 7 days	EMF exposure reduced growth inhibition.	Small (10–20%) effect.	Liburdy et al., 1993
Tamoxifen inhibition of MCF-7 cell growth	60 Hz 1.2 μT 7 days	EMF exposure reduced growth inhibition.		Harland & Liburdy, 1997
Melatonin or Tamoxifen inhibition of MCF-7 cell growth	60 Hz 1.2 μT 7 days	EMF exposure reduced growth inhibition by melatonin and tamoxifen.	Standard errors on growth statistics show considerable overlap.	Blackman, Benane & House, 2001
Melatonin inhibition of cAMP and DNA synthesis in MCF-7 cells	50 Hz 1.2 or 100 μT 7 days	Reduction of melatonin induced inhibition.		Ishido, 2001

Table 52. Continued			
Melatonin inhibition of growth of 3 breast cancer cell lines including MCF-7	2 Hz pulsed field; pulse width 20 ms 0.3 mT 1 h per day for 3 days	No effect on cell growth.	Leman et al., 2001

6.4 Conclusions

The results of volunteer studies as well as residential and occupational studies suggests that the neuroendocrine system is not adversely affected by exposure to power-frequency electric and/or magnetic fields. This applies particularly to the circulating levels of specific hormones of the neuroendocrine system, including melatonin, released by the pineal gland, and a number of hormones involved in the control of body metabolism and physiology, released by the pituitary gland. Subtle differences were sometimes observed in the timing of melatonin release or associated with certain characteristics of exposure, but these results were not consistent. It is very difficult to eliminate possible confounding by a variety of environmental and lifestyle factors that might also affect hormone levels. Most laboratory studies of the effects of ELF exposure on night-time melatonin levels in volunteers found no effect when care was taken to control possible confounding.

From the large number of animal studies investigating power-frequency EMF effects on rat pineal and serum melatonin levels, some reported that exposure resulted in night-time suppression of melatonin. The changes in melatonin levels first observed in early studies of electric-field exposures up to 100 kV m^{-1} could not be replicated. The findings from a series of more recent studies which showed that circularly-polarised magnetic fields suppressed night-time melatonin levels were weakened by inappropriate comparisons between exposed animals and historical controls. The data from other magnetic fields experiments in laboratory rodents, covering intensity levels over three orders of magnitude from a few microtesla to 5 mT, were equivocal, with some results showing depression of melatonin but others showing no change. In seasonally breeding animals, the evidence for an effect of exposure to power-frequency fields on melatonin levels and melatonin-dependent reproductive status is predominantly negative. No convincing effect on melatonin levels has been seen in a study of non-human primates chronically exposed to power-frequency fields, although a preliminary study using two animals reported melatonin suppression in response to an irregular and intermittent exposure.

The effects of ELF exposure on melatonin production or release in isolated pineal glands was variable, although relatively few in vitro studies have been undertaken. The evidence that ELF exposure interferes with the action of melatonin on breast cancer cells in vitro is intriguing and there appears to be some supporting evidence in terms of independent replication

using MCF-7 cells. However this system suffers from the disadvantage that the cell lines frequenctly show genotypic and phenotypic drift in culture that can hinder transferability between laboratories.

With the possible exception of transient (minutes duration) stress following the onset of ELF electric field exposure at levels significantly above perception thresholds, no consistent effects have been seen in the stress-related hormones of the pituitary-adrenal axis in a variety of mammalian species. Similarly, mostly negative or inconsistent effects have been observed in amounts of growth hormone, levels of hormones involved in controlling metabolic activity or associated with the control of reproduction and sexual development, but few studies have been carried out.

Overall, these data do not indicate that ELF electric and/or magnetic fields affect the neuroendocrine system in a way that would have an adverse impact on human health and the evidence is thus considered inadequate.

7 NEURODEGENERATIVE DISORDERS

A number of studies have examined associations between exposure to electromagnetic fields and Alzheimer disease, motor neuron disease and Parkinson disease. These diseases may be classed as neurodegenerative diseases as all involve the death of specific neurons. Although their aetiology seems different (Savitz, 1998; Savitz, Loomis & Tse, 1998), a part of the pathogenic mechanisms may be common. Most investigators examine these diseases separately. In relation to electromagnetic fields, amyotrophic lateral sclerosis (ALS) has been studied most often.

Radical stress, caused by the production of reactive oxygen species (ROS) and other radical species such as reactive nitrogen species (RNS), is thought to be a critical factor in the modest neuronal degeneration that occurs with ageing. It also seems important in the aetiology of Parkinson disease and ALS and may play a part in Alzheimer disease (Felician & Sandson, 1999). Superoxide radicals, hydrogen peroxide (H_2O_2) and hydroxyl radicals are oxygen-centered reactive species (Coyle & Puttfarcken, 1993) that have been implicated in several neurotoxic disorders (Liu et al., 1994). They are produced by many normal biochemical reactions, but their concentrations are kept in a harmless range by potent protective mechanisms (Makar et al., 1994). Increased free radical concentrations, resulting from either increased production or decreased detoxification, can cause oxidative damage to various cellular components, particularly mitochondria, ultimately leading to cell death by apoptosis (Bogdanov et al., 1998).

Several experimental investigations have examined the effect of ELF electromagnetic fields on calcium exchange in nervous tissue and other direct effects on nerve tissue function. A variety of effects of ELF exposure of potential relevance to neurodegenerative disease have previously been reported (Lacy-Hulbert, Metcalfe & Hesketh, 1998). These include small increases (Blackman et al., 1982; 1985), but also decreases (Bawin & Adey, 1976), in Ca^{2+} efflux from brain tissue, in vivo and in vitro, inhibition of outgrowth of neurites from cultured neurons (Blackman, Benane & House, 1993), and an increase in superoxide production from neutrophils (Roy et al., 1995).

It is conceivable that prolonged exposure to ELF fields could alter Ca^{2+} levels in neurons and thus induce oxidative stress through its influence on mitochondrial metabolism. On the other hand, the biological evidence, particularly concerning the response of neurons, is limited.

Neurons can be directly activated by strong electrical currents (see Chapter 5, especially section 5.2.2). Some evidence, discussed in sections 5.1 and 5.2, suggests that ELF exposure might modulate ongoing electrical activity in the CNS, although studies on hormone and neurotransmitter levels have generally reported no effect or only minor influences of ELF exposure (see section 5.4.4). While these effects are unlikely to be damaging, especially in the short term, there is the possibility that prolonged exposure to ELF fields could synchronize certain neurons of high sensitivity (perhaps

especially the large motor neurons), possibly leading to voltage-activated Ca^{2+} entry, which could have a damaging effect on the neurons. There might also be an accumulation of extracellular glutamate relative to GABA (gamma-aminobutyric acid), which could have excitotoxic effects on surrounding neurons.

It is possible that even modest cellular effects of ELF fields may exacerbate pathological changes in otherwise compromised neurons. For instance, intercellular transfer of metabolites and ions via gap junctions has been shown to be affected by exposure to 0.8 mT (but not 0.05 mT) magnetic fields (Li et al., 1999).

In contrast to the effect of ELF it has been suggested that exposure to electric shocks may increase the risk for ALS (Haynal & Regli, 1964). Electric currents may damage brain tissue by disturbing the circulation. It has also been speculated that severe electric shocks cause a massive synchronized discharge of neurons, which might release sufficient glutamate to precipitate toxic changes, as outlined above (AGNIR, 2001a). No mechanism has been identified, however, that could provide a coherent explanation of the observed association between exposure to ELF or electric shocks and these neurodegenerative diseases.

7.1 Alzheimer disease

7.1.1 Pathology

Alzheimer disease (AD) is characterized clinically by progressive loss of memory and other cognitive abilities (e.g. language, attention). Its onset is thought to be heralded by a phase of mild cognitive impairment in which cognition is not normal but not severe enough to warrant a diagnosis of dementia. The exact duration of mild cognitive impairment is unclear, but is likely to last at least a few years. Most data on disease duration come from studies of prevalent AD which suggest that disease duration may average seven or more years, although a recent study estimated that disease duration may actually be closer to 3½ years from the onset of the manifestations of dementia. Many persons with AD also develop motor, behavioral, and affective disturbances. In particular, parkinsonian signs, hallucinations delusions, and depressive symptoms are present in half or more of persons with the disease. Data also suggest that these signs are related to increased risk of death and to rate of cognitive decline. Cholinesterase inhibitor therapy, the mainstay of symptomatic treatment, is not known to definitively affect disease course or outcomes.

Although oxidative stress may be involved in the sporadic forms of AD, the evidence is less compelling. Indices of oxidative damage are significantly increased compared with those in age-matched controls (Felician & Sandson, 1999). Inflammatory and immune responses have also been implicated, although it is difficult to know whether these are secondary to the other pathological changes. Cellular responses to increased oxidative stress

appear to be a mechanism that contributes to the varied cytopathology of AD.

Inflammation in the CNS often occurs in both Parkinson and Alzheimer diseases and chronic neurological disorders such as brain trauma, ischemic stroke (for a review, see Rothwell, 1997). It has long been known that the extent of inflammatory responses in the CNS is less than observed in the periphery (for review, see Lotan & Schwartz, 1994; Perry, Brown & Gordon, 1987). A cascade of inflammatory responses is orchestrated by microglia (resident macrophages) and astrocytes in the CNS.

The fact that microglia become reactive in the aging brain as the natural death of neurons occurs (Sloane et al., 1999) suggests that interactions between neurons and glia play an important role in controlling inflammatory responses in the CNS. Chang et al. (2001) showed that activation of microglia in the ageing brain was linked to the death of neurons.

7.1.2 Epidemiology

Sobel et al. (1995) reported the results of three small case-control studies of AD, two of which had been carried out in Finland and one in the USA. Occupational histories for demented subjects were obtained from the most knowledgeable surrogates and, for non-demented controls, by direct interview. The individuals' primary lifetime occupations were classed blindly by an industrial hygienist as causing low, medium, or high (or medium to high) exposure on the basis of previous knowledge. Dressmakers, seamstresses, and tailors had not previously been classified as occupations with high EMF exposure. The classification of medium to high exposure was confirmed by measurement of the fields produced by four industrial and two home sewing machines.

The first Finnish series consisted in 53 men and women with sporadic AD and 70 with sporadic vascular dementia; the second of 198 men and women admitted to a geriatric institution diagnosed as having AD (sporadic and familial combined) and 298 controls selected in order from the alphabetic listing of patients admitted to the long stay internal medicine wards of the Koskela Hospital in 1978, excluding those with a diagnosis of dementia or mental retardation, psychosis, depression, general or brain arteriosclerosis, Parkinsonism, or multiple sclerosis. The third series consisted in 136 patients admitted to the University of Southern California between 1984 and 1993 with sporadic AD and 106 neuropsychologically normal individuals without any known history of dementia or memory problems in first degree relatives in the communities from which the Alzheimer patients came. The results are summarized in Table 53. The odds ratio for probable medium to high exposure compared to low for the three series combined was 3.0 and was hardly altered (2.9 with 95% CI 1.6–5.4) by adjustment for education and social class and for age at onset, age at examination, and sex. [In this study the newly designated category of dressmakers, seamstresses, and tailors accounted for the greater part of the excess risk from medium to high exposure occupations (23 out of 36 individuals in the AD series and 8 out of

16 in the controls). The limitations of the study are use of different control groups in the three series, particularly patients with vascular dementia who may in fact have had AD; obtaining job histories by questionnaires; lack of validation of exposure of the study population; the measure of high exposures among seamstresses was not confirmed in a later and more extensive study in the US (Kelsh et al., 2003), dependence on proxy respondents for job histories of cases but not for some of the control.]

A further case-control study, based on patients attending an Alzheimer's Disease Treatment & Diagnostic Center in Downey, California, was reported by Sobel et al. (1996) in the following year and may be regarded as constituting a test of the hypothesis formed in the first report. Patients at the Center had been included in several previous studies and information about their primary occupation throughout life was extracted from existing forms. Comparisons were made between 326 patients with probable or definite AD and 152 control patients with cognitive impairment or dementia due to other causes, excluding vascular dementia. These were classified in 20 groups, the largest being head trauma (26) and alcohol abuse (21). These results are also summarized in Table 53. The odds ratio for a primary occupation that caused medium or high exposure to EMF, was 3.93 with 95% CI 1.45–10.56. [Again seamstresses, dressmakers, and tailors combined, in this study, with sewing factory workers and clothing cutters contributed a relatively high proportion of the cases with medium or high exposure. The odds ratios in the study were higher for men than for women, contrary to what had been observed in the previous study. The limitations of this study were that the cases included 24 patients with unclear diagnoses; the controls were not matched by age or gender to the cases and were from the same clinic, which specialized in AD; job histories were obtained by questionnaire; and the exposure of the study population was not validated. The different designs used in this study and in the three other studies of Sobel et al. lead to a diverse collection of relative risks and potential biases].

Table 53. First case-control studies of Alzheimer disease: ELF magnetic field exposure estimated for primary lifetime occupation

Authors		No. of subjects (medium or high exposure / total)		Odds ratio	
		Cases	Controls	Univariate	Adjusted
Sobel et al., 1995	Finnish 1	6 / 53[a]	3 / 70	2.9	2.7
	Finnish 2	19 / 198	10 / 289	3.1**	3.2***
	University S. California	11 / 136	3 / 106	3.0	2.4
Sobel et al., 1996		39 / 326	8 / 152	2.45*	3.93**

[a] Data for one patient missing.

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$

The findings of subsequent studies, which are summarized in Table 54, present a different picture. Savitz, Loomis & Tse (1998) studied men aged 20 years and over who were certified as having died from amyotrophic lateral sclerosis, AD or Parkinson disease in the period 1985–1991 and had recorded occupations in one of the 25 US states that coded occupational information on the death certificate. Three controls were selected from all other men dying in the same states matched with each of the cases and stratified by year of death and age at death in five broad age groups. AD was given as the cause of 256 deaths and the odds ratio for occupations previously defined as involving electrical work, adjusted for age, period, social class and race was 1.2 with 95% CI 1.0–1.4. [The major limitations of this study are the use of death certificates to assess outcome, particularly since AD is difficult to diagnose and is often underreported on death certificates; the small number of cases, and lack of validation in exposure assessment.]

Feychting et al. (1998) studied 77 men and women with dementia, 55 of whom were classed as having probable or possible Alzheimer disease, diagnosed when a sample of individuals drawn from the twins registered in the Swedish Adoption/Twin Study of Ageing were screened for dementia. If both members of a twin-pair had dementia, one was randomly selected for inclusion in the study. Two groups of controls were drawn from the same original sample of twins who, on testing, were mentally intact. Death and refusal diminished the number of controls available for study and the samples were reinforced by a few additional persons from another Swedish twin study. The occupational history of both cases and controls had been recorded at a structured interview, as part of the mental testing procedure, information about demented subjects being obtained from a surrogate (mostly spouse or offspring). Each subject's primary occupation was defined as that held for the greatest number of years. The relevant information about magnetic field exposure was obtained from the records of a previous study in which workday measurements had been made for a large number of occupations held by a sample of the population (Floderus et al., 1993; Floderus, 1996). Lack of data for some occupations and lack of occupational histories for housewives reduced the number of cases available for analysis to 41 for all dementia and 27 for Alzheimer disease, and to 150 and 164 for the two control groups. No clear relationship with exposure from the primary occupation was seen for all dementia: the odds ratios for exposures = 0.2 μT were 1.5 (95% CI 0.6–4.0) and 1.2 (95% CI 0.5–3.2) against the two control groups, nor for AD where the odds ratio for exposure = 0.2 μT were respectively 0.9 (95% CI 0.3–2.8) and 0.8 (95% CI 0.3–2.3). There was, however, some evidence of a relationship with exposure from the last occupation held for both categories: the odds ratios for exposure = 0.2 μT were for all dementias 3.3 (95% CI 1.3–8.6) and 3.8 (95% CI 1.4–10.2); and for AD 2.4 (95% CI 0.8–6.9) and 2.7 (95% CI 0.9–7.8). [It is notable that in this study the relationship with magnetic fields is stronger for all dementias than for AD, and hence stronger still for dementias other than AD, which had been used as the controls in some other studies (Sobel et al., 1995; 1996). The limitations are the small number of cases, particularly of AD; possible selection bias due to twins who refused

to be examined; potential information biases in the job histories which were obtained for cases from proxy respondents; lack of autopsy confirmation of the diagnosis of AD.]

The results of the two cohort studies with measured exposures for large random samples of men with different occupations in the electricity utility industry provide unbiased tests of the hypotheses that the fields can increase the risk of neurodegenerative disease. The studies were designed to find out if exposure to 50 Hz magnetic fields increased the risk of leukaemia, brain cancer, and some other cancers (Johansen & Olsen, 1998b; Savitz & Loomis, 1995) but the causes of all deaths that occurred over prolonged periods were recorded and the results can provide relevant information. Such a test, however, is limited since these are mortality studies which are limited in investigating causes such as Alzheimer disease which might not be reported consistently on the death certificate.

One study covering 21 000 Danish workers followed for up to 19 years was reported by Johansen & Olsen (1998a). The standardized mortality ratio (SMR) for dementia (senile and presenile combined) was less than unity (0.7) for the total population based on six deaths and still lower for the most highly exposed group (0.4). [As specified previously, the use of death certificates for diagnosis of AD is a major limitation, as is the absence of validation of exposure in the study population.]

The second study covered nearly 140 000 workers employed in five US utilities and followed from 1950 or 6 months after the date of hire, whichever was the later, to the end of 1988 (Savitz, Checkoway & Loomis, 1998). The SMR for AD was 1.0, based on 24 deaths. Information was also obtained on the frequency with which the disease was referred to on the death certificates as a contributory cause and the 56 deaths for which it was mentioned as an underlying or contributory cause were related to the individuals' estimated cumulative exposure in terms of μT-years: that is, the time weighted average exposure multiplied by the number of years exposed. This provides no evidence of any association between exposure and death from AD, expressed as relative risk (RR) per μT-year cumulative exposure, either for career exposure or, for what might be the more relevant, as AD commonly lasts for 5 to 10 years before death, for exposure 10–19 years or 20 or more years before death. [Again, the use of death certificates for diagnosis of AD is a major limitation.]

Recently Li, Sung & Wu (2002) reported that among 2198 elderly individuals aged 65 years or over, there was no increased risk of cognitive impairment due higher levels of exposure to power frequency EMFs from a previous occupation, higher residential exposure or both and therefore little support for a link between cognitive impairment and ELF exposure.

Feychting and colleagues (2003) identified all men and women included in the 1980 Swedish census who were working in 1970 or 1980 and alive on January 1, 1981 and followed them until December 31, 1995. All deaths with neurodegenerative disease listed were identified, although AD

and vascular dementia were not separate categories until January 1, 1987, thus the follow-up for these started from that date. Information on subjects' occupational and socioeconomic status (SES) came from census data.

To estimate EMF exposure over the working lifetime, Feychting et al. used Floderus's 1996 job-exposure matrix, which includes some sample occupational 50-Hz magnetic field measurements for the 100 most common jobs held by Swedish men. They also analyzed occupations with the highest estimated EMF exposure in the matrix, plus a group of "electrical occupations" reported earlier by others (Sobel and Savitz) as being associated with higher AD and ALS risk. They calculated person-years of exposure and created groups based on 1st (below 0.11 μT) and 3rd quartiles (0.11 to 0.19 μT), the 90th percentile (0.19 to 0.29 μT) and the 95th percentile (> 0.5 μT). All risk estimates were adjusted for age and SES.

A total of 2 649 300 men and 2 163 346 women were included. Overall, AD was not associated with magnetic field exposure of 0.3 μT or above in men or women. A modest increased risk of AD in men with exposure of 0.5 μT and above in 1970, with a "slightly higher" risk estimate in 1980. Stronger associations were found among men when analyses were limited to mortality before age 75, and even stronger when follow-up was limited to 10 years after the 1980 census. The highest risk ratio (RR) of 3.4 (95% CI 1.6–7.0) was reported for men exposed to 0.5 μT or above in 1980. [The limitations include lack of a complete work history and the reliance on the job-exposure matrix developed for a different study, use of death certificates and reliance on census data for occupation and SES.]

Another investigation in Sweden, by Håkansson et al. (2003) evaluated the relationship between occupational 50-Hz magnetic field exposure and mortality from AD, ALS, Parkinson disease and multiple sclerosis. This population overlapped with a previous study, but focused on highly exposed group of workers (resistance welders) with some exposures in the millitesla range. First, 40 types of occupation where resistance welding could be part of the job description during the study period 1985 to 1994 were identified. Income tax records were used to identify subjects employed at any of the selected work places. A total of 537 692 men and 180 529 women were identified and about 10% of eligible subjects, 53 049 men and 18 478 women, for whom either occupation or exposure data were missing were excluded.

The census data from 1980, 1985 and 1990, which included occupation codes and some job descriptions, were used to identify resistance welders. These 1697 subjects formed the highest exposure group for the analyses. For assignment to other exposure categories, the same Floderus's 1996 job-exposure matrix, plus some additional "exposure information" from a 1993 Swedish study for some rare occupations were used. Further, Håkansson et al. added three other occupations employing mostly women – "domestic service", "computer operator" and "other needlework" – not included in the matrix. They assigned domestic workers to a low exposure categoryandcomputer operators and needleworkers to a high exposure category. As the authors note, overall this cohort was "comparatively young"

with a median age of 35. Causes of death were ascertained from the Swedish national death certificate registry. For workers who moved from a higher exposure level job to a lower one during the study period, the higher level was used for analysis. If information on a subject was lacking for a given census period, the earlier data was used.

Håkansson et al. (2003) report elevated relative risk for AD among exposed men and women, with increasing risk with increasing exposure. Exposure-response analysis yielded an RR of 3.2 for each increase of 1 μT. The risk estimate for men and women in the highest exposure category was 4.64 (95% CI 1.40–11.66), but based on only eight cases. [Results rely on small numbers. No effect is seen if only primary cause of death (without contributing cause) is used. Potential confounding from welders' exposure to metals might be present.]

The most recent study (Qiu et al., 2004) is also from Sweden (Stockholm). It evaluates lifetime occupational exposures to magnetic field and Alzheimer disease in a community cohort of individuals 75 years and older. This cohort was dementia-free at the beginning of the follow-up (1987–89) and was followed to 1994–96. Information on occupational history was obtained from a proxy, exposure to magnetic fields was based on the already mentioned job-exposure matrix and some supplementary information focusing on women. Of 931 individuals 202 were diagnosed with AD based on a structured interview, a clinical examination and psychological assessment. For the deceased subjects the diagnosis was made by the examination of medical records by two physicians. Adjustment was made for numerous potential confounders. Increased risk was seen for men in both medium lifetime average occupational exposure (RR = 1.7; 95% CI 0.6–4.5) and high exposure (RR = 2.0; 95% CI 0.7–5.5), but these elevations were not statistically significant and the broad confidence intervals indicate a high level of uncertainty. The risk was slightly higher but less consistent when adjustments for many potential confounders were made. No risk was evident for women. [Limitations include exposure assessment including information on jobs held and relevance of the job-exposure matrix used especially for women.]

When evaluated across all the studies, there is only very limited evidence of an association between estimated ELF exposure and disease risk. This is mainly confined to the first two studies (Sobel et al., 1995; 1996) and it is not clearly confirmed by the later studies (Feychting et al., 1998; Feychting et al., 2003; Qiu et al., 2004; Savitz, Checkoway & Loomis, 1998; Savitz, Loomis & Tse, 1998). The exception might be a study by Håkansson et al. (2003). The two studies that show excess (Sobel et al., 1995; 1996) may have been affected by selection bias. Because the study populations are undefined, there is no way to determine the extent to which the controls are representative with respect to exposure of the population from which the cases originated. The Håkansson et al. results depend on the use of a contributing cause. Use of mortality information for the evaluation of AD is particularly problematic, because this diagnosis is often not reported as an under-

Table 54. Later studies of Alzheimer disease and dementia unspecified

Authors	Exposure (μT)	No. of deaths	Relative risk (95% CI)	Disease
Savitz, Loomis & Tse, 1998	Electrical occupation	256	1.2 (1.0–1.4)	AD
Feychting et al., 1998	Primary occupation 0.2 / < 0.12	(i) 27 [a] (ii) 27	0.9 (0.3–2.8) 0.8 (0.3–2.3)	AD
	Last occupation 0.2 / < 0.12	(i) 29 (ii) 29	2.4 (0.8–6.9) 2.7 (0.9–7.8)	AD
	Primary occupation 0.2 / < 0.12	(i) 41 (ii) 41	1.5 (0.6–4.0) 1.2 (0.5–3.2)	Dementia
	Last occupation 0.2 / < 0.12	(i) 44 (ii) 44	3.3 (1.3–8.6) 3.8 (1.4–10.2)	Dementia
Savitz, Checkoway & Loomis, 1998	Cumulative career	56	0.97 (0.87–1.08) [b]	AD
	Cumulative 10–19 y before death	56	0.47 (0.21–1.04) [b]	AD
	Cumulative 20 y before death	56	0.97 (0.87–1.09) [b]	AD
Johansen & Olsen, 1998a	Any	6	0.7	Dementia
	Most highly exposed	1	0.4	Dementia
Feychting et al., 2003	Occupation in 1970 (males)			AD
	Reference (< 0.11)	178		
	3rd quartile (0.12–0.19)	696	1.0 (0.9–1.2)	
	90th percentile (0.20–0.29)	239	1.1 (0.9–1.3)	
	95th percentile (> 0.5)	90	1.3 (1.0–1.7)	
Håkansson et al., 2003	Occupational exposure (males & females)			AD
	Reference (< 0.16)	7		
	Medium (0.16–0.25)	17	1.3 (0.5–3.2)	
	High (0.25–0.53)	8	2.2 (0.6–6.3)	
	Very high (> 0.53)	8	4.0 (1.4–11.7)	
Qiu et al., 2004	Lifetime average occupational exposure (males & females)			AD
	Reference (< 0.15)	69		
	Medium (0.16–0.18)	64	1.2 (0.9–1.7)	
	High (> 0.18)	69	1.1 (0.7–1.5)	

[a] (i) & (ii) odds ratios for same cases with two different sets of controls.
[b] Relative risk per μT-year cumulative exposure.

lying cause and is underrepresented as a contributing cause as well. Note that, overall, the studies that did not rely on the death certificates for diagnosis appear to be more positive. This should be considered in the interpretation and development of future studies.

7.2 Amyotrophic lateral sclerosis

7.2.1 Pathology

Amyotrophic lateral sclerosis (ALS) is characterized clinically by progressive motor dysfunction, including painless muscle wasting and spasticity. Most data on disease duration come from clinic samples which suggest that disease duration may average only two to three years. Signs of the disease depend greatly on where the symptoms begin. Brainstem (bulbar) dysfunction may be the first sign in persons presenting with dysphagia or dysarthria. Alternatively, persons may present with painless wasting and weakness of a limb, or one side of the body. Persons with ALS may develop cognitive and autonomic dysfunction. In particular, a frontal lobe dementia and hypotension may develop. Some data suggest that these signs portend a more malignant course of disease. As the disease progresses, pulmonary function and dysphagia result in the need for artificial respiratory support and the insertion of feeding devices to maintain life. Pathologically, the hallmarks of the disease are degeneration of anterior horn cells, ubiquinated inclusions, hardening (sclerosis) of the white matter in the brain and spinal cord, and degeneration of other motor nuclei. Evidence of degeneration and regeneration in muscle is thought to be secondary to the loss of anterior horn cells. About 10% of ALS cases are familial (Brown, 1997).

Trauma has long been suspected as being a cause of motor neuron disease and specifically of ALS. No clear evidence that it was a cause has, however, ever been obtained, partly, perhaps, because of variation in the reports of the type, location, and timing of the trauma in relation to the onset of the disease and partly because of the probability that the many positive findings were affected by recall bias, patients with the disease being more motivated to recall traumatic events than their corresponding controls.

7.2.2 Epidemiology

The results of five case-control studies examining possible etiology of electric shocks and ALS are summarized in Table 55. Four of them specifically noted the prevalence of electric shocks or injuries and four the proportion of people employed in defined electrical occupations. The first study, which gave rise to the hypothesis, was reported from Germany by Haynal & Regli as long ago as 1964. Nine out of 73 patients with ALS had worked in contact with electricity against five out of 150 controls, giving, according to Deapen & Henderson (1986) an odds ratio of 4.1.

No further study was reported until seventeen years later, when Kondo & Tsubaki (1981) described two studies in Japan, one of which involved a substantial number of cases. Both were essentially negative. In the first, information was obtained by personal interview from the spouses of

458 men and 254 women whose deaths were attributed to motor neuron disease, most of whom had ALS (333 men and 178 women) and the findings were compared with those obtained from 216 of the widowers and 421 of the widows, who were used as controls. In the second study, 104 men and 54 women with ALS were interviewed and the findings compared with those in a similarly sized control group matched for sex, age within 5 years, and area of residence, about half of whom were "normal", the others being patients in the same hospitals with relatively mild neurological disease. Very few subjects in either group reported "electrical injuries", that is injuries that resulted in burns, persistent pain, or loss of consciousness, very few were employed in electrical work, and the relative risks were close to unity.

A small study from the UK (Gawel, Zaiwalla & Rose, 1983) reported the findings in response to a questionnaire given to 63 patients with motor neuron disease and 61 undefined controls whose "age and sex distribution ..... was not statistically significant different". Thirteen of the patients had experienced an undefined electric shock against five of the controls and two of the patients had been struck by lightning (one stating that he had been flung to the ground) against none of the controls. The difference between the combined results was statistically significant, but is difficult to interpret in the absence of a clearer description of the method of enquiry. The odds ratio for the combined exposures (4.6) was similar to that of 4.1 for "working in contact with electricity" in Haynal & Regli's (1964) original study.

The fifth, and most important, study was carried out by Deapen & Henderson (1986) in conjunction with the Amyotrophic Lateral Sclerosis Society of America. Histories were obtained from 518 patients with the disease and from a control group of the same size matched for sex and age within 5 years, drawn from individuals nominated by the patients as workmates, neighbours, and other social acquaintances. Information was obtained *inter alia* about the individual's occupation 3 years before the date of diagnosis of the disease (or the corresponding period in the case of the controls) and the occurrence more than 3 years previously of electric shocks severe enough to cause unconsciousness. Odds ratios of 3.8 and 2.8 were calculated respectively for employment in one or other of 19 previously defined electrical occupations and for the occurrence of severe electric shocks. Both were statistically significant. Deapen & Henderson (1986) noted that electric shock was a form of trauma that had been shown to cause demyelinisation, reactive gliosis, and neuronal death in experimental animals, but that previous studies had provided inconsistent results and they were unable to draw any conclusions from their findings, the significance of which they considered to be "not clear". [Limitations of the Deapen & Henderson's study are that the exposure to EMF was assessed from job titles based on responses to the questionnaire; failure to report the criteria for control selection and the potential recall bias inherent in using occupational histories and reports of electric shock.]

A further study of 135 patients with ALS whose disease began under 45 years of age and 85 control patients with multiple sclerosis, is of

limited value. Eight of the ALS patients were noted to have experienced electric shocks before the onset of the disease, severe enough "in some cases" to throw the subject to the ground (Gallagher & Sanders, 1987) but the severity of the shocks in the other cases is not defined and no reference is made to the occurrence (or non-occurrence) of shocks in the controls. Cruz et al. (1999) assessed the association between ALS and several risk factors including electrical shocks. They found a positive association for a familial history of ALS but found no association for electrical shocks.

A cohort study of over 4 million people who were born between 1896 and 1940, were registered in the 1960 Swedish census, and were still alive in 1970 was examined. About 1067 men and 308 women with a known occupation who died between 1970 and 1983 and had ALS given as either the underlying cause or a contributory cause of death on their death certificates (Gunnarsson et al., 1991) were identified. The occupations of the ALS subjects were compared with those of an age-stratified control sample of approximately 250 persons drawn from each 5 year birth cohort from 1896–1900 to 1936–1940. Occupations were classified in 90 groups (54 for men and 36 for women) and significant excesses of ALS were observed for only two (male office workers and male farm workers). It was noted, however, that, in agreement with Deapen & Henderson's (1986) findings "there seemed to be an association between ALS and work with electricity" (OR = 1.5 for male electricity workers). [This study can be viewed only as hypothesis generating.]

In 1997 Davanipour et al. found that 28 patients with ALS had had, on average, more intense occupational exposure to ELF fields than 32 controls. In their study, the controls were relatives of the patients and selected to be of similar age and, if possible, of the same gender. Unfortunately the requirements were too stringent and they obtained the two controls intended (one blood and one non-blood relative) for 12 cases and only one control for the remaining eight. Detailed occupational histories were obtained and exposure to ELF electromagnetic fields was classed for each job held in one of five categories, from low to high, and exposure indices were calculated taking into account the numbers of years worked in each job. The odds ratio per unit value of the exposure index (which ranged from 3 to 383) was positive (1.006) but not quite statistically significant (95% CI 0.99–1.01). Gender made little difference to the results and the odds ratio cited is one for all subjects irrespective of sex. Davanipour et al. (1997) considered that recent findings had made the concept that ELF fields were an aetiological factor in the development of ALS more plausible and that, despite the defects of the control group, their findings indicated that "long term occupational exposure to ELF may increase the risk of ALS". [The study is limited by the small sample size and potential control selection bias.]

Table 55. Case-control studies of amyotrophic lateral sclerosis before 1997: electrical employment and electric shocks [a]

Authors	Exposure	No. of subjects		Odds ratio
		Cases	Controls	
Haynal & Regli, 1964	Occupation in contact with electricity	9 / 73	5 / 150	4.1*
Kondo & Tsubaki, 1981 first study [b]	Electric injuries	2 / 458 (M) 3 / 254 (F	1 / 216 (M) 2 / 421 (F)	1.0
Kondo & Tsubaki, 1981 second study		6 / 104 (M) 1 / 54 (F)	7 / 104 (M) 2 / 54 (F)	1.0
Kondo & Tsubaki, 1981 first study	Occupation electric work	3 / 458 (M)	1 / 216 (M)	1.4
Gawel, Zaiwalla & Rose, 1983	Struck by lightning Other electric shock	2 / 63 13 / 63	0 / 61 5 / 61	4.6*
Deapen & Henderson, 1986	Occupation electricity related	19 / 518	5 / 518	3.8*
	Electric shock	14 / 518	5 / 518	2.8*

[a] A sixth study (Gallagher & Sanders, 1987) is omitted (see text).

[b] First study was on motor neuron disease, included 333 men and 178 women with ALS; second study limited to ALS. No woman was reported with an electric work occupation in either study, neither was any man in the second study.

* $p \leq 0.05$

Estimates of the risks associated with electric work were also provided in five of the later studies described under Alzheimer disease. These are summarized in Table 56.

In the Savitz, Loomis & Tse (1998) proportional mortality study, electrical work, as previously defined, was recorded slightly more often for the 114 men with amyotrophic lateral sclerosis than for the 1614 controls, giving an odds ratio of 1.3 adjusted for age, period, social class, and race, which was statistically significant (95% CI 1.1–1.6). [The diagnosis of ALS from death certificates in this study was based on ICD9, which groups ALS with other motor neuron diseases. Other limitations of this study include the fact that only one occupation was taken from death certificates and the absence of data on important confounders, such as familial neurodegenerative diseases or exposure to electric shocks].

Johansen & Olsen's (1998a) cohort study of Danish electricity workers recorded only 14 deaths from ALS, but the SMR (2.0; 95% CI 1.1–3.4) was, nevertheless, statistically significant and was higher, though no longer significant, for men with the highest average exposure of = 0.1 μT (SMR = 2.8; 95% CI 0.8–7.3). In this population the mortality from electricity accidents was 18 times the national average (based on 10 deaths) and 31 times that expected in the group with the highest average exposure.

In a study of the morbidity from neurodegenerative diseases and other disorders of the central nervous system, data on the entire Danish cohort (n = 30 631) were linked to the population-based National Register of Patients, which records more than 99% of all hospital discharges for somatic diseases (Danish National Board of Health, 1981). Data on all 30 631 employees were linked to the Register for follow-up for central nervous system diseases between 1 January 1978 or the date of first employment, whichever came last, and the date of death, emigration or 31 December 1993, whichever came first. Medical records were obtained for cases of ALS and other motor neuron diseases to verify the diagnosis and to obtain information on episodes of electric shocks or other occupational exposure before development of the disease. Men had an increased risk for all motor neuron diseases combined (SIR = 1.89; 95% CI = 1.16–2.93), based on 20 cases, which was confined to the 15 men with a diagnosis of ALS (SIR = 1.72; 95% CI 0.96–2.83). They also had an increased risk for other motor neuron diseases (SIR = 2.75; 95% CI 0.88–6.41) and for demyelinating diseases, with four cases observed (SIR = 1.90; 95% CI = 0.51–4.86) (Johansen, 2000).

The Savitz, Checkoway & Loomis (1998) cohort study of US utility workers recorded 28 deaths from ALS giving an SMR of 0.8. When, however, all the 33 deaths in which ALS was mentioned on the death certificate as either the underlying or a contributory cause of death, were related to the individuals' estimated cumulative exposure in terms of μT-years, that is the time-weighted average exposure multiplied by the number of years exposed, a positive but non-significant association was observed (relative risk per μT-year = 1.03; 95% CI 0.90–1.18). Unlike Alzheimer disease, ALS progresses rapidly over 1 or 2 years and this may be the most relevant association. Should, however, any effect of exposure have a long latent period, it is notable that the only positive relationship for a specific period was that for 20 or more years in the past (relative risk per μT-year = 1.07; 95% CI 0.91–1.26). [Limitations of this study are the modest number of ALS cases, diagnosis from death certificates, and the absence of the data on electric shocks or the family's disease history].

In a previously described study, Feychting et al. (2003) found no increased risk for ALS in any of their analyses, including occupations having the highest EMF exposure. They also analyzed the "electrician" category separately because this job reports the largest number of electric shock accidents in Sweden. When looking at risk for men only by job title alone, Feychting et al. observed an increased risk (statistically significant) of ALS among welders based on 24 cases, and a slightly elevated risk among radio and television assemblers (seven cases) and telephone and telegraph installers/repairmen (six cases), but these were not statistically significant. No risk was observed for electricians.

For ALS Håkansson et al. (2003) report the statistically significant risk estimate RR = 2.2 (95% CI 1.0–4.7) for both men and women in the very high exposure group (based on 13 cases). Additonally, they report an exposure-response relationship with an RR of 1.5 for an increase of 1 μT.

Table 56. Later studies of amyotrophic lateral sclerosis

Authors	Exposure	No. of deaths	Relative risk (95% CI)
Savitz, Loomis & Tse, 1998	Electrical occupation	114	1.3 (1.1–1.6)
Savitz, Checkoway & Loomis, 1998	Cumulative, career	33	1.03 (0.90–1.18) [a]
	Cumulative, 10–19 y before death	33	0.82 (0.40–1.65) [a]
	Cumulative, 20 y before death	33	1.07 (0.91–1.26) [a]
Johansen & Olsen, 1998a	Any	14	2.0 (1.1–3.4)*
	1.0 μT average	4	2.8 (0.8–7.3)
Feychting et al., 2003	Occupation in 1970 (males)		
	reference group < 0.11 μT	227	
	3rd quartile 0.12–0.19 μT	723	0.9 (0.7–1.0)
	90th percentile 0.20–0.29 μT	210	0.8 (0.7–1.0)
	95th percentile > 0.5 μT	70	0.8 (0.6–1.0)
Håkansson et al., 2003	Occupational exposure (males & females)		
	reference < 0.16 μT	15	
	medium 0.16–0.25 μT	52	1.6 (0.9–2.8)
	high 0.25–0.53 μT	17	1.9 (1.0–4.0)
	very high > 0.530 μT	13	2.1 (1.0–4.7)

[a] Relative risk for μT-year cumulative exposure.
* $p < 0.05$

Most of these studies do not allow examination of possible confounding from electric shock. It is conceivable that exposure to electric shocks increases ALS risk and, also, clearly work in the utility industry carries a risk of experiencing electric shocks. Some to the reviewed studies did report analyses that indeed linked electric shocks to ALS (Deapen & Henderson, 1986; Gunnarsson et al., 1992; Johansen & Olsen, 1998a), but none of the studies provided an analysis in which the relation between EMF and ALS was studied with control for electric shocks. A crude calculation can be made from the data provided by Deapen and Hendersen, and this seems to indicate the EMF association holds up even after control for electric shock experience.

There is no obvious biological explanation for the epidemiological evidence for a link between severe electric shocks and ALS. However, it is

possible that the massive, synchronized discharge of neurons (especially the large motor neurons) might release sufficient glutamate to precipitate excitotoxic changes. It might also trigger more subtle and persistent changes in the excitability of neurons. In many parts of the brain a tetanic burst of impulses arriving at a synapse can lead to a prolonged increase in the efficacy of that synapse and neighbouring synapses in activating the post-synaptic cell (a phenomenon called Long-Term Potentiation or LTP). In many situations, LTP appears to involve activation of the N-methyl-D-aspartate (NMDA) receptor by glutamate. The ionic channel of the NMDA receptor is blocked by intracellular Mg^{2+} at normal intracellular potentials, but this block is released if the cell is substantially depolarised by a preceding burst of impulses. Any impulse that follows a burst will then cause Ca^{2+} influx through the NMDA receptor channel, and this is thought to trigger reactions that lead to an increase in the effectiveness of the synapse, which can last for months (Kandel, Schwartz & Jessell, 1991). If severe electric shocks do produce LTP, the increased excitability of cells might produce cumulative pathological changes, perhaps involving Ca^{2+} influx through voltage-activated channels or increased metabolic demand, with spillover of reactive oxygen species.

The pathogenetic mechanisms leading to the selective loss of certain populations of dopaminergic neurons are not clear. It has been suggested that the dopamine transporter and vesicular monoamine transporter proteins, which are heavily expressed in the dopaminergic neurons of the substantia nigra, might act as portals of entry for toxins that are structurally related to monoamines (Speciale et al., 1998; Uhl, 1998).

7.3 Parkinson disease, Multiple Sclerosis

7.3.1 Pathology

Parkinson disease is characterized clinically by progressive motor dysfunction, including bradykinesia, gait disturbance, rigidity, and tremor. Most data on disease duration come from clinical samples which suggest that disease duration may average seven or more years. Many persons with Parkinson disease develop cognitive, behavioral, and autonomic signs: visible or measureable indications of changes in responses controlled by the autonomic nervous system, such as skin colour, sweating, pupil diametre and blood pressure. In particular, dementia, hallucinations, delusions, and hypotension develop in many persons with the disease. While the behavioral disturbances and autonomic signs are worsened by the dopaminergic agents commonly prescribed to treat the disease, these agents improve quality of life and probably prolong life. Some data suggest that behavioral disturbances and autonomic signs portend a more malignant course of disease. Pathologically, an important hallmark of the disease is degeneration of the substantia nigra (e.g. neuronal loss) .

7.3.2 Epidemiology

Occupation has been considered as a possible cause of Parkinson disease in several studies. The study by Wechsler et al. (1991) included jobs likely to involve relatively high exposures to EMF and reported three of 19 affected men were welders against zero out of nine controls and that two other affected men had worked as electricians or electrical engineers. However, Savitz, Loomis & Tse (1998) found very little evidence of an increased risk in electrical workers. Overall the odds ratio derived from the occupations of 168 men dying from Parkinson disease and 1614 controls was 1.1 (95% CI 0.9–1.2).

In the Danish cohort study (Johansen & Olsen, 1998a), the SMR for Parkinsonism was 0.8, based on 14 deaths and even lower for the more heavily exposed men (0.5). In the US study by Savitz, Loomis & Tse (1998), positive relationships were observed with both cumulative cancer exposure and exposure more than 20 years before death, neither of which were, however, statistically significant (relative risks 1.03 per μT-year, 95% CI 0.90–1.18, and 1.07 per μT-year, 95% CI 0.91–1.26). Noonan et al. (2002) reported a positive association with an OR of 1.5 for the highest exposure category for Parkinson disease and magnetic field exposure in electrical workers.

Feychting et al. (2003) found no increased risk for vascular dementia, senile dementia, pre-senile dementia, Parkinson disease, multiple sclerosis or epilepsy for either men or women. Håkansson et al. (2003) also found no increased risk for Parkinson disease or multiple sclerosis (MS) and they observed a decreased RR for epilepsy.

In one Danish study (Johansen et al., 1999) of the risk for MS, data on the entire cohort (n = 31 990) were linked to the files of the Danish Multiple Sclerosis Registry, which was founded in January 1948 as a nationwide program to register all cases of MS in Denmark. All cases of suspected or verified MS are currently notified to the Register from all 22 Danish neurological departments and the two rehabilitation centers of the Danish Multiple Sclerosis Society. Only verified cases of MS were included in the present study. Overall, 32 cases of MS were diagnosed, as compared with 23.7 expected from national incidence rates, to yield a standardized incidence ratio of 1.35 (95% CI 0.92–1.91).

7.4 Discussion

Of the four neurodegenerative diseases that have been considered, Parkinson disease and MS have received the least attention in epidemiology. No study has provided clear evidence of an association with above-average exposure to extremely low frequency EMFs and, in the absence of laboratory evidence to the contrary, it seems unlikely that such fields are involved in the disease.

The evidence relating to Alzheimer disease is more difficult to assess. The initial reports that gave rise to the idea suggested that the increased risk could be substantial (Sobel et al., 1995). Despite the fact that the initial

report was based on the combined results of three independent studies, it should be regarded only as hypothesis forming, as the greater risk was largely the result of classifying groups of garment workers in the heavily exposed groups that had not previously been so classified. The finding was quickly confirmed (by some of the authors of the original report) in another case-control study and was weakly supported by the proportional mortality ratio of causes of death as recorded on US death certificates. It was not supported, however, by the three studies that could provide quantified estimates of people's exposures. One, a case-control study, that did not show risk associated with the individual's primary occupation, did show a substantial and statistically significant risk with the last recorded occupation, which would have been the association recorded in the death certificate study. Neither of the cohort studies, however, provided evidence of a risk with increasing exposure nor, in the one study that provided the information, any excess mortality in power plant workers as a group. The three more recent studies have provided a mixed evidence as well: one providing a limited evidence for males in the highest exposure group, another (overlapping) study focusing on the resistance welders showed an effect, and a third one showing an effect in males, but not in females. In conclusion, there is only inadequate evidence to suggest that 50/60 Hz fields could cause Alzheimer disease.

More evidence is available for ALS. Eight reports of the relationship between electrical work or the experience of electrical shocks have been published since the original suggestion was made that electric shocks might increase the risk of the disease. Two early studies from Japan, where the prevalence of electrical work (as recorded in the medical history) and of electrical shock was low, failed to provide any support for the hypothesis. The others all provided some support. In three, including one of the two cohort studies with measured exposure, the excess associated with exposure was statistically significant. Electric shocks were recorded only in four early reports, in two of which (one from the UK and one from the US) the prevalence was significantly raised. The two most recent and overlapping studies from Sweden focusing on magnetic field exposure and electric shock are inconsistent, with one showing no effect and the other indicting a relative risk of about 2 in the two highest exposure categories. The epidemiological evidence suggests that employment in electrical occupations may increase the risk of ALS, however, separating the increased risk due to receiving an electric shock from the increased exposure to EMFs is difficult.

In considering a possible causal relationship between neurodegenerative disease and the electrical environment, the relevant exposure has been assumed to be some aspect (e.g. time weighted average, number of exposures above some critical level, etc.) of ELF magnetic fields, contact currents and/or electrical shock[1]. “Contact current” is defined here as an electrical current that

1. There are other environmental exposures that can cause electrical effects in the human body, such as the environmental electric field. Except in special circumstances such as near high voltage transmission lines, however, the effect of this source is usually smaller than either of the other two sources.

passes through the body between two points when they are in "contact" with an external electrical system. An electrical shock occurs as "a reflex response to the passage of current through the body" and thus is the result of contact currents large enough to be perceived. Although it is clear from these definitions that contact current and electrical shock are closely related, it may appear that the ELF magnetic field is a distinctly different exposure because ambient magnetic fields, with specific exceptions (e.g. MRI machines) are not nearly large enough to produce neural stimulation. This is not entirely correct. In fact, there are several important connections between the two that should be understood before the possible effects of one exposure can be separated from those of the other.

The first connection is that each exposure can be responsible for inducing an electric field and a corresponding electric current density within the human body. Biophysicists consider *the induced electric field* as the metric most relevant for evaluating biological interactions from EMF or contact current exposure[1]. Thus, a biological effect due to an electric field in the body may be caused by exposure to an ELF magnetic field, a contact current or some other aspect of the electrical environment that can cause an electric field in the body. What might allow one to discern the origin of the effect is recognition that the distribution of the magnitude and orientation within the body of the electric field induced by an ELF magnetic field and that due to a contact current can be significantly different.

It is well known that a time varying ELF magnetic field in the body can cause electric fields and currents to be induced in the body via Faraday's law. This induced electric field is limited by the size of the body and the magnitude of the magnetic field. In fact, it is generally well recognized that the electric fields induced by typical environmental 50/60-Hertz magnetic fields are usually thought to be too small to cause biological effects. Contact currents with commonly experienced amplitudes, on the other hand, have been estimated to produce electric fields in the body that are orders of magnitude larger than induced electric fields from typical levels of ambient magnetic fields. Further, the electric field produced by a magnetic field is larger near the periphery of the body while the electric field produced by contact currents is larger in the path between contact points and hence often in the limbs and the body's interior. These differences in amplitude and spatial distribution within the body may be suggestive of a cause and effect relationship with diseases that have their origin in specific parts of the body. For these reasons, contact currents and the related electrical shocks are important exposures and should be considered when conducting studies of possible health outcomes due to the electrical environment.

The second connection between the ELF magnetic field and contact currents is the fact that environmental magnetic fields may induce voltages

1. Several other mechanisms have been proposed by which ELF magnetic fields might directly interact with the body. However, they are either thought to be implausible or unlikely at environmental field levels.

in electrical systems that in turn cause current, i.e. contact current, in a human body that is in contact with this system. In addition, conducted currents on residential grounding systems may be related to nearby ELF magnetic fields. When either is the case, the amplitudes of the ELF magnetic field and the contact current are related.

The identification of which of these two exposures (if either) is associated with a health outcome, is a very important question. Properly configured studies should be designed to identify the specific exposure responsible for a specific biological effect.

The measurement of magnetic fields is a well-established enterprise. The measurement of electrical contact current and or shock current, however, is not as well advanced. It would require either that the current entering the body during normal life or work be measured or that the circuit contacted by the body be characterized by a simple equivalent circuit. It is only recently that an instrument for measuring the currents entering the body has been developed and it has not been extensively tested. Measurements that lead to a simple equivalent for a circuit that can be contacted by a human, however, have been made. In either case, methodology to allow evaluation of "contact current" exposure should be tested further. If acceptable, it should be used in further studies of the relationship between the electrical environment and neurodegenerative diseases.

Quantitatively, the flow of electricity through the brain is likely to be substantially greater from the use of electro-convulsive therapy for the treatment of psychiatric conditions than from even severe electric shock received occupationally or from non-fatal strikes by lightning. However, no large, long-term study of patients has been reported in sufficient detail to permit the detection of (say) a five-fold risk of a disease that normally causes about one death in 100 adults.

7.5 Conclusions

It has been hypothesized that exposure to ELF fields is associated with several neurodegenerative diseases. For Parkinson disease and multiple sclerosis the number of studies has been small and there is no evidence for an association with these diseases. For Alzheimer disease and amyotrophic lateral sclerosis (ALS) more studies have been published. Some of these reports suggest that people employed in electrical occupations have an increased risk of ALS. So far no biological mechanism has been established which can explain this association, although it could have arisen because of confounders related to electrical occupations such as electric shocks. Overall, the evidence for the association between ELF exposure and ALS is considered inadequate.

The few studies investigating the association between ELF exposure and Alzheimer disease are inconsistent. However, the higher quality studies that focused on Alzheimer morbidity rather than mortality do not indicate an association. Altogether, the evidence for an association between ELF exposure and Alzheimer disease is inadequate.

8 CARDIOVASCULAR DISORDERS

Concerns about chronic cardiovascular changes resulting from exposure to ELF fields originated from descriptions in the 1960s and early 1970s of the symptoms among Russian high voltage switchyard operators and workers (Asanova & Rakov, 1966; 1972). Further studies carried out in the Russian Federation in the 1980's and 90's reported various functional changes in the cardiovascular system, such as hypertension in workers in 500 kV, 750 kV and 1150 kV power installations (Rubtsova, Tikhonova & Gurvich, 1999). More recent investigations have focused mainly on direct cardiac effects of EMF exposure, mostly related to heart rate variability and subsequent acute cardiovascular events.

8.1 Acute effects

Current flow through the human body appears to be necessary in order to result in major cardiovascular effects from EMF exposure, such as the effects due to electric shock (Hocking, 1994). Normally electric shock requires direct electrical contact of a conductor with the body. It may, however, also occur if the body is exposed to very strong electric or magnetic fields (Foster, 1992). Minor effects have also been reported in other situations of low-level EMF exposure. Most human studies on EMF effects on the cardiovascular system have focused on acute rather than long-term effects.

8.1.1 Electrocardiogram changes, heart rate, and heart rate variability

Silny (1981) found no effects on the electrocardiogram (ECG) in 100 persons exposed to time-varying magnetic fields (5 Hz to 1 kHz, less than 100 mT). Hauf (1989) has performed human tests exposing the subjects to 50-Hz fields (20 kV m^{-1} and 0.3 mT) with a current of 500 μA passing through the body. The experiments did not indicate any significant effects on the heart rate of the subjects. In another study, there were no significant changes in heart rate in persons exposed locally to pulsed magnetic fields up to 2.2 μT by transcranial magnetic stimulation (TMS) (see 5.2.2) (Chokroverty et al., 1995).

In a series of studies carried out by the Midwest Research Institute in the US, effects of ELF fields on the heart rate in humans have been investigated. In a set of studies by Graham et al. (1994), subjects were exposed to different levels of combined electric and magnetic fields (low: 6 kV m^{-1} and 10 μT; medium: 9 kV m^{-1} and 20 μT; high: 12 kV m^{-1} and 30 μT). In the medium group a significantly decreased heart rate was observed, while in the other groups no change was found. In another study by the same group, six physiological parameters were examined at five sampling points with and without exercise (Maresh et al., 1988). During no-exercise sessions the cardiac interbeat interval was increased at two sampling points when subjects were exposed to 60-Hz fields. No other difference between the sham and exposed groups was found. A similar effect was found by another study of the same group (Cook et al., 1992).

In a replication study by Whittington, Podd & Rapley (1996), no effect of a higher magnetic field (100 μT, 50 Hz) on heart rate or blood pressure was found, however. Humans exposed for 1 hour to EMFs under a 400-kV power line exhibited no difference in pulse rate during autonomic function tests (Korpinen & Partanen, 1994a). The same researchers reported that exposure to 50-Hz fields (up to 10 kV m^{-1} and 15 μT for several hours) did not affect the incidence of extrasystoles or arrhythmia (Korpinen & Partanen, 1994b; Korpinen, Partanen & Uusitalo, 1993). A 2% decrease of heart rate was also observed by Sait et al. (1999) after a 100 to 150-s exposure to a 50 Hz, 28 μT magnetic field. From these studies, it can be noted that the positive but inconsistent results from the US Midwest Research Institute of reduced heart rates after exposure to EMF have not been confirmed by other studies. The heart rate effects, where such have been found, are generally of small magnitude, and can currently not serve as an indicator of an acute health effect (Hauf, 1982).

Sastre, Cook & Graham (1998) performed studies on heart rate variability (HRV) of 77 healthy men exposed to 60-Hz magnetic fields of 14.1 μT or 28.3 μT. Statistically significant alterations in HRV were observed during intermittent exposure to the higher field strength, while no effects occurred at the lower field strengths or when the exposure was continuous. A reduction in the power ratio in the low band of the HRV spectra (0.02–0.15 Hz) to the high band (0.16–1.0 Hz) was also observed by Sait, Wood & Sadafi (1999) after a 100 to 150-s exposure to a 50 Hz, 28 μT magnetic field with the exposure conditions already mentioned. In two studies on the same issue, HRV was evaluated during intermittent exposure to 28.3 μT (Graham, Cook & Riffle, 1997; 1998). In the latter study, three different frequencies were used (16, 40, 60 Hz). Exposure to 16 Hz was associated with significant alterations of the HRV spectrum. However, in a later pooled analysis of several studies conducted at the same institute, Graham et al. (1999) reported that this effect occurred only in studies where hourly blood sampling was performed. The authors hypothesised that blood sampling altered the level of subject arousal, allowing EMF interaction to affect HRV. A multi-study analysis indicates that the effect on HRV happens when EMF exposure is accompanied by increases in physiologic arousal, stress, or a disturbance in sleep, such as blood collection, but not otherwise (Graham et al. 2000a).

Recently, Graham et al. (2000e) performed studies using a much higher magnetic field (127.3 μT) and both continuous and intermittent exposure. No alterations in HRV were observed by either exposure condition, and the researchers concluded that, taking into account earlier reports, direct excitation of the human heart is extremely unlikely under exposure to magnetic fields lower than 127.3 μT.

A summary of the studies into the effects of ELF fields on ECG and heart rate is given in Table 57.

Table 57. Studies of ECG and heart rates after ELF exposure

Test	Exposure	Response	Comments	Authors
ECG	5 Hz–1 kHz < 100 mT	No change.		Silny, 1981
Cardiac interbeat interval	60 Hz 9 kV m^{-1}, 16 A m^{-1}	Longer cardiac interbeat interval.		Maresh et al., 1988
Pulse rate	50 Hz 20 kV m^{-1}, 300 µT or combined + 200 and 500 µA-currents at 50 Hz	No change.	Protocol looks confused, mixing haematological and physiological parameters.	Hauf, 1989
Pain, ECG, heart rate	Not defined: magneto-stimulation	No pain, no change in ECG and heart rate.	No dosimetry	Nagano et al., 1991
Interbeat interval before, during and after exposure 30 male subjects	60 Hz 9 kV m^{-1}, 20 µT 2x3 h day^{-1}, 4 days	Interbeat interval longer during and immediately after exposure.	Double-blind, counterbalanced study.	Cook et al., 1992
Extrasystoles, pulse rate	50 Hz 0.14–10 kV m^{-1}, 1.0-5.4 µT 0.5 h – few hours	No more extrasystoles in the field than out the field. Small decrease in pulse rate can be due to changes in work load.		Korpinen, Partanen & Uusitalo, 1993 Korpinen & Partanen, 1994b
Interbeat interval before, during and after exposure 54 male subjects	60 Hz 6 kV m^{-1}, 10 µT 9 kV m^{-1}, 20 µT 12 kV m^{-1}, 30 µT	Interbeat interval longer during and immediately after exposure only at the intermediate level of exposure.	Double-blind, counterbalanced study.	Graham et al., 1994
Pulse rate	50 Hz 3.5–4.3 kV m^{-1}, 1.4–6.6 µT 1 h	No change in pulse rate.		Korpinen & Partanen, 1994a
ECG, systolic and diastolic blood pressure, orthostatic test, valsalva maneuver, deep breathing test	50 Hz 3.5–4.3 kV m^{-1}, 1.4–6.6 µT 1 h	No change.	CV autonomic tests were performed 0.5 h before and after the 1 h-exposure.	Korpinen & Partanen, 1995
Heart rate	pulsed magnetic fields of up to 2.2 µT used in TMS	No change		Chokroverty et al., 1995

Table 57. Continued

Heart rate and blood pressure 100 (male and female) subjects	50 Hz 100 µT, intermittent 9 min	No effect.	Double-blind, counterbalanced study.	Whittington, Podd & Rapley, 1996
Heart rate variability 33 male subjects (exp 1) 40 male subjects (exps 2 and 3)	60 Hz 1 or 20 µT, intermittent Overnight (23.00–07.00)	Altered heart rate variability at 20 µT, but not at 1 µT.	Double-blind (all studies) and counterbalanced (exps 2 and 3).	Graham, Cook & Riffle, 1997 Sastre, Cook & Graham, 1998
Heart rate and heart rate variability 18 (pilot study) and 35 subjects (follow-up study)	50 Hz 28 µT, sinusoidal continuous or intermittent (15 s on-off), or square-wave for 100–150 s	Altered heart rate and heart rate variability by continuous sinusoidal fields, but not by intermittent or square-wave fields.	Blind and counterbalanced.	Sait, Wood & Sadafi, 1999
Heart rate variability 172 male subjects (pooled from 7 studies)	60 Hz 28.3 or 127.3 µT, intermittent or continuous Overnight	Altered heart rate variability in some conditions.	Blood sampling (for another study) at night was critical for this effect. Double-blind studies.	Graham et al., 1999; 2000e; 2000d

8.1.2 Blood pressure

No changes were observed in blood pressure, neither in subjects exposed to a 50 Hz field (20 kV m^{-1} and 0.3 mT) with a current of 500 µA passing through the body (Hauf, 1989), neither in humans exposed for 1 hour to EMFs under a 400-kV power line (Korpinen & Partanen, 1996), nor in persons exposed locally to pulsed magnetic fields up to 2.2 µT by TMS (Chokroverty et al., 1995). These studies are summarized in Table 58.

Table 58. Studies of blood pressure after ELF exposure

Test	Exposure	Response	Comments	Authors
Blood pressure	50 Hz 20 kV m^{-1}, 300 µT or combined + 200 and 500 µA-currents at 50 Hz	No change.		Hauf, 1989
Blood pressure	pulsed magnetic fields of up to 2.2 µT used in TMS	No change.		Chokroverty et al., 1995
Blood pressure	50 Hz 3.5–4.3 kV m^{-1}, 1.4– 6.6 µT 1 h	No change.		Korpinen & Partanen, 1996

8.2 Long-term effects

Knave et al. (1979) and Stopps, Janischewskyj & Alcock (1979) found no significant effects on cardiovascular function in male workers who were exposed occupationally for more than 5 years to electric fields from 400 kV power lines. Checcucci (1985) found no effect on the cardiovascular system in 1200 workers at high-voltage railway substations (1–4.6 kV m^{-1} and 4–15 μT). In a health survey of 627 railway high-voltage substation workers, Baroncelli et al. (1986) found no difference in the ECG between exposed and control groups. Table 59 gives a summary of these studies.

Table 59. Studies of cardiovascular effects after long-term ELF exposure

Test	Exposure	Response	Comments	Authors
CV parameters and diseases	50 Hz 400 kV power lines > 5 years	No effect.	Better psychologic performance linked to higher education level, and lower fertility predominant on boys, anterior to the exposure period.	Knave et al., 1979
CV parameters and diseases	50 Hz 400 kV power lines > 5 years	No effect.		Stopps, Janischewskyj & Alcock, 1979
CV parameters and diseases	1–4.6 kV m^{-1}, 4–15 μT	No effect.		Checcucci, 1985
Haematology electro-cardiogram	50 Hz HV railway substation < 5 kV m^{-1}, 15 μT 0, 1, 10 and 20 h / week	No effect.		Baroncelli et al., 1986

Based on the idea put forth by Sastre, Savitz (1999) hypothesized an association between exposure to EMF and cardiovascular disease. This hypothesis was based on two independent lines of evidence. The first was experimental data on heart rate variability described above in which intermittent 60-Hz magnetic fields were found to reduce the normal HRV (Sastre, Cook & Graham, 1998). The second came from several prospective cohort studies which indicated that reductions in some components of the HRV increase the risk for: (1) heart disease (Dekker et al., 1997; Liao et al., 1997; Martin et al., 1987; Tsuji et al., 1996); (2) overall mortality rate in survivors of myocardial infarction (Kleiger et al., 1987; Lombardi et al., 1987; Vaishnav et al., 1994); and (3) risk for sudden cardiovascular death (Malik, Farrell

& Camm, 1990). Thus, they postulated that occupational exposure to EMF will increase the risk for cardiac arrhythmia-related conditions and acute myocardial infarction, but not for chronic cardiovascular disease.

Several studies, published before the specific hypothesis of an effect on HRV was suggested, examined general cardiovascular mortality in relation to EMF (Table 60). In a Canadian retrospective cohort study of 21 744 men employed in an electrical utility company in the province of Quebec between 1 January 1970 and 31 December 1988, the standardised mortality ratio (SMR) for circulatory diseases was below 1 in all job categories and with all exposure levels to magnetic fields, electric fields and pulsed electromagnetic fields (Baris et al., 1996b). Exposure information was obtained from a job-exposure matrix (JEM) constructed on the basis of the last job held in the industry. The JEM was constructed for a larger study of employees in the utility industry in Canada and France (Theriault et al., 1994) and included a measurement protocol of magnetic fields, electric fields and pulsed electromagnetic fields among 466 employees for one week. Among employees exposed to magnetic fields > 0.16 μT, 137 persons died from circulatory diseases (adjusted RR = 0.91; 95% CI 0.73–1.14). The SMRs, when using electric fields and pulsed electromagnetic fields as the exposure variables, were close to those observed for exposure to magnetic fields. [It must be noted that no definition of diagnoses included as "circulatory diseases" are given. Likewise, there is no reference to the quality of the Canadian mortality statistics in this paper, or to what extent it is the underlying cause of death, the contributory cause of death or a combination of the two, which is used as the outcome measurement.]

A retrospective cohort study from the US (Kelsh & Sahl, 1997) of 40 335 men and women employed between 1960 and 1991 in a Californian utility company observed a significantly reduced SMR of 0.62 (95% CI 0.59–0.65) for both sexes combined. This was based on a comparison with the general population of the geographical area of the utility company and included 1561 cases of cardiovascular death (ICD-9, 3900–4489). The risk estimates in different occupational categories were very close to each other and all but the category "Meter readers/Field service" had significantly decreased mortality. Exposure information was primarily based on job title and work environment and included no measurement protocol. Each employee was assigned to one of seven categories based on the occupation held for the longest time. Information on mortality was obtained from three public sources and also from company records, indicating some underreporting to the primary sources. In internal analyses conducted across employment categories and using administrative employees as a reference group, mortality from "Major Cardiovascular" (category not defined) was significantly increased in all categories, the highest RR being 1.71 (95% CI 1.13–2.58) in the "Meter Reader/Field service" category. When stratifying the internal analyses by work employment period (before or after 1960) no clear pattern emerged. [A clear healthy worker effect seems to explain the results of the external analyses. However, no clear explanation can be given for the increased risk of death from "Major Cardiovascular" as no precise and

detailed information was available for exposure to known risk factors for these disorders (tobacco smoking, alcohol consumption or physical activity).] A re-analysis of this study cohort (Sahl et al., 2002) is described below.

In a nationwide retrospective cohort study in Denmark of 21 236 men employed in utility companies between 1900 and 1993 the causes of death were ascertained for 1 January 1974 through 31 December 1993, and cause-specific mortality was analysed by latency and estimated levels of exposure to 50 Hz electromagnetic fields (Johansen & Olsen, 1998b). A dedicated job-exposure matrix was designed that distinguished between 25 different job titles held by utility company employees and 19 work areas within this industry. Each of the 475 combinations of job title and work area was assigned an average level of exposure to 50 Hz EMF during a working day, which in turn was grouped into five categories of exposure to ELF fields. The conversion program was constructed by four engineers from the utility companies experienced in the planning and operation of electric utilities in Denmark. The construction of the matrix was based partly on a series of 196 24-hour measurements of 50 Hz EMF among 129 employees in six Danish utility companies and partly on judgements. The individual exposure assignment was based on the characteristics of the first employment held. Overall, 3540 deaths were observed as compared with 3709 expected from national mortality rates, yielding a standardized mortality ratio of 0.96 (95% CI 0.93–0.99). Overall mortality caused by acute myocardial infarction (ICD-8, 410) yielded an SMR of 0.95 (95% CI 0.9–1.0) based on 713 cases. SMR for cardiac sclerosis (ICD-8, 412) was 0.9 (95% CI 0.8–1.0) based on 300 cases and for mortality caused by other heart disorders (ICD-8, 394–402; 413; 420–429; 450 and 782) the SMR was 0.9 (95% CI 0.8–1.0). When analysing the cause-specific mortality by time since first employment or categories of estimated EMF exposure no increased mortality for these disorders appeared. [No information was available about known risk factors for cardiovascular disease. The exposure assessment in this study is based on few measurements and historical records and one cannot exclude that misclassification has taken place. In addition the use of mortality records as the measurement of the outcome may have caused some additional misclassification as the autopsy rates in Denmark has been decreasing in the study period. This study only use external comparisons as the method of analyses and this does not take into account a possible healthy worker effect.] This study cohort was later followed up for risk of pacemaker implantation – summarized below (Johansen et al., 2002).

In a recent follow-up study of Thai employees of the Electricity Generating Authority of Thailand, changes in levels of vascular risk factors over 12 years, and the associations of baseline risk factors with mortality were examined (Sritara et al., 2003). Over the 12-year period, levels of all major vascular risk factors, apart from smoking, worsened in this occupational study population. Although the authors note that the increases appear to exceed those expected from ageing of the cohort alone, very little regarding the impact of exposure on disease and mortality can be inferred from this study.

In the first study conducted with the specific aim to test the hypothesis of an association between EMF and acute cardiovascular disease risk another US retrospective cohort study of utility workers (Savitz et al., 1999) was analysed. It included 138 903 men employed for six months or more between 1950 and 1986. The authors report a significantly increased risk of mortality from arrhythmia-related conditions and acute myocardial infarction among workers with long duration of work (with rate ratios of 1.4–1.5 for the longest employment intervals) and with high exposure to magnetic fields (with rate ratios of 1.6–2.4 in the highest exposure category). As postulated a positive association was seen for acute myocardial infarction (AMI) and an inverse association for chronic cardiovascular disease (CVD). The EMF exposure categories were based on 2842 complete work shift time weighted average magnetic field exposure measurements and information on outcome (death certificate) was obtained from 97% of the deceased men. This cohort was reanalysed by Van Wijngaarden et al. (2001a), however, not providing further information on the hypothesis of an association between EMF exposure and mortality of arrhythmia-related cardiovascular diseases or AMI. Finkelstein (1999) questioned the use of death certificates as a source of information on a diagnosis of loss of autonomic cardiovascular control by Savitz et al. (1999) and pointed out that etiologic conclusions could not be drawn on the basis of death certificate codes (Finkelstein, 1999). Problems in using subtypes of CVD as coded on death certificates, which are of uncertain validity and reliability, are particularly evident in this study where the excess of deaths in acute cardiovascular categories coincides with a deficit of deaths in chronic categories for all exposure groups except the highest group. This either suggests specificity of effect or miscoding. In addition, they could not examine the temporal relation between exposure and outcome in any detail other than to look at jobs (with their estimated mean) and death, but not diagnosis. They also lacked information on other CVD risk factors.

The hypothesis of an association between exposure to EMF and the risk for arrhythmia-related cardiovascular disorders was further addressed in the Danish cohort of utility workers (Johansen et al., 2002). The incidence of severe cardiac arrhythmia as indicated by the need for a pacemaker was investigated by a linkage to the nationwide, population-based Danish Pacemaker Register. The study identified all cases of pacemaker implantation among 24 056 male utility workers between 1982 and 2000 and compared this number with the corresponding numbers in the general population. In addition, the data on utility workers was fitted to a multiplicative Poisson regression model in relation to estimated levels of exposure to 50 Hz electromagnetic fields. Overall, the risk was not increased for severe cardiac arrhythmia among employees in the utility companies, based on 135 men with pacemakers with 140 expected, yielding a risk estimate of 0.96 (95% CI 0.8 –1.1). No clear dose-response pattern emerged with increasing level of exposure to EMF or duration of employment. [The study investigated the risk of a morbidity, which leads to the implantation of a pacemaker. One may also consider that other arrhythmias, which are not associated with a pacemaker implantation, and thus not included here, may be associated with the

exposure under study. Furthermore the files of the workers were established years before the events reported to the Danish Pacemaker Registry and were supported by personal data from the nationwide, compulsory pension fund and the public payroll system kept for administrative purposes. The completeness of these registries of employments and pacemaker implantation highly reduces the likelihood of selection and information bias. Comparisons with the general population might have been influenced by the healthy worker effect. This was not the case, however, in the internal comparisons within the cohort of different exposure groups. No control of confounding for other risk factors was made. As mentioned before, the exposure assessment in this study is based on few measurements and historical records and one cannot exclude that misclassification has taken place.]

A re-analysis of the data reported by Kelsh & Sahl (1997) did not confirm the findings from Savitz' study (Sahl et al., 2002). In this cohort of 35 391 male utility workers in southern California, USA, with follow-up from 1960 to 1992, 369 cases of chronic coronary heart disease and 407 cases of myocardial infarct were identified. For cumulative exposure, adjusting for socioeconomic factors, no association was observed with mortality from acute myocardial infarction (rate ratio per μT-year = 1.01, 95% CI 0.99–1.02) or chronic cardiovascular heart disease (rate ratio per μT-year = 1.00, 95% CI 0.99–1.02). In this study (Sahl et al., 2002) the analyses were performed by the same methods and analytical models as those used by Savitz et al. (1999) in an attempt to conduct as a close a replication as possible of the Savitz work. In the previous study (Kelsh & Sahl, 1997) men aged > 80 years were excluded, EMF exposure was defined on the basis of the worker's usual occupation as opposed to a detailed occupational history, and different reference groups were used in the internal analyses. One group with a significantly increased mortality from cardiovascular disease, but with low EMF exposure, was assigned to the reference group in the present study (Sahl et al., 2002). This might explain some of the observed changes in risk estimates. [Weaknesses include the inability to control for potentially important factors that may influence mortality due to cardiovascular disease, the use of death certificates to identify the cause of death, and the reliability of the distinction between AMI and chronic cardiovascular heart disease as recorded on the death certificate. Strengths include large number of exposed, improved exposure assessment and an attempt to indirectly examine smoking as a potential confounder.]

A population-based case-control study from Sweden (Ahlbom et al., 2004) investigating risk factors for acute myocardial infarction in the city of Stockholm included information on occupational EMF exposure based on job titles one, five, and ten years prior to diagnosis. The analysis was restricted to the 695 cases and 1133 controls with information on job titles. Of these, 595 cases and 949 controls had jobs that were common enough to have been classified according to a previously developed JEM. The study used two approaches to classify exposure. First, specific individual job titles with presumed elevated EMF exposure were investigated and secondly, the subjects were classified according to a JEM. Both analytical approaches

revealed risk estimates for acute myocardial infarction below or close to one. [The strengths of this study include the fact that it is population based, looks at morbidity rather than mortality, the high participation rates and finally the high validity of the AMI diagnoses. This study is the first to include information on potential confounders, in particular blood pressure, serum cholesterol, socio-economic status, and cigarette smoking. The limitations of this study include the use of the previously developed JEM. Although this has been utilized in several other studies and seemingly performed well, its sensitivity and specificity in relation to classification of EMF exposure are not assessed. Thus, it is not entirely inconceivable that non-differential recall bias plays a role. On the other hand, several specific job titles were also analyzed and gave consistent results.]

Another Swedish study of the association between EMF exposure and mortality from heart diseases utilised data from the Swedish twin registry including close to 28 000 twins from two different cohorts of twins in Sweden (Håkansson et al., 2003). These twins were interviewed in 1967 and 1973 and at that time their occupation was recorded. In addition the interview covered information on smoking, alcohol consumption, level of physical activity and body mass index. The analyses were based on the primary and contributory cause of death followed up until 1996 utilizing the previously described exposure matrix (Ahlbom et al., 2004) adjusted for the previously mentioned risk factors. The results did not show an overall increased risk for arrhythmia related death, ischemic heart disease other than AMI or atherosclerosis. A non-significantly increased risk for AMI was observed in the highest exposure group (RR = 1.3; 95% CI 0.9–1.9; exposure level > 0.3 μT). Since this study was conducted within a twin cohort a sub-analysis that took into account the twin information was conducted. In this analysis the authors observed a larger increase in risk for AMI and magnetic fields in genetically susceptible subgroups (i.e. among the monozygotic twins, one of whom previously had an AMI) for which there is no obvious explanation. [Note that this study included subjects from the general population and its exposure assessment was based on a single question on the subjects' "main occupation" at one point in time in the past.]

The latest study of utility workers examined a cohort of 83 997 workers in the UK employed for at least six months between 1973 and 1982 and followed up from 1973 to 1997 (Sorahan & Nichols, 2004). Estimates were obtained for lifetime exposure and exposures accumulated during the most recent 5 years using comprehensive occupational magnetic field exposure assessment. Causes of death (both underlying and contributing) from cardiovascular diseases were grouped into four categories: (1) arrhythmia related, (2) acute myocardial infarction, (3) atherosclerosis related, and (4) chronic/sub-chronic coronary heart disease. Poisson regression modeling with adjustments for age, sex, calendar time, beginning year of employment, and an indicator for socioeconomic status was used. Only for arrhythmia-related death, the relative risk estimates were greater than one for all exposure categories, however, the estimates were based on small numbers, showed no monotonic trend with increasing exposure, and were not statisti-

cally significant. (RR per 10 μT-years = 1.1; 95% CI 0.8–1.6). [Of note in this study is the exposure assessment, which was based on elaborate methods that considered individual job histories, job environments, and local sources of magnetic fields in individual job locations, which is likely to have reduced misclassification.]

Table 60. Studies of general cardiovascular mortality in relation to EMF

Population	Design	Exposure	Outcome	Size	Results (95% CI)	Authors
Workers employed in electrical company between 1970–1988	Cohort SMR and internal comparisons	Member of cohort, job-exposure matrix	Circulatory disease mortality	Circulatory deaths: 137 Cohort: 21 744	Highest exposure category: SMR = 0.63 (0.53–0.74) RR = 0.91 (0.73–1.14)	Baris et al., 1996b
Utility workers, employed 1 y between 1960–1991, followed - 1992	Cohort SMR and internal comparisons	Member of cohort, certain occupational categories	CVD mortality	CVD deaths: 1561 Cohort: 40 335	Total cohort: SMR = 0.62 (0.59–0.65) Linemen: RR = 1.42 (1.18–1.71)	Kelsh & Sahl, 1997
Male utility workers, employed 3 months between 1990–1993, followed 1974–1993	Cohort SMR	Member of cohort, classification of workplaces based on measurements	CVD mortality	CVD deaths: 713 Cohort: 21 236	High exposure workplace, AMI: SMR = 0.095 (0.9–1.0)	Johansen & Olsen, 1998b
Male utility workers, employed 6 months between 1950–1986, followed - 1988	Cohort SMR and internal comparisons	Duration of work in jobs with elevated EMF	CVD mortality	CVD deaths: 6802 Cohort: 138 903	Highest μT-year category, AMI: RR = 1.62 (1.45–1.82) Chronic CHD: RR = 1.0 (0.86-1.77)	Savitz et al., 1999
Male utility workers, employed 3 months between 1990–1993, followed 1974–1993	Cohort SMR	Member of cohort, classification of workplaces based on measurements	Pacemaker implantation	Implants: 135 Cohort: 24 056	Highest exposure category total SIR = 1.00 (0.6–1.5)	Johansen et al., 2002

Table 60. Continued

Male utility workers in Kelsh & Sahl, 1997	Cohort SMR and internal comparisons	Duration of work in jobs with elevated EMF	CVD mortality	AMI deaths: 407 CCHD deaths: 369 Cohort: 35 391	Highest μT-year category, AMI: RR = 0.99 (0.65–1.51) Chronic CHD: RR = 1.19 (0.79–1.77)	Sahl et al., 2002
Swedish twins responding to job questionnaire in 1967 or 1973	Cohort Cox analysis	Job-exposure matrix	CVD mortality	Twin cohort: 27 790	Highest exposure group, AMI: RR = 1.3 (0.9–1.9)	Håkansson et al., 2003
Male population of Stockholm 1992–1993	Population-based case-control	Job titles, job-exposure matrix	AMI morbidity	695 and 1133 cases and controls	Highest exposure category: RR = 0.57 (0.36–0.89)	Ahlbom et al., 2004
Utility workers, employed 6 months between 1973–1982, followed – 1997	Cohort SMR and internal comparisons	Duration of work in jobs and locations with elevated EMF	CVD mortality	CVD deaths: 6802 Cohort: 79 972	Highest μT-year category, AMI: RR = 1.03 (0.88–1.21) Chronic CHD: RR = 0.92 (0.73-1.16)	Sorahan & Nichols, 2004

8.3 Discussion

8.3.1 Heart rate variability hypothesis

Occupational exposure to electromagnetic fields has been suggested to increase the risk for cardiac arrhythmia-related conditions and acute myocardial infarction (Savitz et al., 1999). This hypothesized association between exposure to EMF and cardiovascular disorders was based on experimental data on HRV (Sastre, Cook & Graham, 1998). These experimental data were obtained in a double-blind laboratory investigation in which exposure to 20 μT of intermittent 60 Hz magnetic fields was found to reduce the normal variation of the HRV (Sastre, Cook & Graham, 1998). However, these findings have not been reproduced, and subsequent studies with volunteers did not always produce consistent results regarding HRV and exposures to magnetic fields. After conducting a multi-study analysis, it was concluded that differences in study design factors related to physiologic arousal might explain the apparent inconsistency (Graham et al., 2000d).

In addition, several prospective cohort studies have indicated that reductions in some components of the variation in heart rate increase: (1) the risk for heart disease (Dekker et al., 1997; Liao et al., 1997; Martin et al., 1987; Tsuji et al., 1996), (2) overall mortality rate in survivors of myocardial infarction (Kleiger et al., 1987; Lombardi et al., 1987; Vaishnav et al., 1994), and (3) the risk for sudden cardiovascular death (Malik, Farrell & Camm, 1990). Changed HRV reflects changed cardiac autonomic control (Akselrod et al., 1981; Willich et al., 1993), suggesting this is a possible mechanism of action of EMF exposure on the heart

Thus, while reduced HRV seems to be predictive for the development and survival from heart disease, it is difficult to explain how the mechanism underlying the transient changes in heart rate variability seen in healthy young men after EMF exposure in controlled settings (Graham et al., 2000a; Sastre, Cook & Graham, 1998; Tabor, Michalski & Rokita, 2004) can also explain deaths from arrhythmia and infarction many years after long-term occupational exposure to ELF fields. Furthermore, the influence of EMF on HRV seems questionable.

8.3.2 Epidemiologic evidence

The biologically plausible model described above gave Savitz et al. (1999) the impetus to look at cardiovascular mortality in a cohort of utility workers. As postulated *a priori* Savitz observed an increased risk from AMI and arrhythmia related death, but not from chronic cardiovascular disease (Savitz et al., 1999). The only and limited support for the original observation comes from a study based on data from the Swedish twin registry (Håkansson et al., 2003), which observed a nonsignificantly increased risk for AMI. However, seven other studies failed to support to this hypothesis. The first three of these studies were done before the HRV hypothesis was introduced and were mainly descriptive and did not focus on cardiovascular disease. The other four studies were specifically designed to test this hypothesis from different point of views: two (Sahl et al., 2002; Sorahan & Nichols, 2004) were replications of the original study, and like Savitz et al. (1999), focused on cohorts of utility workers. One study focused specifically on arrhythmia (Johansen et al., 2002); one study investigated cardiovascular morbidity and was the first study to have detailed information on confounding factors and thus an ability to control for them (Ahlbom et al., 2004).

Thus only mortality studies of the association between occupational exposure to EMF and cardiovascular diseases have reported an association (Håkansson et al., 2003; Savitz et al., 1999). Studies of cardiovascular diseases which rely on mortality records as the measure of outcome are limited because the disease under study may not be mentioned on the death certificate, and if so, the accuracy of the diagnosis may not be correct. It is well known that death certificates do not provide the same quality of outcome measure as compared to incidence records which mainly can be obtained in disease registries or prospectively designed cohort or case-control studies. There are limitations to speculating about causal mechanisms of types of CVD as coded on death certificates of uncertain validity and reliability

(Finkelstein, 1999). A recent UK study identified inaccuracy in identifying underlying cause of death on the death certificates and difficulties in differentiating between acute and chronic cardiac causes (Mant et al., 2006). Thus, on balance, the evidence supporting an etiologic relation between occupational EMF exposures has been overturned by more focused and rigorous studies.

8.4 Conclusions

Experimental studies of both short- and long-term exposure indicate that, while electric shock is an obvious health hazard, other hazardous cardiovascular effects associated with ELF fields are unlikely to occur at exposure levels commonly encountered environmentally or occupationally. Although various cardiovascular changes have been reported in the literature, the majority of effects are small and the results have not been consistent within and between studies. With one exception, none of the studies of cardiovascular disease morbidity and mortality has shown an association with exposure. Whether a specific association exists between exposure and altered autonomic control of the heart remains speculative. Overall, the evidence does not support an association between ELF exposure and cardiovascular disease.

9 IMMUNE SYSTEM AND HAEMATOLOGY

Haematology is the branch of medicine that is concerned with blood, the blood-forming organs and blood diseases. Studies encompass the growth and development of the leukocyte (white blood cell) populations that form part of the immune system in addition to the erythrocyte (red cell) populations and the non-cellular serum constituents such as serum iron and serum alkaline phosphatase concentrations. Haemopoiesis, the formation of blood cells, occurs primarily in bone marrow, where there is progressive division and maturation from stem cells through to the formation of mature erythrocytes and leukocytes. Erythrocytes and leukocytes circulate in the bloodstream, from which cell populations and other haematological parameters may be readily sampled. However, there is a continual and active exchange of leukocytes with other body compartments such as the lymphoid system. In the adult human body, for example, only about 2% of the total lymphocyte pool is present in the blood and the lymphocyte subset composition can be varied by a number of different factors including disease. Few studies have examined ELF effects either on immune system function or on heamatology. The tables below summarize the results of studies conducted on the immune system and haematology. Only the more significant ones are discussed in the text.

9.1 Immune system

The immune system identifies and responds to invading microorganisms such as viruses, bacteria, and various single-celled or multicellular organisms, and to "foreign" macromolecules including proteins and polysaccharides. Thus, it serves to protect individuals from infectious diseases and can also act against tumour cells, although these responses are fairly weak. Immunological responses are mediated through intercellular signalling pathways via chemical messengers such as cytokines and interleukins.

The first line of defence against pathogens is sustained by relatively nonspecific (natural or innate) parts of the immune system. These are natural killer (NK)-cells, mononuclear phagocytes and granulocytes. The protein "complement system" mediates many of the cytolytic and inflammatory effects of humoral (non-cell-mediated) immunity. These innate responses are followed by the adaptive (or aquired) antigen-specific responses of the immune system. The cells that mediate the antigen-specific (or acquired) responses are the B-lymphocytes, which secrete antibodies (humoral immunity) that circulate in body fluids, and the T-lymphocytes, that can function as cytotoxic cells (cell-mediated immunity) or as helper T-cells which assist in B- or T-cell activation. Activated cytotoxic T-lymphocytes specifically recognise and kill cells having foreign molecules on their surface and are implicated in anti-tumour responses. The acquired immune responses also involve the recruitment and amplification of the responses of the innate parts of the immune system.

9.1.1 Human studies

Selmaoui, Lambrozo & Touitou (1996) showed that a one-night (23.00 to 08.00) exposure to either continuous or intermittent (1 hour off and 1 hour with on/off switching every 15 s) 50-Hz, 10-T magnetic fields did not affect immunological parameters (CD3-, CD4-, CD8-lymphocytes, NK-cells and B-cell populations) in 16 healthy men aged 20–30 years as compared to 16 healthy sham-exposed men.

In 2000, Tuschl et al. (2000) published some results on immune parameters of ten workers exposed to the magnetic fields associated with induction heaters (50–600 Hz, up to 2 mT, or 2.8–21 kHz, 0.13–2 mT, for at least two years). Overall, there were no differences between exposed and control subjects in the levels of B- and T-cells, cytokines and immunoglobulins. However, the numbers of NK-cells and oxidative bursts of monocytes, implicated in cytotoxic responses were significantly increased in the exposed group while monocytes had significantly reduced phagocytic activity compared with those from unexposed personnel. The authors considered that overall the non-specific immunity of the exposed subjects was normal and that the most peculiar finding was the increase in NK-cell population.

Recently, the Mandeville group has reported effects of 60 Hz magnetic fields on 60 workers of power utilities (Ichinose et al., 2004). They monitored the activity of ornithine decarboxylase (ODC) in white blood cell, the activity of NK-cells, lymphocyte phenotypes, and differential cell counts. They monitored exposure over three consecutive days before collecting peripheral blood. There was no alteration of NK-cell activity nor of the number of circulating neutrophils, eosinophils, basophils, or T-lymphocytes. However, there was an association between exposure intensity and a decreased ODC activity and lower NK-cell counts.

The production of melatonin, which is known to stimulate the immune system, was quantified on the night preceding immune marker determinations. While no alteration in melatonin levels could be observed in the exposed subjects, the decrease in ODC activity, counts of NK- and B-cells, and monocytes were strongest for the workers with lowest melatonin production. According to the authors, the health consequences associated with these changes are not known.

Using a cross-section approach, Chinese scientists investigated the effects of ELF fields on the immune system. Zhu and coworkers (2002; 2001) systematically explored its effects on red blood cell, platelets and white blood cells of peripheral blood taken from people who were working with the electric railway system. They reported that the fields (50 Hz, 0.01–0.938 mT, or 0–12 kV m^{-1}) decreased the number of white blood cells and the level of IgA and IgG (Immunoglobulins A and G) antibodies. They also found that the percentage of lymphocytes showing DNA damage was higher in the exposed group than in the control group. The authors concluded that ELF fields might induce DNA damage in lymphocytes, then cause apoptosis

of these cells, and further result in the decrease of cell number and immunoglobulin level in the blood.

Dasdag et al. (2002) compared blood cell counts, hematocrit and lymphocyte surface antigens of a group of 16 welders with that of a group of 14 healthy male control subjects. Although CD4 and CD8 levels were decreased in the welders and the hematocrit increased, the authors concluded that the differences were not clinically significant and that the results were not suggestive of an ELF effect on immunologic parameters.

Table 61 summarizes the studies on immune responses in humans exposed to ELF fields.

Table 61. Immune system responses in humans

Test	Exposure	Results	Comments	Authors
Numbers of CD3+, CD4+, CD8+ lymphocytes, of NK- cells and B-cells Healthy young men exposed: n=16 sham-exposed: n=16	50 Hz 10 µT Continuous or intermittent (1 h off, 1 h with on/off switching every 15 s) Exposure for one night (23:00 to 08:00).	No effect with either exposure protocol.	Well controlled study. Low power.	Selmaoui, Lambrozo & Touitou, 1996
Number of B- and T-cells, levels of cytokines and immunoglobulins Numbers of NK cells and oxidative bursts of monocytes Monocyte phagocytic activity Workers exposed to induction heaters (n=10)	50–600 Hz up to 2 mT or 2.8–21 kHz 0.13–2 mT Exposure for at least two years	No effect on B- and T-cells, cytokines and immunoglobulins. Increase in NK cells and in bursts of monocytes. Decreased phagocytic activity.		Tuschl et al., 2000
Activity of ornithine decarboxylase (ODC) in white blood cells Activity of NK cells Lymphocyte phenotypes Differential cell counts Power-utility workers (n=60)	60 Hz Personal magnetic field monitor for 3 consecutive working days	Decreased ODC activity. No alteration of NK activity. No change in number of circulating neutrophils, eosinophils, basophils, and T-lymphocytes, lower NK-cell counts		Ichinose et al., 2004

Table 61. Continued

Numbers of blood cells, levels of immunoglobulins, levels of DNA damage in lymphocytes (comet assay) Daily exposed workers: n=192 Unexposed control workers: n=106	50 Hz 0-12 kV m^{-1}, 0.01-0.92 mT 4.59±2.64 h / day, 9.72±3.09 year	Increase in red blood cells, platelets, and haemoglobin. Decrease in white blood cells and lymphocytes. Decrease in IgA and IgG. Increase in DNA damage of lymphocytes.		Zhu, Way & Zhu, 2001
Numbers of blood cells, levels of immunoglobulins, levels of DNA damage in lymphocytes (comet assay) Daily exposed workers: n=33 Unexposed control workers: n=106	50 Hz 1.69-3.25 kV m^{-1}, 0.245-0.938 mT 4.59±2.64 h / day, 9.4±3.2 year	Increase in red blood cells and platelets. Decrease in white blood cells and lymphocytes. Decrease in IgA and IgG. Increase in DNA damage of lymphocytes.	Extension of Zhu et al., 2001	Zhu et al., 2002
Red blood cells; hemoglobin; hematocrit; platelets; total white blood cells; neutrophils; lymphocytes; eosinophils; and CD3, CD4, CD8, and CD4/CD8 Male welders: n=16 Male controls: n=14	Welders exposed 3-4 hours per day per week and for at least 10 years	CD4, CD8 lower, hematocrit higher in welders. Differences “not clinically significant”.		Dasdag et al., 2002

9.1.2 Animal studies

Animal studies have been carried out using several approaches: some authors have examined the responsiveness of the whole immune system, while other used blood cell counts and standard in vitro tests on cells taken from the peripheral blood or spleen of exposed animals. This section discusses all experiments done with exposure of the animals even if the tests on their immune cells were done in vitro. Many of these studies have been previously reviewed by ICNIRP (2003) and the general conclusion was that “there is little consistent evidence on any inhibitory effect of power-frequency EMF exposure on various aspects of immune system function”.

The Löscher group (Mevissen et al., 1996) had reported a decreased spleen T-lymphocyte proliferation in rats chronically exposed to 50 Hz magnetic fields. In a follow-up study, the same authors (Mevissen et al., 1998) found that this proliferation was initially increased, after 2 weeks, but then decreased, after 13weeks, compared to sham-exposed animals.

Later, the same group (Häussler et al., 1999) reported on two independent experiments on the ex vivo production of interleukins (ILs) by mitogen-stimulated splenic lymphocytes from female Sprague-Dawley rats exposed to 100 μT 50 Hz magnetic fields. In the first experiment, the rats were treated with DMBA and exposed or sham-exposed for 14 weeks. There was no difference between exposed and sham-exposed groups in the level of production of IL-1 by mitogen-activated splenic B-cells. In the second experiment, rats were exposed for 1 day, 1 week, or 2 weeks, followed by collection and activation of spleen lymphocytes. There was no difference in IL-1 or IL-2 production from stimulated B- or T-cells. According to the authors, these negative findings suggested that the reported changes in T-cell proliferation in response to magnetic field exposure (Mevissen et al., 1996; 1998) was not mediated via alterations in IL production.

In another experiment, Thun-Battersby, Westermann & Löscher (1999) exposed female Sprague-Dawley rats to a 50 Hz, 100 μT field for periods of 3 or 14 days or 13 weeks. They performed analyses of T-lymphocyte subsets and other immune cells: NK- cells, B-lymphocytes, macrophages, and granulocytes in blood, spleen and mesenteric lymph nodes. They also detected proliferating and apoptotic cells in the compartments of spleen tissue. No effect was found on different types of leukocytes, including lymphocyte subsets for any of the exposure durations. The authors concluded that exposure did not affect lymphocyte homeostasis, but did not exclude that functional alterations in T-cell responses to mitogens and in NK-cell activity, as described in some studies of exposed rodents, may be one of the mechanisms involved in the carcinogenic effects of magnetic field exposure observed in some models of co-carcinogenesis, such as the DMBA model used by this group.

A number of tests of NK-cell activity have been carried out, mainly on exposed mice. House et al. (1996) reported that the NK-cell activity of young B6C3F(1) female mice was reduced in some experiments after exposure to continuous or intermittent 60 Hz magnetic fields (2–1000 μT) but not in male mice nor in male or female rats. The authors later did the experiment with older female mice, and observed a similar decrease in NK-cell activity at 1000 μT but not at the lower field intensities (House & McCormick, 2000). They concluded that the inhibition of NK-cell activity caused by exposure was consistent across their experiments but had little biological significance, as it was not associated with an increase in neoplasms in separate investigations with the same type of exposure.

Arafa et al. (2003) investigated the bioeffects of repeated exposure to 50 Hz high-strength (20 mT) magnetic fields on some immune parameters in mice. The animals were exposed daily for 30 minutes three times per week for 2 weeks. Immune endpoints included total body weight, spleen/body weight ratio, splenocytes viability, total and differential white blood cell (WBC) counts, as well as lymphocyte proliferation induced by phytohaemagglutinin, concanavalin-A and lipoploysaccharide. Magnetic field

exposure decreased splenocyte viability, WBC count, as well as mitogen-induced lymphocyte proliferation (by approximately 20%).

The authors also tested the effects of two distinct anti-radical compounds: L-carnitine and Q10. Both drugs were given 1 h prior to each ELF exposure. L-carnitine, but not Q10 attenuated the adverse effects of exposure on the vast majority of the immune parameters tested. It was speculated by the authors that the effect of L-carnitine was due to its anti-ROS properties.

Ushiyama & Ohkubo (2004) and Ushiyama et al. (2004) studied the acute and subchronic effects of whole-body exposure to 50 Hz magnetic field on leukocyte-endothelium interaction using a dorsal skinfold chamber technique in conscious BALB/c mice. They perfomed an acute exposure experiment by exposing for 30 min at 0, 3, 30 and 30 mT and a subchronic exposure experiment by continuous exposure for 17 days at 0, 0.3, 1 and 3 mT. The intra-microvascular leukocyte adherence to endothelial cells significantly increased at 30 mT in the acute exposure and at 3 mT in the subchronic exposure conditions. In a companion study Ushiyama et al. (2004), however, they failed to find changes in serum tumour necrosis factor-α (TNF-α) and IL-l β levels under exposure to subchronic exposure to 30 mT.

The effect of long-term exposure to ELF electric and magnetic fields on the thymocytes of rats was studied by Quaglino et al. (2004). The 2-month-old Sprague-Dawley rats were exposed or sham exposed for 8 months to 50 Hz fields (1 kV m^{-1}, 5 μT or 5 kV m^{-1}, 100 μT). Simultaneous exposure to continuous light and ELF fields did not change significantly the rate of mitoses compared to sham-exposed rats, but the amount of cell death was significantly increased. The conclusion of the authors was that, in vivo, stress, such as that caused by continuous exposure to light and ELF exposure can act in synergy to cause a more rapid involution of the thymus and suggested that this could be responsible for an increased susceptibility to the potentially hazardous effects of ELF-EMF.

Table 62 summarizes the studies on immune system responses found in experimental animals.

9.1.3 Cellular studies

Jandova et al. (1999; 2001) found that the adherence of leukocytes taken from cancer patients to solid surfaces (such as glass surfaces or plastic materials) was increased after 1 hour of exposure to a 50 Hz sinusoidal magnetic field (1 mT and 10 mT), while it was decreased in T-lymphocytes taken from healthy donors. The leukocyte surface properties manifest cell-mediated immunity, since, in the presence of antigens, leucocytes taken from cancer patients exhibit less adherence than leucocytes from healthy humans. The authors concluded that the response of cell-mediated immunity was altered by external magnetic field exposure and hypothesized about different biophysical mechanisms, among which were the free radical reactions.

Table 62. Immune system responses in animals

Biological endpoint	Exposure conditions	Results	Comments	Authors
T-cell proliferation				
Spleen lymphocyte proliferation Swiss-Webster mice	60 Hz 100 kV m^{-1} 90–150 days	No effect.		Morris & Phillips, 1982
Spleen T-lymphocyte proliferation Sprague-Dawley rats	50 Hz 50 µT 13 weeks	Decreased T-cell proliferation		Mevissen et al., 1996
Spleen T-lymphocyte proliferation Sprague-Dawley rats	50 Hz 100 T 13 weeks	Increase in T-cell proliferation after 2 weeks; decrease after 13 weeks; no effect on B-cells		Mevissen et al., 1998
Peripheral blood lymphocyte proliferation Baboons	Pilot study: 60 Hz 9 kV m^{-1}, 20 µT 5 weeks Main study: 60 Hz 30 kV m^{-1}, 50 µT 5 weeks	Reduced B-lymphocyte response in pilot study. No effect in main study.	Considerable heterogeneity in results of sham exposed animals.	Murthy, Rogers & Smith, 1995
T-cell function				
Ex vivo production of interleukins (ILs) by mitogen-stimulated splenic lymphocytes Female Sprague-Dawley rats treated with DMBA	50 Hz 100 µT 14 weeks 1 day, 1 week, 2 weeks	No effect on production of IL-1. No difference in IL-1 or IL-2-production by stimulated B- or T-cells.		Häussler et al., 1999

Table 62. Continued

T-lymphocyte subsets; NK-cells, B-lymphocytes, macrophages and granulocytes in blood, spleen and mesenteric lymph nodes; proliferating and apoptotic cells in the compartments of spleen tissue Sprague-Dawley rats	50 Hz 100 µT 3 or 14 days or 13 weeks.	No effects.		Thun-Battersby, Westermann & Löscher, 1999
Delayed-type hypersensitivity to oxazolone B6C3F1 mice	60 Hz 2, 200, 1000 µT continuous, 1000 µT intermittent (1 h on/off) 13 weeks	No consistent effect.	Generally well described study.	House et al., 1996
Resistance to Listeria monocytogenes infection Mice (BALB/C)	60 Hz 2, 200, 1000 µT continuous, 1000 µT intermittent (1 h on/off) 4 or 13 weeks	No effect.	Experimental and control data not shown.	House et al., 1996
Long-term effects on IL-1 and IL-2 activity Sheep	60 Hz transmission lines 1.07, 3.5 µT 12–27 mo	No effect.		Hefeneider et al., 2001
NK-cell activity				
Spleen and blood NK cells SENCAR mice treated with DMBA and TPA	60 Hz 2 mT 6 h / day, 5 days / week, 21 weeks	No significant effect.		McLean et al., 1991

Table 62. Continued

Spleen natural killer cells BALB/C mice	0.8 Hz (pulsed) 10–120 mT 10 h / day, 5 days	Enhanced activity at 30 mT and above.		de Seze et al., 1993
NK-cell activity Young mice and rats	60 Hz 2–1000 µT, continuous or intermittent	Reduced NK-cell activity in some experiments in female mice but not in male mice nor in male or female rats.	Generally well described study, replicate experiments.	House et al., 1996
NK-cell activity Older mice	Repeat of above study	Reduced NK-cell activity.		House & McCormick, 2000
Spleen NK-cells F344 rats	60 Hz 2, 200, 1000 µT continuous, 1000 µT intermittent (1 h on/off) 6 or 13 weeks	No consistent effect in males or females.	Generally well described study, replicate experiments.	House et al., 1996
Spleen NK-cells F344 rats	60 Hz 20 µT–2 mT 20 h / day, 6 weeks	Trend for enhanced activity with exposure.	Fully described study; but significant effects with control rather than sham comparison.	Tremblay et al., 1996
Macrophage activity				
Peritoneal macrophages F344 rats	60 Hz 20 µT–2 mT 20 h / day, 6 weeks	Trend for enhanced hydrogen peroxide release with exposure.	Fully described study; but significant effects with control rather than sham comparison.	Tremblay et al., 1996
Antibody cell activity				
Circulating antibody levels to keyhole limpet haemocyanin Immunised Swiss Webster mice	60 Hz 100 kV m^{-1} 30 or 60 days	No effect.		Morris & Phillips, 1982

Table 62. Continued

Antibody-forming spleen cells Immunised BALB/C mice	60 Hz 500 µT 5 h on three alternate days	No effect.		Putinas & Michaelson, 1990
Antibody-forming spleen cells Immunised BALB/C mice	0.8 Hz (pulsed) 10–120 mT 10 h / day, 5 days	No effect.		de Seze et al., 1993
Antibody-forming spleen cells Immunised B6C3F1 mice	60 Hz 2, 200, 1000 µT continuous 1000 µT intermittent (1 h on/ off) 3 or 13 weeks	No effect.	Generally well described study; positive controls.	House et al., 1996
Body weight, spleen/body weight ratio, splenocytes viability, total and differential WBC counts, lymphocyte proliferation induced by PHA, Con-A and LPS Effect of anti-radical compounds L-carnitine and Q10 Mice	50 Hz 20 mT 30 min / day, 3 days /week, 2 weeks	Decreased splenocyte viability, WBCs count, and mitogen-induced lymphocyte proliferation. Only L-carnitine attenuated the effects of exposure.		Arafa et al., 2003
Leukocyte-endothelial interaction BALB/c mice	50 Hz 0, 3, 10 and 30 mT 30 min	Increased leukocyte adherence at 30 mT.		Ushiyama & Ohkubo, 2004
Leukocyte-endothelial interaction; serum TNF-alpha and IL-I beta BALB/c mice	50 Hz 0, 0.3, 1 and 3 mT continuous for 17 days	Increased leukocyte adherence at 3 mT, no change in serum TNF-alpha and IL-I beta levels.		Ushiyama et al., 2004
Rate of mitosis in thymocytes 2-month-old Sprague-Dawley rats	50 Hz 1 kV m^{-1}, 5 µT 5 kV m^{-1}, 100 µT 8 months	No change in rate of mitoses; cell death significantly increased.		Quaglino et al., 2004

Ikeda et al. (2003) studied the immunological functions of human peripheral blood mononuclear cells (PBMCs) from healthy male volunteers. They assessed the activities of NK and lymphokine activated killer (LAK) cells and the production of interferon-γ (IFN-γ), tumour necrosis factor-α (TNF-α), interleukin-2 (IL-2), and interleukin-10 (IL-10). The PBMCs were exposed for 24 hours to linearly (vertical), or circularly, or elliptically polarised fields, at 50 and 60 Hz (2–500 μT for the vertical field and 500 μT for the rotating fields). They found no effect of exposure on the cytotoxic activities and the cytokines production of human PBMCs.

The Simko-group in Germany has been very active in recent years studying the effects of 50 Hz, 1 mT magnetic fields on various immune cells. The effects on the production of free radicals was studied by Lupke, Rollwitz & Simko (2004) in monocytes from the blood of human umbilical cord and in human Mono Mac6 cells. In monocytes a significant increase of superoxide radical anion production was observed (up to 40%) and an increase in ROS release (up to 20%) upon 45-min exposure of monocytes. The increases were even larger in Mono Mac6 cells.

Rollwitz, Lupke & Simko (2004) gave some evidence of the cell-activating capacity of ELF magnetic fields by reporting a significant increase in free radical production after exposure of mouse bone marrow-derived (MBM) promonocytes and macrophages. The superoxide anion radicals were produced in both types of cells. The authors suggested that the NADH-oxidase pathway was stimulated by exposure, but not the NADPH pathway.

The same research group (Simko & Mattsson, 2004) has concluded that some of the effects of ELF magnetic field exposure might be caused by increasing levels of free radicals. They considered four different types of processes: (i) direct activation of macrophages (or other immune cells) by short-term exposure leading to phagocytosis (or other cell specific responses) and consequently, free radical production, (ii) exposure-induced macrophage activation including direct stimulation of free radical production, (iii) increase in the lifetime of free radicals under exposure leading to long-term elevation of free radical concentrations, (iv) long-term exposure leading to a durable increase in the level of free radicals, subsequently causing an inhibition of the effects of the pineal gland hormone melatonin. However, there are no well-established data showing that free radical production is affected by ELF magnetic field exposure.

Table 63 summarizes the results of ELF in vitro studies on immune system responses.

Table 63. Immune system in vitro studies

Biological endpoint	Exposure conditions	Results	Authors
Adherence assay Leukocytes taken from venous blood of normal donors and cancer patients	50 Hz 1 and 10 mT (measurements gave 1.02 and 9.52 mT, respectively) 1 h Test tubes placed in the center of a coil. Exposure performed at 37°C. Sham exposure not mentioned.	Decreased adherence in normal leukocytes which normally are adherent. Increased adherence in cancer leukocytes that are usually not adherent to solid surfaces. Similar effect for longer exposure duration (2, 3 and 4 h tested but no data shown).	Jandova et al., 1999; 2001
Several CD markers and transcription and expression of CD4.	50 Hz 24, 48, 72 h	Slight effect on CD4, CD14 and CD16 receptor expression, other CD receptors not affected.	Conti et al., 1999
Peripheral blood mononuclear cells CD4 expression	50 Hz, pulsed (2 msec. impulse duration) generated by a BIOSTIM apparatus 1.5 mT 24, 48 and 72 hours	DNA CD4+ expression increased mRNA CD4+ expression increased in resting cells exposed for 24 h, but not 48 or 72 h Increase in percentage cell cycle progression in S phase	Felaco et al., 1999
Activity of NK and LAK cells; production of IFN-gamma, TNF-alpha, IL-2, and IL-10 PBMCs from healthy male volunteers	50 and 60 Hz linearly (vertical), circularly, or elliptically polarised magnetic fields 2–500 µT (vertical field) 500 µT (rotating fields) 24 h	No effects.	Ikeda et al., 2003
Monocytes from blood of human umbilical cord and human Mono Mac6 cells Production of free radicals	50 Hz 1 mT 45 min	Increase in superoxide radical anion production in monocytes; increase in ROS release upon 45-min exposure of monocytes (larger in Mono Mac6 cells).	Lupke, Rollwitz & Simko, 2004
Mouse bone marrow-derived (MBM) promonocytes and macrophages Production of free radicals	50 Hz 1 mT 45 min to 24 hours	Increase of free radical production: superoxide anion radicals were produced in both types of cells.	Rollwitz, Lupke & Simko, 2004

9.2 Haematological system

Haematological parameters include: leukocyte and erythrocyte counts, haemoglobin concentration, reticulocyte and thrombocyte counts, bone marrow cellularity and prothrombin times, serum iron and serum alkaline phosphatase concentrations and serum triglyceride values. Most studies have included assessments of the differential white blood cell count, that is, the overall concentration of white cells (leukocytes) and their various subgroups. However, the importance of small alterations of the levels of circulating leukocytes is not clear as there is a continual and active exchange with other body compartments such as the lymphoid system which can be affected by a number of different factors including disease.

9.2.1 Human studies

Very few studies have been performed on volunteers and none in recent years.

Selmaoui et al. (1996) exposed or sham exposed 32 male volunteers to 10 μT, 50 Hz horizontally polarised magnetic fields between 23.00 and 08.00 on two separate days. Blood samples were taken from each subject at 3-hourly intervals from 11.00 to 20.00 and hourly from 22.00 to 08.00. One month later, the exposed group was subjected to an intermittent 10 μT, 50 Hz magnetic field between 23.00 and 08.00. In the intermittent regimen, the magnetic field was turned on for one hour and off for the next hour; during the on-period, the field was cycled on and off every 15 s. Counts of all cell types showed a strong circadian rhythm with the possible exception of neutrophils and NK-cells; However, values in the group exposed continuously and in those exposed intermittently were always very similar to values in the sham exposed groups. Moreover, inter- and intra-individual variations were so high that small effects due to exposure were unlikely to be detected.

Bonhomme-Faivre et al. (1998) monitored a few subjects exposed for 8 hours per day for more than 1year in their hospital laboratory to 50 Hz, 0.2–6.6 μT magnetic fields. CD3 and CD4 lymphocyte counts were significantly lower than those measured in six control workers, but NK-cell counts were increased. Since exposure levels were measured at ankle level, the whole-body exposure of the individuals was unknown and no health consequences could be attributed to field exposure.

These studies are summarized in Table 64.

9.2.2 Animal studies

Boorman et al. (1997) exposed Fischer 344/N rats and B6C3F1 mice to 60 Hz magnetic fields (2200 and 1000 μT) for 8 weeks (18.5 h per day, 7 days per week). An additional group of rats and mice was exposed intermittently (1 h on and 1 h off) to 1000 μT magnetic fields. There were no haematological alterations that could be attributed to magnetic field exposure.

Table 64. Human haematological studies

Biological endpoint	Exposure conditions	Results	Comments	Authors
Counts of all blood cell types	50 Hz 10 μT 23.00 to 08.00 on two separate days	No effect but strong inter and intra-individual variations.	Well controlled study. Low power.	Selmaoui et al., 1996
CD3 and CD4 lymphocytes and NK counts	50 Hz 0.2–6.6 μT at ankle level 8 h / day, 1 year	Decrease in CD3 and CD4 and increase in NK cells.	Dosimetry not provided. Low number of subjects (6 exposed, 6 controls).	Bonhomme-Faivre et al., 1998

Zecca et al. (1998) assessed haematological variables before exposure and at 12-week intervals during exposure up to 32 weeks. Male Sprague-Dawley rats (64 animals per group) were exposed for 8 h per day, 5 days per week for 32 weeks at 50 Hz (5 μT and 1 kV m^{-1}, and 100 μT and 5 kV m^{-1}). Blood samples were collected at 0, 12, 24, and 32 weeks. No pathological changes were observed under any exposure conditions in animal growth rate, in morphology and histology of the tissues collected from the liver, heart, mesenteric lymph nodes, testes and bone marrow or in serum chemistry.

Three studies were performed by Korneva et al. (1999) in male CBA mice exposed to 50 Hz, 22 μT magnetic fields for 1 h, at the same time of day, for 5 successive days. In the first study, spleen colony formation was examined and the number of colony-forming units was not higher than in sham-exposed animals. Significant changes were seen in the thymus weight and thymus index of exposed animals when compared to sham-exposed animals. In a second study, mice were given a sublethal dose of X-rays (6 Gy) followed 2 h later with the same magnetic field exposure as above. The number of colonies per spleen showed a consistent, significant increase with exposure and the number of colony forming units per femur was decreased. In the third study, bone marrow was taken from mice that had been exposed in still the same way, and injected into mice that had been exposed to a lethal dose of X-rays (9 Gy). The number of colony forming units per femur in the recipient mice was significantly reduced at days 1 and 4 after injection.

A summary of these studies is presented in Table 65.

Table 65. Animal haematological studies

Biological end-point	Exposure conditions	Results	Comments	Authors
Differential white blood cell count Swiss-Webster mice and Sprague-Dawley rats	60 Hz 100 kV m^{-1} 15 (rats only), 30, 60 or 120 days	No consistent effects seen in replicate studies.	Replicate studies; some results variable.	Ragan et al., 1983
Differential white blood cell and bone marrow progenitor cell count CBA/H mice	50 Hz 20 mT 7 days	No effect.		Lorimore et al., 1990
Splenic lymphocyte subgroup analysis B6C3F1 mice	60 Hz 2, 200, 1000 µT continuous 1000 µT intermittent (1 h on/off) 4 or 13 weeks	No effect.	Generally well described study.	House et al., 1996
Differential white blood cell count F344 rats	60 Hz 20 µT–2 mT 20 h / day, 6 weeks	Trend for reduced T-cell count with exposure; reduced total, cytotoxic and helper T-cells.	Fully described study; significant effects with control rather than sham comparison.	Tremblay et al., 1996
Differential white blood cell count Sprague-Dawley rats	50 Hz 100 µT 3 days, 14 days or 13 weeks	No effect.	Extensive lymphocyte sub-set analysis.	Thun-Battersby, Westermann & Löscher, 1999
Differential white blood cell count Baboons	Pilot study: 60 Hz 9 kV m^{-1}, 20 µT 5 weeks Main study: 60 Hz 30 kV m^{-1}, 50 µT	Reduced helper T-lymphocyte count in pilot study; no effect in main study.	Considerable heterogeneity in sham exposed results.	Murthy, Rogers & Smith, 1995
Haematology Fischer rats and B6C3F1 mice	60 Hz 1000 or 2200 µT continuous 1000 µT Intermittent (1 h on, 1 h off) 18.5 h / day, 7 days / week, 8 weeks	No effect.		Boorman et al., 1997

Table 65. Continued

Blood cells count before exposure, at 12, 24 and 32 weeks of exposure Morphology and histology of different organs (liver, heart, mesenteric lymph nodes, testes, bone marrow) Groups of 64 rats sham-exposed	50 Hz 5 µT, 1 kV m^{-1} 100 µT, 5 kV m^{-1} 8 h / day, 5 days / week, 32 weeks	No effects.	Zecca et al., 1998
Spleen colony formation Bone marrow injected to mice exposed to 9 Gy X-rays Male CBA mice	50 Hz 22 µT 1 h / day, same time of day, 5 successive days 6 Gy X-rays followed after 2 h by same exposure as above	No effect of EMF alone. Increase in number of colonies per spleen; decrease in colony forming units per femur. Number of colony forming units per femur significantly reduced in the recipient mice.	Korneva et al., 1999
Total and differential white blood cell counts Mice	50 Hz 20 mT 30 min / day, 3 days / week, 2 weeks	Decreased white blood cells count.	Arafa et al., 2003

9.2.3 Cellular studies

Only one paper has been published recently on the effects on cells of the haematopoietic system: Van Den Heuvel et al. (2001) studied the effects of 50 Hz, 80 µT magnetic fields on the proliferation of different types of stem cells, including haemopoietic cells. The cytotoxic effects of exposure were investigated on the proliferation of undifferentiated murine 3T3 cells using the neutral red test. Magnetic fields had no cytotoxic effect on this cell line.

When exposed to the same fields, a reduction in the proliferation and differentiation of the granulocyte-macrophage progenitor (CFU-GM) grown from the bone marrow of male and female mice was shown compared to non-exposed cells. Stromal stem cell proliferation (CFU-f) from female mice showed a reduction while CFU-f from male mice did not decrease. The authors concluded that these effects on CFU-f are equivocal.

Table 66 summarizes the results of ELF in vitro studies.

Table 66. Cell proliferation studies

Biological endpoint	Exposure conditions	Results	Authors
Cell numbers and colony following efficiency Mouse haemopoetic progenitor cells FDCP mix A4	Nulled fields, 50 Hz vertical fields, Ca2+ ion cyclotron resonance conditions at 50 Hz 0.006, 1 and 2 mT 2 hours immediately after seeding 1, 4 or 7 days, one hour after seeding	No effects.	Reipert et al., 1997
Cell number K562 myeloid leukaemia cells	50 Hz 0.2–200 µT up to 24 h	No effects.	Fiorani et al., 1992
^{3}H-thymidine uptake CCRF-CEM human lymphoblastoid cells	72 Hz pulsed 3.5 mT 0.5–24 h	No effects.	Phillips & McChesney, 1991
Proliferation Stem cells Undifferentiated murine 3T3 cells	50 Hz 80 µT 4 days	No effects.	Van Den Heuvel et al., 2001
Proliferation and differentiation of the granulocyte-macrophage progenitor	50 Hz 80 µT 7 days	Reduction in proliferation and differentiation.	Van Den Heuvel et al., 2001
Stromal stem cell proliferation	50 Hz 80 µT 10 days	Decrease in female mice and no change in male mice.	Van Den Heuvel et al., 2001

9.3 Conclusions

Evidence for the effects of ELF electric or magnetic fields on components of the immune system is generally inconsistent. Many of the cell populations and functional markers were unaffected by exposure. However, in some human studies with fields from 10 µT to 2 mT, changes were observed in natural killer cells, which showed both increased and decreased cell numbers, and in white blood cell counts, which showed no change or decreased numbers. In animal studies reduced natural killer cell activity was seen in female, but not male mice or in rats of either sex. White blood cell counts also showed inconsistency, with decreases or no change reported in different studies. The animal exposures had an even broader range of 2 µT to 30 mT. The difficulty in interpreting the potential health impact of these data is due to the large variations in exposure and environmental conditions, the relatively small numbers of subjects tested and the broad range of endpoints.

There have been few studies carried out on the effects of ELF magnetic fields on the haematological system. In experiments evaluating differ-

ential white blood cell counts, exposures range from 2 μT to 2 mT. No consistent effects of acute exposure to magnetic fields or to combined electric and magnetic fields have been found in either human or animal studies.

Overall therefore, the evidence for effects of ELF electric or magnetic fields on the immune system and haematological system is considered inadequate.

10 REPRODUCTION AND DEVELOPMENT

The effects of exposure to low frequency EMFs on fertility, reproduction, prenatal and postnatal growth and development have been investigated in epidemiological and laboratory studies for a number of years. Epidemiological studies have examined reproductive outcome in relation to visual display terminal use, and to residential exposure, especially in relation to electrically heated beds. Experimentally, this issue has been addressed in studies of effects on mammalian and non-mammalian species, particularly birds. Several comprehensive reviews are available (e.g. AGNIR, 1994; Brent et al., 1993; Brent, 1999; Huuskonen, Lindbohm & Juutilainen, 1998; IARC, 2002; ICNIRP, 2003; Juutilainen, 2003; Juutilainen & Lang, 1997; McKinlay et al., 2004; NIEHS, 1998).

10.1 Epidemiology

10.1.1 Maternal exposure

10.1.1.1 Video display terminals

A number of epidemiological studies have investigated possible association of adverse pregnancy outcome with the use of video display terminals during pregnancy (for reviews, see Brent et al., 1993; Delpizzo, 1994; IARC, 2002; Juutilainen, 1991; Parazzini et al., 1993; Shaw, 2001; Shaw & Croen, 1993). The electromagnetic fields emitted by video display terminals include ELF as well as higher frequencies up to 100 kHz. In general, these studies have not suggested increased risks for spontaneous abortion, low birth weight, pre-term delivery, intrauterine growth retardation, or congenital abnormalities. However, most of the studies did not include any measurements of ELF field exposure. The average exposure of a video display operator is typically low (around 0.1 μT), so these studies are not informative for assessing possible effects associated with higher exposures. Lindbohm et al. (1992) carried out measurements of the field emissions of displays used by the study subjects, and observed an increased odds ratio (3.4; 95% CI: 1.4–8.6) for spontaneous abortions among women who used the few video display terminal types that had unusually high ELF magnetic field emissions (> 0.9 μT peak-to-peak value). Another study that included ELF field measurements (Schnorr et al., 1991) did not report any association with field exposure. The strongest fields to which subjects were exposed in this study were weaker than those in the Lindbohm study.

10.1.1.2 Electrically heated beds

Electric blankets and electrically heated waterbeds can significantly increase exposure to ELF magnetic and electric fields, because they are used close to the body for long time periods. Electric blankets produce fields up to about 2.2 μT and the users of waterbeds are exposed to flux densities of 0.3–0.5 μT (Bracken et al., 1995; Florig & Hoburg, 1990; Kaune et al., 1987). The use of these devices may also result in increased maternal heat stress.

The first suggestion of harmful effects of electric blankets and heated waterbeds came from the study by Wertheimer & Leeper (1986). They examined seasonal patterns of foetal growth and spontaneous abortion rate among the users of heated beds, and reported that these outcomes were associated with conception in the winter months, and hence with use of bed heating. This study, however, has been criticized for several methodological shortcomings (Chernoff, Rogers & Kavet, 1992; Hatch, 1992). The findings of the studies on electrically heated beds and birth defects have been mostly negative. The use of electric blankets or heated waterbeds was not related to neural tube defects, oral cleft defects, or urinary tract defects (Dlugosz et al., 1992; Milunsky et al., 1992; Shaw et al., 1999). In the study of Li, Checkoway & Mueller (1995) electric blanket use was not associated with an increased risk of urinary tract anomalies. However, in a subgroup of women (37 cases, 85 controls) with a history of sub-fertility, an odds ratio of 4.4 was observed (95% CI: 0.9-23).

All the above studies were retrospective and assessment of exposure was usually based on self-reported data on the use of heated beds. Thus, incomplete information of exposure level (which varies between different types of electric blankets and waterbeds) and biased reporting of exposure may have influenced the findings. These difficulties were partly overcome in a prospective study (Bracken et al., 1995). In this study, exposure was estimated by measurements of magnetic fields produced by electric blankets and waterbeds and using interview data on hours of daily use. Low birth weight and intrauterine growth retardation were not related to use of electrically heated beds during pregnancy. The same group also examined the occurrence of spontaneous abortion in women who used electric blankets or electrically heated waterbeds (Belanger et al., 1998). The use of electric blankets did result in an increased risk ratio (1.8; 95% CI: 1.1–3.1), whereas the use of waterbeds or wire codes indicating elevated ELF field exposure were not associated with increased risk. In another prospective study (Lee et al., 2000), no increased risks of spontaneous abortions were found for users of electric blankets (OR = 0.8; 95% CI: 0.6–1.2) or waterbeds (OR = 1.0; 95% CI 0.7–1.3). No increase of risk with increasing setting-duration combination of electrically heated bed use was observed. The adjusted odds ratio for the twenty women who used electric blankets at high setting for 1 hour or less was 3.0 (95% CI: 1.1–8,3), but there were no spontaneous abortions among the women (n = 13) who used a high setting for 2 hours or more.

Overall, the studies on electrically heated beds have not provided convincing evidence for an association with adverse pregnancy outcomes. This view is supported by reviews from the UK Advisory Group on Non-Ionising Radiation (AGNIR, 1994) and more recently from the Health Council of the Netherlands (HCN, 2004). There is some indication of different patterns of results for waterbeds and electric blankets. For use of waterbeds during pregnancy, the risk estimates have generally been close to 1.0, while higher (and in some cases statistically significant) risk estimates have been reported for electric blankets, particularly among those women who used the high power setting of electric blankets. This pattern of results could be inter-

preted to reflect the higher magnetic fields produced by electric blankets (compared to waterbeds), or higher thermal stress experienced by the users of electric blankets.

Table 67 summarizes the results of epidemiological studies investigating various reproductive outcomes in humans exposed to different ELF sources.

Table 67. Epidemiological studies on reproductive outcome

Endpoint	Study population	Exposure (EB: electric blankets; WB: electrically heated water beds)	Relative risk (95% CI)	Authors
Miscarriage Low birth weight	673 cases, 583 controls	EB WB	not determined	Wertheimer & Leeper, 1986
Miscarriage	Prospective study, n = 2967	EB, use at conception	1.74 (1.0–3.2)	Belanger et al., 1998
		EB, use at interview	1.61 (0.8–3.2)	
		EB, high setting at conception	1.65 (0.6–4.9)	
		EB, high setting at interview	2.05 (0.7–4.7)	
		WB, use at conception	0.59 (0.3–1.1)	
		WB, use at interview	0.63 (0.4–1.1)	
		WB, high setting at conception	0.59 (0.3–1.1)	
		WB, high setting at interview	0.49 (0.2–1.1)	
Miscarriage	Prospective study, n = 5144	EB	0.8 (0.6–1.2)	Lee et al., 2000
		EB, high setting	1.6 (0.6–3.3)	
		WB	1.0 (0.7–1.3)	
		WB, high setting	1.0 (0.7–1.5)	
Low birth weight Intrauterine growth retardation	Prospective study, n = 2967	EB or WB, low setting [a]	1.2 (0.5–2.8)	Bracken et al., 1995
		EB or WB, high setting [a]	1.2 (0.6–2.5)	
		EB or WB, low setting [a]	0.8 (0.4–1.7)	
		EB or WB, high setting [a]	1.6 (1.0–2.6)	
Neural tube defects Oral cleft defects	535 cases, 535 controls	EB	0.9 (0.5–1.6)	Dlugosz et al., 1992

Table 67. Continued

		WB	1.1 (0.6–1.9)	
		EB	0.7 (0.4–1.2)	
		WB	0.7 (0.4–1.1)	
Neural tube defects	Cohort, n = 23491	EB	1.2 (0.5–2.6)	Milunsky et al., 1992
Neural tube defects	Two studies, 1455 cases, 1754 controls in total	EB (study 1)	1.8 (1.2–2.6)	Shaw et al., 1999
		EB (study 2)	1.2 (0.6–2.3)	
		WB (study 1)	1.2 (0.8–1.8)	
		WB (study 2)	1.2 (0.8–1.9)	
CLP, isolated [b]		EB	0.8 (0.5–1.5)	
		WB	1.0 (0.7–1.5)	
CLP, multiple [c]		EB	1.3 (0.5–3.4)	
		WB	1.8 (1.0–3.2)	
Urinary tract anomalies (UTA)	118 cases, 369 controls	EB	1.1 (0.5–2.3)	Li, Checko-way & Mueller, 1995
UTA, subfertile women	37 cases, 85 controls			
		WB	0.8 (0.3–2.7)	
		EB	4.4 (0.9–23)	

[a] Exposure during 3rd trimester. Odds ratios were lower for exposures estimated for earlier periods of pregnancy.

[b] Cleft lip with/without cleft palate, no other (or only minor) anomalies.

[c] Cleft lip with/without cleft palate with at least one accompanying major anomaly.

10.1.1.3 Other residential and occupational exposure

Several studies have investigated residential ELF exposures other than heated beds. Wertheimer & Leeper (1989), using an approach similar to their earlier study on electric blankets and waterbeds (Wertheimer & Leeper, 1989), reported that monthly rate of foetal loss was correlated with monthly increase of heating degree days (= need of heating) in homes with ceiling cable heat (which was reported to expose the occupants to magnetic fields of about 1 μT), but not in homes without such heating. No association with pregnancy outcome has been seen in studies that have assessed magnetic field exposure using wire codes (a method of classifying dwellings based on proximity to visible electrical installations, widely used in epidemiological studies on childhood cancer – see Chapter 11) or proximity to power lines.

Measurement-based exposure assessment has been used in five studies. One study showed a suggestive association (OR = 5.1; 95% CI: 1.0–26) between early pregnancy loss and magnetic fields above 0.63 μT measured at the front door (Juutilainen et al., 1993). The preclinical miscarriages studied by Juutilainen et al. may be etiologically different from the clinically observed miscarriages investigated in the other studies. Fields above 0.2 μT measured in residences were not associated with miscarriages, low birth weight or pre-term delivery (Savitz & Ananth, 1994). These two studies had small numbers of exposed women, and used spot measurements to characterize the magnetic field levels of the subjects' homes. Spot measurements have been shown to be correlated with personal exposure, but their use may result in significant misclassification (Eskelinen et al., 2002). A prospective study (Bracken et al., 1995) used a wrist-worn meter to assess personal average exposure during seven days. Exposure to fields above 0.2 μT was not statistically significantly associated with low birth weight or intrauterine growth retardation.

Another prospective cohort study assessed the association of personal measured ELF magnetic field exposure with spontaneous abortion (Li et al., 2001). The association with time-weighted average (TWA) magnetic field exposure was not significant. However, a significantly increased risk (OR = 1.8; 95% CI: 1.2–2.7) was found when the exposure metric used was maximum exposure above 1.6 μT. The association was stronger for early miscarriages (<10 weeks of gestation). Analysis of dose-response showed weakly rising risk with magnetic field "dose", measured as the product of field level and duration above 1.6 μT (in μTs). The association was more pronounced (OR = 2.9; 95% CI: 1.6–5.3) among those women who indicated that the measurement (by body-worn meter) had been taken on a "typical day", possibly reflecting lower exposure misclassification among these subjects. The risk was further increased for subjects who had a history of difficulties during pregnancy.

A nested case-control study with personal exposure measurements (Lee et al., 2002) reported findings that were in certain respects similar to those of Li et al. (2001). In the study by Lee et al. miscarriages did not show a significant associated with TWA magnetic fields (although a suggestive step function response was seen with higher TWA quartiles). Statistically significant associations, and dose response trends with increasing exposure quartiles, were found for two personal exposure metrics – maximum exposure and rate-of-change of the magnetic field – but the value of these metrics has not yet been established.

Lee et al. (2002) also conducted a prospective substudy of 219 participants of the same parent cohort. The results of the prospective substudy were consistent with those of the case-control study, suggesting increased miscarriage risk associated with high rate-of-change and maximum field values. Unlike the nested study results, the personal TWA exposure at home (but not total 24-h TWA exposure) showed a significantly increased risk for fields above 0.2 μT (OR = 3.0; 95% CI: 1.1–8,4).

Savitz (2002) hypothesized that the apparent association with peak exposures and magnetic field variability might be explained by lower mobility of subjects who experience nausea, which is known to be less common among women who will miscarry. In their response, Li & Neutra (2002) provided evidence against this hypothesis using data from the prospective study by Li et al. (2001). However, McKinlay et al. (2004) noted that the parameter that provided evidence of a risk – namely maximum magnetic fields – was not chosen *a priori* on the basis of aetiological plausibility (Li & Neutra, 2002). In addition, the results were sensitive to the choice of breakpoint, which was made on the basis of the observations; and the study was not a standard prospective study as more than half of the miscarriages (and all those at all strongly related to maximum field exposure) occurred before the measurements were made. McKinlay et al. (2004) also note that the compliance rate was low and the possibility of selection bias was not excluded. Analyses of four data sets from the Li et al. (2001) study indicate that the magnitude of the maximum, but not the 95th or 99th percentile, is affected by the sampling rate of the meter and the mobility of the wearer (Mezei et al., 2006). This supports the hypothesis proposed by Savitz that the differential mobility of cases and controls could affect the maximum magnetic field measured.

Finally, in a case-control study in France, Robert et al. (1996) looked at congenital abnormalities in relation to distance from power lines. For distance < 50 m the odds ratios was 1.3 (95% CI: 0.5–3.2) and for distance < 100 m it was 1.0 (95% CI: 0.5–2.0). However, this was based on only two cases and since the entire study involved only 11 cases and 22 controls, its statistical power was limited.

Overall, the studies on residential ELF magnetic field exposure have provided some limited evidence for increased miscarriage risk associated with magnetic field exposure. This association is stronger for maximum value and variability of the magnetic field than for time-weighted average field level, but risk estimates above 1.0 were also reported for high TWA magnetic fields. One study provided evidence that the effect might be stronger for early miscarriages, and one study suggested effects on very early (pre-clinical) foetal loss. There is no evidence (but also very few data) of increased risks of adverse pregnancy outcomes other than miscarriage.

The results of epidemiological studies on reproductive outcomes in people exposed to ELF fields in their homes are summarized in Table 68.

Table 68. Epidemiological studies on reproductive outcome and exposure to residential ELF magnetic fields assessed by measurements, wire codes or distance to power line

Study population	Outcome	Exposure [a]	Risk estimate and 95% CI	Authors
257-396 pregnancies	Miscarriage	Home spot measurement 0.2 μT	0.8 (0.3–2.3)	Savitz & Ananth, 1994
		High wire code	0.7 (0.3–1.9)	
	Low birth weight	High wire code	0.7 (0.2–2.3)	
	Preterm delivery	Home spot measurement 0.2 μT	0.7 (0.1–4.0)	
		High wire code	0.2 (0.0–1.5)	
Prospective study, n = 2967	Miscarriage	Very high wire code	0.37 (0.2–1.1)	Belanger et al., 1998
Prospective study, n = 969	Miscarriage (MC)	Personal TWA 0.3 μT	1.2 (0.7–2.2)	Li et al., 2001
		Personal 24-h maximum 1.6 μT	1.8 (1.2–2.7)	
		Total sum above 1.6 μT 476 μTs	2.0 (1.2–3.1)	
	MC before 10 weeks	Personal 24-h maximum 1.6 μT	2.2 (1.2–4.0)	
	MC after 10 weeks	Personal maximum 1.6 μT	1.4 (0.8–2.5)	
155 cases, 509 controls	Miscarriage	Very high wire code	1.2 (0.7–2.1)	Lee et al., 2002
		Home spot measurement 0.2 μT	1.1 (0.5–2.2)	
		Personal TWA 0.128 μT	1.7 (0.9–3.2)	
		Personal 24-h maximum 3.51 μT	2.3 (1.2–4.4)	
		Personal rate-of-change 0.094 μT	3.1 (1.6–6.0)	
Prospective study, n = 219	Miscarriage	Home spot measurement 0.2 μT	3.1 (1.0–9.7)	
		Personal TWA 0.2 μT	1.9 (0.6–6.1)	
		Personal 24-h maximum 2.69 μT	2.6 (0.9–7.6)	

Table 68. Continued

		Personal rate-of-change 0.069 μT	2.4 (0.9–6.6)	
89 cases, 102 controls	Early pregnancy loss	Home spot measurement 0.25 μT	1.1 (0.6–2.3)	Juutilainen et al., 1993
		Home spot measurement 0.63 μT	5.1 (1.0–26)	
Prospective study, n = 2967	Low birth weight	Very high wire code	0.83 (0.3–2.1)	Bracken et al., 1995
		Personal TWA 0.2 μT	1.35 (0.3–6.1)	
	Intrauterine growth retardation	Very high wire code	0.75 (0.4–1.6)	
		Personal TWA 0.2 μT	1.16 (0.4–3.1)	
11 cases, 22 controls	All abnormalities	Distance to power line 100 m	0.95 (0.5–2.0)	Robert et al., 1996
		Distance to power line 50 m	1.25 (0.5–3.2)	

[a] In many studies, the results were reported for several different exposure levels. The highest exposure levels were selected for this table.

10.1.2 Paternal exposure

Reproductive outcomes have also been occasionally related to paternal magnetic field exposure. Buiatti et al. (1984) reported that cases with infertility reported radioelectric work as their usual occupation more often than the controls. No association was observed between semen abnormalities and job titles linked to magnetic field exposure (Lundsberg, Bracken & Belanger, 1995). Schnitzer, Olshan & Erickson (1995) reported an excess of birth defects in the children of electronic equipment operators. Increased frequency of abnormal pregnancy outcome (congenital malformations and fertility difficulties) was observed among high-voltage switchyard workers (Nordström, Birk & Gustavsson, 1983). No significant increase of abnormal birth outcome was found for offspring of power-industry workers (Tornqvist, 1998). Two studies suggested an association between magnetic field exposure and decreased male/female ratio in the offspring (Irgens et al., 1997; Mubarak, 1996).

The results of the studies on paternal exposure are inconclusive and share the methodological limitation that occupation is used as a surrogate for electromagnetic field exposure. While some studies indicated increased risks associated with electrical occupations, there is very little evidence for a causal role of ELF fields in these associations.

10.2 Effects on laboratory mammals

10.2.1 Electric fields

Several studies have addressed effects of 60 Hz electric fields on reproduction and development in rats, using field strengths from 10 kV m^{-1} to 150 kV m^{-1} (for review, see IARC, 2002). The studies involved large group sizes and exposure over multiple generations. In general, the studies did not report any consistent adverse effects. For example, malformations were increased and fertility was decreased in one experiment (Rommereim et al., 1987). These effects were not confirmed in further studies by the same group (Rommereim et al., 1990; 1996).

Exposure to 50 Hz electric fields at 50 kV m^{-1} did not induce significant effects on growth and development in eight-week-old male rats exposed 8 h per day for 4 weeks, or rabbits exposed 16 h per day from the last two weeks of gestation to six weeks after birth (Portet & Cabanes, 1988).

Sikov et al. (1987) conducted a three-generation study on Hanford Miniature swine. The exposed group was kept in a 60 Hz, 30 kV m^{-1} electric field for 20 h per day, 7 days per week. Two teratological evaluations were performed on the offspring of the F_0 generation. Malformations were decreased in the first teratological evaluation (significant only if analysed by foetus), but increased in the second evaluation. Increased malformations were also found among offspring of the F_1 generation at 18 months, but not in another offspring 10 months later. The inconsistency of the results makes it impossible to conclude that there is a causal relationship between ELF electric field exposure and developmental effects in swine.

10.2.2 Magnetic fields

10.2.2.1 Effects on prenatal development

Several studies have investigated effects of low frequency magnetic fields on prenatal development of rodents, and have been reviewed previously (Huuskonen, Lindbohm & Juutilainen, 1998; IARC, 2002). The magnetic flux densities varied from 2 μT to 30 mT. In general, the results do not show any consistent effects on gross external or visceral malformations or increase of foetal loss. The only findings that show some consistency are increases in minor skeletal alterations in several experiments in rats (Huuskonen, Juutilainen & Komulainen, 1993; Mevissen, Buntenkotter & Löscher, 1994; Ryan et al., 2000; Stuchly et al., 1988) and mice (Huuskonen et al., 1998b; Kowalczuk et al., 1994). However, in many other studies in rats (Chung et al., 2003; Negishi et al., 2002; Rommereim et al., 1996) and mice (Chiang et al., 1995; Frolen, Svedenstal & Paulsson, 1993; Ohnishi et al., 2002; Wiley et al., 1992) this effect was not observed. The lowest flux density reported to induce this kind of effect was 13 μT (Huuskonen, Juutilainen & Komulainen, 1993; Huuskonen et al., 1998b). Skeletal variations are relatively common findings in teratological studies and often considered biologically insignificant. Some of the groups concluded that the increased skeletal changes observed in their studies resulted from statistical fluctuation rather

than effects of the magnetic field exposure. Another possible explanation is that these findings indicate subtle developmental effects similar to the developmental instability reported by Graham et al. (2000c) in Drosophila (see 3.2). The use of low frequency magnetic fields for facilitating bone healing (for review, see IARC, 2002) may imply effects on growth and development of bone tissue.

Table 69 summarizes the results of ELF studies on prenatal development in mammals.

Table 69. Low frequency magnetic fields and prenatal development in mammals

Animal strain	Frequency waveform	Flux density (μT)	Exposure time (days)	Findings [a]	Other findings, notes	Authors
CBA/Ca mouse	50 Hz sinusoidal	12.6, 126	0–18	M- S+ R-		Huuskonen et al., 1998b
CD-1 mouse	50 Hz sinusoidal	20 000	0–17	M- S- R-	Body weight and length increased.	Kowalczuk et al., 1994
Swiss Webster mouse	15.6 kHz sawtooth	40 (p-p)	5–16	M+ S- R-	Combined exposure with cytosine arabinoside.	Chiang et al., 1995
CBA/S mouse	20 kHz sawtooth	15 (p-p)	0–18 1–18 4–18 6–18	M- S- R+		Frolen, Svedenstål & Paulsson, 1993
CBA/S mouse	20 kHz sawtooth	15 (p-p)	0–4.5 0–6	M- R-	Number of dead fetuses increased, weight and length decreased.	Svedenstål & Johansson, 1995
CBA/S mouse	20 kHz sawtooth	15 (p-p)	0–18	M- S- R-		Huuskonen et al., 1998a
CBA/Ca mouse	20 kHz sawtooth	15 (p-p)	0–18	M- S+ R-		Huuskonen et al., 1998b
CD-1 mouse	20 kHz sawtooth	3.6, 17, 200 (p-p)	0–17	M- S- R-		Wiley et al., 1992
Wistar rat	50 Hz sinusoidal	12.6	0–20	M- S+ R-		Huuskonen, Juutilainen & Komulainen, 1993

Table 69. Continued

Wistar rat	50 Hz sinusoidal	30 000	0–19	M- S+ R-		Mevissen, Buntenkotter & Löscher, 1994
SD rat	60 Hz sinusoidal	0.6, 1000	0–20	M- S- R-		Rommereim et al., 1996
SD rat	60 Hz sinusoidal	2, 200, 1000	6–19	M- S- R-		Ryan et al., 1996
SD rat	60, 180 or 60+180 Hz sinusoidal	200	6–19	M- S+ R-		Ryan et al., 2000
SD rat	50 Hz sinusoidal	7, 70, 350	0–7 8–15	M- S- R-		Negishi et al., 2002
ICR mouse	50 Hz sinusoidal	500, 5000	0–18	M- S-	Exposure before mating.	Ohnishi et al., 2002
SD rat	60 Hz sinusoidal	5, 83.3, 500	6–20	M- S- R-	Visceral variations decreased, resorptions increased nonsignificantly .	Chung et al., 2003
Wistar rat	10 kHz sinusoidal	95, 240, 950	0–22	M- S- R-		Dawson et al., 1998
SD rat	18 kHz, sawtooth	5.7, 23, 66 (p-p)	0–21	M- S+ R-	Exposure before mating.	Stuchly et al., 1988
Wistar rat	20 kHz, sawtooth	15 (p-p)	0–20	M- S+ R-		Huuskonen, Juutilainen & Komulainen, 1993
ICR mouse	20 kHz, sawtooth	6.25 μT (peak)	2.5–15.5	M- R-		Kim et al., 2004

[a] M=major external or visceral malformations; S=minor skeleton anomalies; R=resorptions; + positive finding; - no statistically significant difference from controls.

Effects of a 50 Hz, 20 mT magnetic field on postnatal development and behaviour of prenatally exposed CD1 mice were studied by Sienkiewicz et al. (1994). Three possible field-dependent effects were found: the exposed animals performed the air-righting reflex earlier (about 2 days), the exposed males were significantly lighter in weight at 30 days of age and the exposed animals remained on a Rota-rod for less time as juveniles. A reduction in run-

ning time on a Rota-rod which was found in juvenile mice may represent a magnetic field-induced impairment in motor coordination during adolescence.

Seven pregnant CD1 mice were exposed for the period of gestation to a vertical, sinusoidal, 50 Hz, magnetic field at 5 mT and eight control animals were sham-exposed. Ten males per group were tested at 82–84 days of age for deficits in spatial learning and memory in radial arm maze. No effects on performance were observed (Sienkiewicz, Larder & Saunders, 1996).

Chung, Kim & Myung (2004) exposed Sprague-Dawley rats (24 per group) for 21 h per day from gestational day 6 through lactational day 21 to 60 Hz magnetic fields at flux densities of 5, 83.3 or 500 μT. Growth, physical development, behaviour, and reproductive performance of the offspring was evaluated. A fraction of the F_1 pups were evaluated for visceral and skeletal abnormalities, and the F_2 foetuses were evaluated for external visible malformations. The behavioural tests included righting reflex, negative geotaxis, traction test, papillary reflex, acoustic startle response, Rota-rod test, open field test and water-filled T-maze test. The statistically significant findings included decrease of anogenital distance in males of the 5 μT group and females of the 5 and 500 μT groups, performance in the open field test in males of the 5 μT group, performance in one of the tests performed with the water maze with the females of the 5 μT group, changes in some organ weights, and increased incidence of visceral variations in the 83.3 μT group. However, as these findings showed no dose-response relationship and a high number of statistical comparisons were performed, they are most probably chance findings.

10.2.2.3 Multi-generation studies

A reproductive assessment by continuous breeding (RACB) study on the toxicity of 60 Hz magnetic fields was conducted by Ryan et al. (1999). The RACB protocol permits the evaluation of reproductive performance over multiple generations. Groups of Sprague-Dawley rats, 40 breeding pairs per group were exposed continuously for 18.5 hours per day to sinusoidal 60 Hz magnetic fields at field strengths of 0, 2, 200 or 1000 μT or to an intermittent (1 hour on, 1 hour off) field at 1000 μT. No exposure-related toxicity was observed in any of the three generations examined. Foetal viability and body weight were similar in all groups, and there were no differences in any measure of reproductive performance (litters per breeding pair, percent fertile pairs, latency to parturition, litter size, and sex ratio). Teratological examinations were not performed.

10.2.2.4 Effects on mammalian embryos in vitro

Huuskonen, Juutilainen & Kumolainen (2001) studied the effects of 13 μT, 50 Hz magnetic fields on the development of preimplantation CBA/S mouse embryos. The development of the embryos was followed for eight days (up to the blastocyst stage). Significantly fewer embryos died at the 5–8-cell and >8-cell stages in the exposed group than in the control group, but no

differences were seen in other developmental stages. There was no overall difference in survival, and no abnormalities or effects on developmental rate were observed. In contrast, Beraldi et al. (2003) reported significantly decreased survival in cultured mouse embryos exposed to 50 Hz fields at 60, 120 or 220 μT. The effect (tested at 60 μT) was more pronounced in embryos obtained by in vitro fertilization than in those resulting from natural breeding. No effects were observed on the morphology or developmental rate of the embryos.

10.2.2.5 Effects of paternal exposure

Possible effects of 50 Hz magnetic fields on the fertility of male Sprague-Dawley rats were investigated by Al-Akhras et al. (2001). Ten males per group (13 in the control group) were exposed to a sinusoidal, 50 Hz magnetic field at 25 μT for 90 days before they were mated with unexposed females (two females per male). The number of pregnancies decreased significantly from 24/26 (92%) in the control group to 10/20 (50%) in the exposed group. The effect persisted in a second mating after 45 days, but not at 90 days after removal from the magnetic field. Number of implantations per litter and viable foetuses per litter were not significantly affected. Effects on fertility in females (10 animals per group) were also evaluated in the same study. The 90-day exposure resulted in a statistically significant decrease of pregnancies, from 100% in the controls to 6/10 in the exposed females. The mean number of implantations per litter also decreased from 9.9 to 4.7 and the mean number of viable foetuses per litter from 9.6 to 4.3. These differences were statistically significant, but the numbers of animals in the groups were small.

In another study with similar design, the same investigators reported no adverse effects on fertility and reproduction in Swiss mice (Elbetieha, Al-Akhras & Darmani, 2002).

Picazo et al. (1995) exposed young male and female OF1 mice until adulthood to a sinusoidal 50 Hz, 15 μT magnetic field. The animals were then mated, and the offspring were kept under the same experimental conditions until they acquired sexual maturity. A significant increase of testis size and weight and of testosterone levels was observed in male offspring that had been exposed compared with a control group. However, complete spermatogenesis occurred in both control and exposed animals.

The effects of a 50 Hz, 1.7 mT sinusoidal magnetic field on mouse spermatogenesis (De Vita et al., 1995) was examined by flow cytometry. Groups of five male hybrid FI mice (C57Bl/Cne x C3H/Cne) were exposed for 2 or 4 hours, and measurements were performed at 7, 14, 21, 28, 35, and 42 days after exposure. The only statistically significant difference was a decrease in elongated spermatids at 28 days after treatment in the animals exposed for 4 h.

Kato et al. (1994b) reported no effects of circularly polarized 50 Hz magnetic fields at 1, 5 or 50 μT on plasma testosterone concentration in male Wistar-King rats.

10.3 Effects on non-mammalian species

10.3.1 Bird embryos

10.3.1.1 Development

Delgado et al. (1982) reported that weak pulsed ELF magnetic fields (0.12–12 μT; 10, 1000 or 1000 Hz) affected the early development of chicken embryos examined after 48 h of incubation. After this initial finding, the same research group published several papers reporting similar effects (Leal et al., 1989; Ubeda et al., 1983; Ubeda et al., 1994; Ubeda, Trillo & Leal, 1987).

The initial results of Delgado were not replicated in an independent study (Maffeo, Miller & Carstensen, 1984). A large well-designed international study ("Henhouse project") aimed at replicating Delgado's results has been carried out in six separate laboratories (Berman et al., 1990). Identical equipment and standardized experimental procedures were used. While the combined data showed a significant ($p < 0.001$) increase of abnormal embryos in the exposed group, the results were not consistently positive – only two laboratories found a statistically significant increase of abnormalities.

One of the laboratories that participated in the Henhouse project has reported a large additional investigation using pulsed waveforms and 50 Hz sinusoidal fields (Koch et al., 1993). Several different strains were tested to investigate possible strain-specific differences in sensitivity to magnetic fields. No significant magnetic field effects were observed.

Studies by Juutilainen and co-workers (1986) showed that the percentage of abnormalities was increased in chick embryos exposed during their first two days of development to 100 Hz magnetic fields with a pulsed, sinusoidal and rectangular waveforms. In another series of experiments with sinusoidal waveform, similar effects were found in a wide range of frequencies (Juutilainen & Saali, 1986). The effects of 100 Hz sinusoidal fields with a field strength of 1 A m^{-1} were confirmed in experiments with a large number of eggs (Juutilainen, 1986). Further experiments showed similar effects also at 50 Hz (sinusoidal), and indicated a threshold at 1.3 μT (Juutilainen, Läära & Saali, 1987).

Apart from the series of experiments by Juutilainen and colleagues, there have been few other studies on sinusoidal fields. Cox et al. (1993) attempted to partly replicate the findings of Juutilainen et al. No difference from control embryos was observed in 200 embryos exposed to a 10 μT, 50 Hz magnetic field.

Farrell et al. (1997) conducted an extensive series of experiments on the effects of pulsed and sinusoidal magnetic fields on chick embryo development, involving a total of more than 2500 embryos. Both 60 Hz, 4 μT sinusoidal fields and a 100 Hz field with 1 μT peak amplitude (similar to the field used in the Henhouse project) were used. Overall, the abnormality

rate was more than doubled by magnetic field exposure, and the effect was statistically significant for both 100 Hz and 60 Hz fields.

Quail embryo development has been reported to be affected by exposure to ELF magnetic fields (Terol & Panchon, 1995). The exposures were 50 or 100 Hz with rectangular waveform and intensities of 0.2, 1.2, 3.3 and 3.2 μT, and the embryos were examined at 48 h. There was a significant increase in embryonic deaths and abnormal development in the 100 Hz group, but not in the 50 Hz group.

10.3.1.2 Interaction with known teratogens

Pafkova & Jerabek (1994) reported that exposure to a 50 Hz, 10 mT magnetic field modified the embryotoxic effect of ionizing radiation on chick embryos examined at day 9 of development, although no effects of magnetic fields alone were detected. Embryotoxicity was expressed as the sum of embryonic deaths and malformations. Exposure to the magnetic field prior to the X-ray treatment seemed to protect the embryos from X-ray induced toxicity, while an enhancement of the embryotoxicity was seen when the magnetic field exposure followed the X-ray irradiation. The effects were seen consistently in several experiments and were statistically significant. The same group has also shown a similar protective effect of 50 Hz, 10 mT magnetic field exposure against subsequent exposures to the chemical teratogens insulin and tetracyclin (Pafkova et al., 1996).

Another research group has reported that the survival of chicken embryos exposed to UV-radiation is modified by exposure to a 60 Hz, 8 μT magnetic field (Dicarlo et al., 1999). Similarly to Pafkova's findings, the direction of the effect (enhancement or protection) depended on the exposure protocol. In this case magnetic field exposure always preceded UV exposure, but short exposure (2 h) seemed to protect the embryos, while longer exposure (96 h) increased the UV-induced mortality.

10.3.2 Other non-mammalian species

Exposure to sinusoidal magnetic fields has been reported to delay the development of fish embryos at 60 Hz, 0.1 mT (Cameron, Hunter & Winters, 1985), sea urchin embryos at 60 Hz, 0.1 mT (Zimmerman et al., 1990), and fish embryos at 50 Hz, 1 mT (Skauli, Reitan & Walther, 2000). No malformations were found in these studies.

Graham et al. (2000c) studied the effects of 60 Hz magnetic fields on "developmental stability" in *Drosophila melanogaster*. Developmental stability is a concept that describes the ability of an organism to maintain a consistent phenotype under given genetic and environmental conditions (this relatively new concept is potentially a useful tool for detecting weak environmental effects (Graham et al., 2000c). An individual with low developmental stability has reduced ability to correct disturbances in development. The standard measure of developmental instability is fluctuating asymmetry, random deviations from perfect bilateral symmetry. This measure has been shown to respond to environmental agents such as DDT, lead, and benzene.

Another measure of developmental instability is the frequency of phenodeviants in a population. Graham et al. exposed the fruit flies for their entire lives, egg to adult, to 60 Hz fields at 1.5 or 80 μT. The magnetic field exposures caused a significant reduction in body weight. The flies exposed to 80 μT showed reduced developmental stability measured both by fluctuating asymmetry (asymmetrical wing veins) and frequency of phenodeviants (fused abdominal segments). Mirabolghasemi & Azarnia (2002) have reported increased abnormalities in adult *D. melanogaster* flies after exposure of larvae to a 11 mT, 50 Hz field.

10.4 Conclusions

On the whole, epidemiological studies have not shown an association between adverse human reproductive outcomes and maternal or paternal exposure to ELF fields. There is some evidence for increased risk of miscarriage associated with measured maternal magnetic field exposure, but this evidence is inadequate.

ELF electric fields of up to 150 kV m^{-1} have been evaluated in several mammalian species, including studies with large group sizes and exposure over several generations. The results consistently show no adverse developmental effects.

The exposure of mammals to ELF magnetic fields of up to 20 mT does not result in gross external, visceral or skeletal malformations. Some studies show an increase in minor skeletal anomalies, in both rats and mice. Skeletal variations are relatively common findings in teratological studies and often considered biologically insignificant. However, subtle effects of magnetic fields on skeletal development cannot be ruled out. Very few studies have been published which address reproductive effects and no conclusions can be drawn from them.

Several studies on non-mammalian experimental models (chick embryos, fish, sea urchins and insects) have reported findings indicating that ELF magnetic fields at microtesla levels may disturb early development. However, the findings of non-mammalian experimental models generally carry less weight in the overall evaluation of developmental toxicity than those of corresponding mammalian studies.

Overall the evidence for developmental effects and for reproductive effects is inadequate.

11 CANCER

The possibility that exposure to low frequency EMFs increases the risk of cancer has been subject to much epidemiological and experimental research over the last two decades and has been widely reviewed by national and international expert groups (e.g. AGNIR, 2001b; Ahlbom & Feychting, 2001; IARC, 2002; ICNIRP, 2003; NIEHS, 1998). The association between childhood leukaemia and residential ELF magnetic fields, first identified by Wertheimer & Leeper (1979) and subsequently found in a number of epidemiological studies, has driven experimental and epidemiological research and risk assessment forwards in this area and led to the classification of ELF magnetic fields by the International Agency for Research on Cancer (IARC) as a "possible human carcinogen" (IARC, 2002). This evaluation of the carcinogenicity of EMFs is of particular relevance to this Environmental Health Criteria document. However, a number of relevant studies have been published following this assessment.

A cancer is an uncontrolled growth of cells that may invade and disrupt surrounding tissues and spread through the body via the blood and lymphatic vessels. In contrast to normal cells, malignant cells in vitro commonly show persistent and autonomous proliferation in absence of any proper attachment (immortalisation and "anchorage free" growth). Carcinogenesis itself is a multi-stage process and is classically divided into two principal stages: initiation, which is the induction of irreversible changes (mutations in genes), and promotion, which is reversible and needs to be sustained by repeated stimuli to the initiated cell. Promotion then stimulates further development (outgrowth) into a tumour. Because of the low energy levels in molecular interactions, it is physically highly implausible that ELF fields cause direct genetic damage (i.e. damage DNA molecules from which genes are made). However, it has been theorised that ELF may enhance such damage from other sources (e.g. endogenous radicals), or that epigenetic (non-genotoxic) interference in signal transduction may enhance cancer formation (see section 11.4). Once the potential for full malignancy has been established in a primary tumour, the progression of the disease may be influenced by other factors such as immune surveillance and hormonal dependency. It has also been hypothesised that ELF fields may interfere with these factors that play a role in a "late-stage" of tumour development (see Chapter 6 on the neuroendocrine system and Chapter 9.1 on the immune system).

This chapter reviews the experimental and epidemiological evidence concerning ELF exposure and the risk of cancer, focussing on studies published subsequent to the IARC assessment in 2002. In contrast to other chapters, the experimental evidence is discussed before the epidemiological evidence. In particular, the section discussing childhood leukaemia presents a detailed risk assessment, drawing on the other evidence presented and leads on to chapters on overall risk assessment and protective measures.

11.1 IARC 2002 evaluation: summary

Since the first report suggesting an association between residential ELF magnetic fields and childhood leukaemia was published in 1979, dozens of increasingly sophisticated epidemiological studies have examined this association (see Tables 1 and 2 from IARC, 2002). In addition, there have been numerous comprehensive reviews, meta-analyses, and two pooled analyses. In one pooled analysis based on nine well-conducted studies, virtually no association was noted for exposure to ELF magnetic fields below 0.4 μT and an odds ratio of around 2 was seen, indicating an twofold excess risk, for exposure above 0.4 μT (Ahlbom et al., 2000). The other pooled analysis included 15 studies based on less restrictive inclusion criteria and used 0.3 μT as the highest cut-point (Greenland et al., 2000). A relative risk of 1.7 for exposure above 0.3 μT was reported. The two analyses are in close agreement. In contrast to these results for ELF magnetic fields, evidence that electric fields are associated with childhood leukaemia is insufficient for firm conclusions but does not suggest any risk.

The association between childhood leukaemia and estimates of time-weighted average exposures to magnetic fields is unlikely to be due to chance, but bias may explain some of the association. In particular, selection (including participation) bias may account for part of the association in some of the studies. Case-control studies which relied on in-home measurements are especially vulnerable to this bias, because of the low response rates in many studies. Studies conducted in the Nordic countries, which relied on historical calculated magnetic fields, are not subject to any selection bias yet identified, but risk estimates are imprecise due to low numbers of exposed subjects. There have been dramatic improvements in the assessment of exposure to electric and magnetic fields over time, yet all of the studies are subject to misclassification. Non-differential misclassification of exposure (similar degrees of misclassification in cases and controls) is likely to result in bias towards the null. Bias due to unknown confounding factors is very unlikely to explain the entire observed effect. However, some bias due to confounding is quite possible, which could operate in either direction. It cannot be excluded that a combination of selection bias, some degree of confounding and chance could explain the results. Conversely, if the observed relationship were causal, the exposure-associated risk could also be greater than what is reported.

With regard to other childhood cancers, no consistent relationship has been reported in studies of childhood brain tumours or cancers at other sites and residential ELF electric and magnetic fields. However, these studies have generally been smaller and of lower quality and associations can not be ruled out for all those outcomes.

Numerous studies of the relationship between electrical appliance use and various childhood cancers have been published. In general, these studies provide no discernible pattern of increased risks associated with increased duration and frequency of use of appliances. Since many of the studies collected information from interviews that took place many years

after the time period of etiological interest, recall bias is likely to be a major problem. Studies on parental occupational exposure to ELF electric and magnetic fields in the preconception period or during gestation are methodologically weak and the results are not consistent.

Concerning adult cancer risk and residential exposures, the evidence was considered sparse and methodologically limited, and although there had been a considerable number of reports, a consistent association between residential exposure and adult leukaemia and brain cancer was not established. For breast and other cancers, the existing data were not considered adequate to test for an association with electric or magnetic fields. Concerning studies of occupational exposure, most had focused on leukaemia and brain cancer. There was no consistent finding across studies of an exposure-response relationship and no consistency in the association with specific sub-types of leukaemia or brain tumour. Evidence for cancers at other sites was not considered adequate for evaluation.

In general, the animal studies, which included a number of life-time studies and studies of animals predisposed to develop cancer, and in vitro studies of cellular processes implicated in carcinogenesis, did not support the hypothesis that ELF EMFs were carcinogenic.

In summary, taking this information into consideration, the overall IARC (2002) evaluation for the carcinogenicity of EMFs was:

- There is *limited* evidence in humans for the carcinogenicity of extremely low-frequency magnetic fields in relation to childhood leukaemia.
- There is *inadequate* evidence in humans for the carcinogenicity of extremely low-frequency magnetic fields in relation to all other cancers.
- There is *inadequate* evidence in humans for the carcinogenicity of static electric or magnetic fields and extremely low-frequency electric fields.
- There is *inadequate* evidence in experimental animals for the carcinogenicity of extremely low-frequency magnetic fields.
- No data relevant to the carcinogenicity of extremely low-frequency electric fields in experimental animals were available.

Leading to the conclusion that:

- Extremely low-frequency magnetic fields are *possibly carcinogenic to humans (Group 2B)*.
- …extremely low-frequency electric fields are *not classifiable as to their carcinogenicity to humans (Group 3)*.

Table 70. Case–control studies of childhood leukaemia and exposure to ELF magnetic fields [a] [b]

Study area, population	Exposure	# cases	OR (95% CI)	Comments	Authors
Denver, CO, USA 155 deceased cases, 155 controls aged 0–19 y	*Wire code* [c] LCC HCC	 92 (126 controls) 63 (29 controls)		No risk estimates presented; lack of blinding for the exposure assessment; hypothesis-generating study.	Wertheimer & Leeper, 1979
Los Angeles County, CA, USA 211 cases, 205 controls aged 0–10 y	*Wire code* UG/VLCC (baseline) OLCC OHCC VHCC	 31 58 80 42	 1.0 0.95 (0.53–1.7) 1.4 (0.81–2.6) 2.2 (1.1–4.3)	Matched analysis, no further adjustments; low response rates for measurements; no wire coding of subjects who refused to participate.	London et al., 1991
164 cases, 144 controls aged 0–10 y	*Mean magnetic fields (24-h bedroom measurement)* < 0.067 μT (baseline) 0.068–0.118 μT 0.119–0.267 μT ≥ 0.268 μT	 85 35 24 20	 1.0 0.68 (0.39–1.2) 0.89 (0.46–1.7) 1.5 (0.66–3.3)		
Sweden (corridors along power lines) 39 cases, 558 controls aged 0–15 y	*Calculated historical magnetic fields* < 0.1 μT (baseline) 0.1–0.19 μT ≥ 0.2 μT	 27 4 7	 1.0 2.1 (0.6–6.1) 2.7 (1.0–6.3)	Adjusted for sex, age, year of diagnosis, type of house, Stockholm county (yes/no); in subsequent analysis also for socioeconomic status and air pollution from traffic; no contact with subjects required.	Feychting & Ahlbom, 1993

Table 70. Continued

Denmark 833 cases, 1666 controls aged 0–14 y	*Calculated historical magnetic fields* < 0.1 μT (baseline) 0.1–0.24 μT ≥ 0.25 μT	 829 1 3	 1.0 0.5 (0.1–4.3) 1.5 (0.3–6.7)	Adjusted for sex and age at diagnosis; socioeconomic status, distribution similar between cases and controls; no contact with subjects required.	Olsen, Nielsen & Schulgen, 1993
Norway (census wards crossed by power lines) 148 cases, 579 controls aged 0–14 y	*Calculated historical magnetic fields* < 0.05 μT (baseline) 0.05–< 0.14 μT ≥ 0.14 μT	 139 8 1	 1.0 1.8 (0.7–4.2) 0.3 (0.0–2.1)	Adjusted for sex, age and municipality, socioeconomic status, type of house, and number of dwellings; no contact with subjects required.	Tynes & Haldorsen, 1997
Lower Saxony and Berlin (Germany) 176 cases, 414 controls aged 0–14 y	*Median magnetic fields (24-h bedroom measurement)* < 0.2 μT (baseline) ≥ 0.2 μT	 167 9	 1.0 2.3 (0.8–6.7)	Adjusted for sex, age and part of Germany (East, West), socioeconomic status and degree of urbanization; information on a variety of potential confounders available; low response rates.	Michaelis et al., 1998
Canada: five provinces, subjects living within 100 km of major cities 351 cases, 362 controls aged 0–14 y	*Wire code* UG (baseline) VLCC OLCC OHCC VHCC	 79 73 77 83 39	 1.0 0.70 (0.41–1.2) 0.76 (0.45–1.3) 0.64 (0.38–1.1) 1.2 (0.58–2.3)	Adjusted for age, sex, province, maternal age at birth of child, maternal education, family income, ethnicity and number of residences since birth; information on a variety of potential confounding factors available; relatively low response rates for personal monitoring portion; children with Down syndrome excluded.	McBride et al., 1999
293 cases, 339 controls aged 0–14 y	*Personal monitoring (48-h)* < 0.08 μT (baseline) 0.08–< 0.15 μT 0.15–< 0.27 μT ≥ 0.27 μT	 149 67 45 32	 1.0 0.57 (0.37–0.87) 1.1 (0.61–1.8) 0.68 (0.37–1.3)		

Table 70. Continued

England, Wales and Scotland 1073 cases, 1073 controls aged 0–14 y	*Time-weighted average magnetic fields (1.5–48-h measurement)* < 0.1 μT (baseline) 0.1–< 0.2 μT ≥ 0.2 μT 0.2–< 0.4 μT ≥ 0.4 μT	 995 57 21 16 5	 1.0 0.78 (0.55–1.1) 0.90 (0.49–1.6) 0.78 (0.40–1.5) 1.7 (0.40–7.1)	Adjusted for sex, date of birth and region, socioeconomic status; information on a variety of potential confounders available; low reponse rates.	UKCCSI, 1999
West Germany 514 cases, 1301 controls aged 0–14 y	*Median magnetic fields (24-h bedroom measurement)* < 0.1 μT (baseline) 0.1–< 0.2 μT 0.2–< 0.4 μT ≥ 0.4 μT *Night-time magnetic fields* < 0.1 μT (baseline) 0.1–< 0.2 μT 0.2–< 0.4 μT ≥ 0.4 μT	 472 33 6 3 468 34 7 5	 1.0 1.2 (0.73–1.8) 1.2 (0.43–3.1) 5.8 (0.78–43) 1.0 1.4 (0.90–2.2) 2.5 (0.86–7.5) 5.5 (1.2–27)	Adjusted for sex, age, year of birth, socioeconomic status and degree of urbanization; information on a variety of potential confounders available; low response rates; relatively long time lag between date of diagnosis and date of the measurement.	Schüz et al., 2001
Nine mid-western and mid-Atlantic states, USA 408 cases, 408 controls aged 0–14 y	*Wire code* UG/VLCC (baseline) OLCC OHCC VHCC	 175 116 87 24	*Matched* 1.0 1.1 (0.74–1.5) 0.99 (0.67–1.5) 0.88 (0.48–1.6)	Unmatched analysis additionally adjusted for age, sex, mother's education and family income; information on a variety of potential confounding factors available; wire coding of subjects who refused to participate; relatively low response	Linet et al., 1997

Table 70. Continued

638 cases, 620 controls aged 0–14 y	*Time-weighted average (24-h bedroom measurement plus spot measurements in two rooms)*			rates for measurements in controls; only acute lymphoblastic leukaemia; children with Down syndrome excluded from this study (Schüz et al., 2001).
			Unmatched	
	< 0.065 μT (baseline)	267	1.0	
	0.065–0.099 μT			
	0.100–0.199 μT	123	1.1 (0.81–1.5)	
	≥ 0.200 μT	151	1.1 (0.83–1.5)	
		83	1.2 (0.86–1.8)	
			Matched	
		206	1.0	
		92	0.96 (0.65–1.4)	
		107	1.2 (0.79–1.7)	
		58	1.5 (0.91–2.6)	

[a] Source: (IARC, 2002).

[b] In this table, only studies that contributed substantially to the overall summary are considered and only results that were part of the analysis strategy of IARC are presented. Exposure metrics and cut-points vary across studies.

[c] UG, underground wires; VLCC, very low current configuration; OLCC, ordinary low current configuration; OHCC, ordinary high current configuration; VHCC, very high current configuration; LCC, low current configuration; HCC, high current configuration.

Note that in the IARC procedure, the term "limited evidence of carcinogenicity" means that a positive association has been observed for which a causal interpretation is considered credible, but that chance, bias or confounding could not be ruled out with reasonable confidence. The term "inadequate evidence of carcinogenicity" indicates that either the available studies are of insufficient quality, consistency or statistical power to permit a conclusion, or that no data on cancer are available.

In Tables 70 and 71 the key studies discussed by IARC (2002) are summarized.

Table 71. Pooled analysis of total leukaemia in children [a]

Authors	0.1–< 0.2 μT [b]	0.2–< 0.4 μT	≥ 0.4 μT	Observed [c]	Expected	Continuous analysis
Measurement studies						
Canada McBride et al., 1999	1.3 (0.84–2.0)	1.4 (0.78–2.5)	1.6 (0.65–3.7)	13	10.3	1.2 (0.96–1.5)
Germany Michaelis et al., 1998	1.2 (0.58–2.6)	1.7 (0.48–5.8)	2.0 (0.26–15)	2	0.9	1.3 (0.76–2.3)
New Zealand Dockerty et al., 1998; 1999	0.67 (0.20–2.2)	4 cases, 0 controls	0 cases 0 controls	0	0	1.4 (0.40–4.6)
United Kingdom UKCCSI, 1999	0.84 (0.57–1.2)	0.98 (0.50–1.9)	1.0 (0.30–3.4)	4	4.4	0.93 (0.69–1.3)
USA Linet et al., 1997	1.1 (0.81–1.5)	1.0 (0.65–1.6)	3.4 (1.2–9.5)	17	4.7	1.3 (1.0–1.7)
Calculated field studies						
Denmark Olsen, Nielsen & Schulgen, 1993	2.7 (0.24–31)	0 cases 8 controls	2 cases 0 controls	2	0	1.5 (0.85–2.7)
Finland Verkasalo et al., 1993	0 cases/ 19 controls	4.1 (0.48–35)	6.2 (0.68–57)	1	0.2	1.2 (0.79–1.7)
Norway Tynes & Haldorsen, 1997	1.8 (0.65–4.7)	1.1 (0.21–5.2)	0 cases 10 controls	0	2.7	0.78 (0.50–1.2)
Sweden Feychting & Ahlbom, 1993	1.8 (0.48–6.4)	0.57 (0.07–4.7)	3.7 (1.2–11.4)	5	1.5	1.3 (0.98–1.7)

Table 71. Continued

Summary [d]						
Measurement studies	1.1 (0.86–1.3)	1.2 (0.85–1.5)	1.9 (1.1–3.2)	36	20.1	1.2 (1.0–1.3)
Calculated field studies	1.6 (0.77–3.3)	0.79 (0.27–2.3)	2.1 (0.93–4.9)	8	4.4	1.1 (0.94–1.3)
All studies	1.1 (0.89–1.3)	1.1 (0.84–1.5)	2.0 (1.3–3.1)	44	24.2	1.2 (1.0–1.3)

[a] Source: (IARC, 2002).

[b] Relative risks (95% CI) by exposure level and with exposure as continuous variable (relative risk per 0.2 μT) with adjustment for age, sex and socioeconomic status (measurement studies) and residence (in East or West Germany). The reference level is < 0.1 μT.

[c] Observed and expected case numbers at ≥ 0.4 μT, with expected numbers given by modelling the probability of membership of each exposure category based on distribution of controls including covariates.

[d] From Ahlbom et al. (2000).

11.2 Epidemiological studies

11.2.1 Childhood leukaemia

Since childhood leukaemia is the outcome for which the epidemiological evidence is the most consistent it has attracted particular attention, especially following the IARC (2002) assessment. This section provides an update on studies that have been published since the IARC classification and discusses possible interpretations.

11.2.1.1 Epidemiology

Leukaemias are cancers of the blood and bone marrow. The classification of leukaemias is conventionally based on the cell types of origin (lymphocytes, myelocytes, monocytes) and on the rate at which the disease progresses (acute and chronic). Leukaemia is the most common childhood malignancy, constituting more then a third of all childhood cancers. Acute lymphocytic leukaemias (ALL) account for 75% of all cases of childhood leukaemia. Acute myeloid leukaemia (AML) accounts for most non-ALL childhood leukaemias; only a fraction of childhood leukaemia cases are diagnosed with other subtypes.

11.2.1.1.1 Incidence

For children under 15 years of age, the estimated number of new leukaemia cases in 2000 was approximately 49 000 globally, translating into an incidence rate of about 3 cases per 100 000 (IARC, 2000). The incidence of childhood leukaemia in different regions of the world is given in Table 72.

Table 72. Global incidence of childhood leukaemia in 2000			
Region	**Population 0-14 year olds [a]**	**New cases [b]**	**Incidence (per 100 000)**
Africa	339 631 000	3 848	1.13
Asia	1 119 233 000	31 062	2.78
Europe	127 382 000	4 878	3.83
Latin America	165 828 000	6 367	3.84
North America	68 083 000	2 841	4.17
Oceania	8 018 000	283	3.53
World	1 828 175 000	49 000	2.68

[a] Estimates for 2000: International Association of Cancer Registries (IARC, 2000).

[b] Estimates for 2000: United Nations - World Population Prospects (UN, 2002).

There are marked differences in leukaemia rates among various regional and ethnic groups. In the USA, the highest rates are observed among Hispanics in Los Angeles and Filipinos, Chinese, and Japanese in California and Hawaii. Moderate-to-high rates occur among Caucasians; for African-Americans, rates are significantly lower. The white-to-black ratio of overall leukaemia incidence rates is about 2 throughout various age groups (Linet & Devesa, 1991). Within the United States, there are also clear regional differences, with rates ranging from 2.2–5.6 per 100 000 for boys and 1.4–6.3 per 100 000 for girls (Linet & Devesa, 1991).

International comparisons of overall childhood leukaemia incidence rates indicate a 4–6-fold variability. The highest overall incidence rates of over 6 cases per 100 000 per year have been reported in Costa Rica and among the non-Maori population in New Zealand (Kinlen, 1994; Linet & Devesa, 1991). High incidence rates have also been reported in the Scandinavian countries, Australia, Hong Kong, and the Philippines; rates range between 4.5 and 5.5 cases per 100 000 annually, similar to rates reported among Hispanic males in Los Angeles (Kinlen, 1994; Linet & Devesa, 1991). Intermediately high incidence rates have been observed in European countries, such as Germany, Great Britain, France, and Hungary, as well as in Japan and China and among Jews in Israel (Bhatia et al., 1999; Greenberg & Shuster, 1985; Kinlen, 1994; Linet & Devesa, 1991). Low incidence rates occur in India, among Kuwaitis in Kuwait, and among black children in Africa (Bhatia et al., 1999; Greaves & Alexander, 1993; Greenberg & Shuster, 1985). Although absolute rates vary, the sex ratio of incidence rates and the patterns of age-specific rates are similar among the various countries, except that the early childhood peak in ALL incidence is apparently absent among African children. There is, however, a significant international variation between ALL and non-ALL ratios. As in the United States, the large majority of cases in European and Latin-American countries have ALL, whereas in many Asian countries, such as China, the Philippines, and India,

the proportion of non-ALL cases is higher, composing close to 50% of childhood leukaemia cases (Greaves & Alexander, 1993).

Whether the wide international variation in childhood leukaemia incidence rates represents real differences in incidence rates or reflects only differences in completeness of case ascertainment and registration is controversial. Alternative explanations are that inherited genetic factors may predispose certain ethnic groups to childhood leukaemia, or some so-far-unidentified environmental factors or higher socioeconomic status may predispose children in more developed nations to a higher risk of leukaemia. Incidence rates for leukaemia are consistently 10–50% higher among boys than among girls (Gurney et al., 1995; Linet & Devesa, 1991; Zahm & Devesa, 1995). This difference results primarily from higher rates of the most common type of leukaemia, ALL, among boys (Gurney et al., 1995; Linet & Devesa, 1991; Rechavi, Ramot & Ben-Bassat, 1992). Others types of leukaemia do not clearly show such a strong predominance in males. For example, gender-specific AML incidence rates tend to be similar overall.

Incidence rates for ALL cases have a characteristic age pattern. During the first couple of years of life incidence rates dramatically increase, reaching a peak at 2–3 years of age, followed by a slow decline until about age 10, when the rate stabilizes. AML incidence has a different age distribution: the highest incidence rate occurs during the first 2 years of life and lower rates later in childhood (Ries et al., 2001).

Development of the characteristic peak of ALL incidence in early childhood was first shown from mortality data in the 1920s in Britain (Cartwright & Staines, 1992; Milham & Ossiander, 2001). In the United States, this peak was shown to develop about 3–4 decades earlier among white children (in the 1920s and 1930s) than among black children (in the1960s) (Bhatia et al., 1999; Greaves & Alexander, 1993; Milham & Ossiander, 2001).

11.2.1.1.2 Etiology

Leukaemia results from chromosomal alterations and mutations that disrupt the normal process by which lymphoid or myeloid progenitor cells differentiate. The underlying triggers for molecular damage may be inherited at conception, may occur during fetal development or during infancy. Most likely, there is an accumulation of a series of detrimental genetic changes over time (Bhatia et al., 1999). Subtypes of AML and ALL are frequently characterized by genetic alterations, including changes in chromosome number (hyperdiploidy or hypodiploidy) and chromosomal translocations that may involve chimeric or fusion genes (Greaves, 2002; Lightfoot, 2005). There is strong evidence that these rearrangements may originate *in utero*. Other data suggest that the conversion of the preleukemic clone to overt disease is low. The implication is that the development of childhood ALL is a multistep process requiring at least one prenatal event in combination with additional prenatal and/or postnatal events. While the “first hit”, the initiating *in utero* event, is believed to be common, the “second hit”,

possibly occurring postnatally, is rare, and therefore acts as the rate-determining step in the development of the disease. However, although there have been significant advances in diagnostic techniques and improvements in treatment, the etiology of leukaemia in children still remains unclear.

A wide variety of factors have been hypothesized to be involved in the etiology of childhood leukaemia. Among environmental exposures possibly associated with childhood leukaemia, ionizing radiation is a generally accepted risk factor (Bhatia et al., 1999). The list of chemical agents for which some evidence points to a link with leukemogenesis includes solvents, pesticides, tobacco smoke, and certain dietary agents. The possible role of viral or other infectious agents in triggering leukaemia development has also been hypothesized (Mezei & Kheifets, 2002) and has received support from a recently published study (Gilham et al., 2005) carried out as part of the United Kingdom Childhood Cancer Study (UKCCS) into the aetiology of childhood leukaemia. More recently, Kinlen's hypothesis of population mixing (perhaps involving rare reactions to infectious vectors) has received additional support (e.g. Dickinson & Parker, 1999). Generally accepted associations, however, explain only 10% of childhood leukaemia incidence (Kheifets & Shimkhada, 2005), leaving the majority with unexplained etiology.

11.2.1.2 Trends and ecologic correlations

Despite the well known pitfalls of using ecological correlations to infer causality, assumed rapid increase in magnetic field exposures and lack of corresponding increase in leukaemia incidence has been used as an argument against causal association between magnetic fields and childhood leuekmia. For completeness, historical changes in exposures are presented and compared to changes in childhood leukaemia rates. As expected, however, when this comparison is made, there is, in fact, relatively little that can be deduced.

11.2.1.2.1 Trends in exposures

Magnetic fields are produced by currents in electricity systems. The electricity consumed in most countries has increased dramatically over the twentieth century (this is a statement of the obvious, as there was no public electricity supply anywhere before the late 1800s). It is natural to assume this increase in electricity use has led to an increase in currents in electricity circuits and hence an increase in magnetic fields. This approach has been followed by, e.g., Jackson (1992), Olsen, Nielsen & Shulgen (1993), Petridou et al. (1993), Kraut, Tate & Tran (1994) and Sokejima, Kagamino & Tatsumura (1996), who all assumed average magnetic fields are proportional to a measure of per capita electricity consumption.

It is possible to criticise this assumption. For instance, the increase in electricity use will have been accommodated partly by building new circuits rather than by increasing the load on existing circuits, and there may have been other changes in engineering practice which affect the link

between magnetic fields and electricity consumption. Unfortunately, there are no historical measurements that allow this to be tested, and instead, modelling is required. Swanson (1996), for the UK, broke down average exposure into three main components and considered these separately, taking account of changes in engineering practice. The conclusion was that in the UK, average exposure to magnetic fields from 1949 to 1989 had increased by slightly more than per capita electricity consumption – a factor of 4.5 compared to 3.2. Importantly, Swanson recognised a number of uncertainties in this modelling, but showed that the likely effect of the uncertainties was to make the estimated increase an underestimate rather than an overestimate. Note however, that average exposure to magnetic fields in the UK seemed to have stabilized around 1970 and has remained relatively constant ever since.

It is still possible to postulate changes in electricity distribution practices in other countries that break or reduce the link in those countries between consumption and exposure. For instance, it has been suggested that the decreasing use of "knob and tube" wiring in homes in the USA has reduced exposures (Leeper et al., 1991). However, whether this is significant is speculative. The only available evidence supports a working assumption that average exposures have risen by an amount comparable to that of electricity consumption.

11.2.1.2.2 Trends in incidence

There is general agreement that in most countries where data are available (in practice, westernised countries only), childhood cancer registration rates for most but not all cancer types as recorded in registries appear to have risen during the twentieth century (Draper, Kroll & Stiller, 1994). In the UK, a large country with a good national registry, childhood cancer registration rates have risen by 35% from 1962 to 1998, an average of 0.8% per year (Cancer Research UK, 2004). For earlier periods, before registries existed but when most childhood cancers and certainly leukaemia were almost always fatal, mortality can be used as a surrogate for incidence. However, any increase in registration (or incidence or mortality rates) could be caused by (a) the survival of children long enough to get cancer, who in earlier years would have died of other causes such as infections; (b) improved diagnosis of cancer; and (c) improved registration efficiency. The improved diagnosis affects the distinction between different types of leukaemia, but should apply less to total leukaemia rates (Draper, Kroll & Stiller, 1994). These factors almost certainly account for some of the increase in registration rates, but it seems likely that there is a genuine increase in some childhood cancer incidence rates as well. In the US, a very slight overall increase in childhood leukaemia incidence was described for the period from the mid-1970s to the late 1990s, indicating an estimated annual increase of 0.5% for all leukaemias and 1.1% for ALL (Linet et al., 1999; Ries et al., 2001). However, Linet et al. (1999) concluded that this modest increase was confined to short intervals in the mid 1980s, and the pattern suggests that reporting or diagnostic changes, rather than environmental influences, were responsible.

Another relevant phenomenon, decribed earlier, is the appearance of a peak in childhood ALL incidence in children aged 2–4 in the early twentieth century. There is some evidence this peak appeared earlier in more industrialised countries, and also appears differently in different ethnic groups.

11.2.1.2.3 Comparison of trends in incidence and exposure

Suppose that magnetic fields are a risk factor for childhood leukaemia, that average exposure to magnetic fields has increased over time and that all other risk factors did not change over time. Then the childhood leukaemia incidence rate would have increased as a consequence of the increase in average exposure, and the size of the increase in incidence rate would be a measure of the fraction of leukaemia incidence attributable to magnetic field exposure.

The calculations presented in the appendix, based on the pooled analyses of the epidemiological data on magnetic field exposure and childhood leukaemia incidence, and again taking the hypothetical case of a causal relationship, suggest that the attributable fraction for magnetic field exposure ranges from 0.5% in a low-exposure country such as the UK to 5% in a high-exposure country such as the USA. Increases at the lower end of this range are essentially indistinguishable from the random fluctuations in incidence-rate data. Further, numerous other factors are suspected to be linked to the development of childhood leukaemia. The assumption that all those other risk factors have remained unchanged is implausible, and it would take only a small change in those factors to mask any change in effects, if any, of magnetic field exposure. Furthermore, reliable incidence data in most countries is available only from about 1970, a time where the exponential increase in exposure may have ceased. Therefore, while available data on incidence rates are compatible with the attributable fraction derived from the pooled analyses, they are also compatible with the alternatives of no cases attributable to magnetic fields or of a larger fraction being attributable. It is therefore impossible to draw any conclusions from a comparison of trends in exposures and incidence rates.

Milham & Ossiander (2001) have suggested that the appearance of the peak incidence at around age 3 in childhood ALL is linked with electrification and therefore with exposures. Again, the data are compatible with this hypothesis. However, many other features of society have also changed with progressive industrialisation, and there is in addition considerable uncertainty whether this peak appeared as a consequence of improved survival from other causes. Therefore, it is not valid to claim this as evidence of a link between EMFs and cancer (Kheifets, Swanson & Greenland, 2006).

11.2.1.3 New data

Two studies have been published since the IARC evaluation: Kabuto et al. (2006) in Japan and Draper et al. (2005) in the UK.

Kabuto et al. (2006) conducted a study of ALL and AML in children aged 15 years or less and diagnosed between 1999 and 2002 in the catchment area consisting of 18 prefectures and covering 10.7 million (53.5%) of the total 20.0 million children aged 0–15 years in Japan. For each case, up to 3 controls were selected matched on gender, age and residential area. Exposure assessment included 5-min magnetic field measurements in a room where a child spends the longest time daily, as well as in four corners of the house and at an entrance, and 1-week measurements made in the child's bedroom. The distance from each house to the closest overhead power transmission line (22–500 kV) located within 100 meters was measured. Measurements were done in the current house. Based on the family's residential history the length of stay at the current house for the period from conception to the date of diagnosis was assessed. In order to reduce possible information bias due to seasonal variation of magnetic field levels, measurements for each set of case and controls were made close in time and within 2.6 days on average; four sets with more than 100 days between the measurements were excluded. The main exposure metric consisted of a weekly arithmetic mean magnetic fields in the child's bedroom, categorized with cut-off points of 0.1, 0.2, and 0.4 μT for comparability with the pooled analysis. From 1439 childhood leukaemia cases diagnosed in all Japan, request for participation was sent to 781 (ALL+AML) cases living in the catchment area through the child's physicians. Among them 381 cases agreed to participate, but an additional 60 were later excluded due to change of residence after diagnosis, missing measurements, or lack of controls. The final analysis was based on 251 ALL and 61 AML cases and 495 and 108 controls, respectively (9 additional cases and 31 controls were lost due to matching). All conditional logistic regression analyses were adjusted for mother's education as an indicator of socio-economic status. When compared with children who were exposed to magnetic fields < 0.1 μT, the odds ratio for exposure 0.4 μT was 2.63 (95% CI: 0.77–8.96) for all leukaemia combined. No elevation in risk was observed below 0.4 μT. The risk was higher for ALL: OR = 4.73 (95% CI: 1.14–19.7) and the risk was not increased (no cases in the highest category) for AML. [The results are roughly consistent with those of the pooled analyses, but are limited by the small sample size leading to a broad range of uncertainty. The low response rate was a limitation of this study. Thus the addition of this study to the database will not add much as far as the overall results are concerned.]

In the study by Draper et al. (2005), 33 000 children from birth to 14 years old who had a cancer diagnosis in England, Scotland, or Wales between 1962 and 1995 were identified from various cancer registries. One control for each case matched on gender, birth date within 6 months, and birth registration district was selected. The final data set included 9700 matched case-control pairs for leukaemia who had a known birth address that allowed mapping in relation to transmission lines. The postal code at birth was used to identify subjects within 1 km of a 275- or 400-kV transmission line and a few 132-kV lines. Exposure was based on the shortest distance to any line that had existed in the year of birth. When possible, previous line

locations were recreated. A distance-dependent excess risk was observed for leukaemia (ranging from RR = 1.36 for distance-to-line 500–599 m to RR = 1.67 for distance of 0–49 m, compared to distance greater than 600 m). Adjustment for the deprivation index did not change the results. [Given its large size the risk estimates in the paper should be stable. Furthermore, because contact with the subject was not necessary, selection bias due to the differential participation among cases and controls, which plagued some of the previous studies, has been avoided. Thus the dependence of the results on the chosen control group and observation of the excess risk so far from the power lines, both noted by the authors and others, is surprising. Furthermore, distance is known to be a very poor predictor of magnetic field exposure, and therefore, results of this material based on calculated magnetic fields, when completed, should be much more informative.]

11.2.1.4 Evaluating epidemiological evidence: possible explanations

The consistent association observed between childhood leukaemia and average magnetic field exposure above 0.3–0.4 μT can be due to chance, selection bias, misclassification and other factors which confound the association, or can be a true causal relationship. Each of these interpretations will be discussed in turn below.

11.2.1.4.1 Random error

In the earlier studies only very small numbers were included, particularly for the very-high exposed categories. These studies were thus subject to substantially potentail random error. However, recent pooled analyses are based on large numbers including for children in the highly exposed categories and as a consequence these pooled analyses are unlikely to be substantially affected by random error.

11.2.1.4.2 Systematic error

Selection bias

Since practically all epidemiological studies of ELF and childhood leukaemia have been case-control studies, it has been proposed that control selection bias – a common and potentially serious problem of all case-control studies – may be fully or, at least, partially responsible for the consistently described epidemiological association between ELF magnetic fields and childhood leukaemia. In a case-control study, control selection bias occurs when the ratio of the selection probabilities of exposed and unexposed cases is different than the ratio of the selection probabilities of exposed and unexposed controls. The overall requirement of the controls is that they are representative of the source population of the cases.

Low participation rates alone or even selection or response rates that are associated only with disease or only with exposure do not result in selection bias; selection bias develops only if the selection/inclusion probabilities are differential for cases and controls based on their exposure status.

Low subject participation rates in a case-control epidemiological study, however, may allow for a significantly greater potential for control selection bias to occur. A particular problem arises with hospital-based case-control studies and with studies that use methods such as random digit dialing for selection of controls. The problems arise because of a possible difference between the source population of the cases and the source population of the controls.

Subject participation rates differed greatly in previous epidemiological studies of ELF and childhood leukaemia. Participation rates often depended on the type of study and the way study subjects were recruited. Registry-based studies, where subjects were not contacted, were able to include 94–100% of the selected subjects. Studies requiring interviews and in-home measurements generally had significantly lower participation rates (68–37% of eligible subjects), while matching in a case-control study frequently resulted in further decrease in the number of subjects included in the analysis; in one study only 31% and 9% of the eligible cases and controls, respectively, were included. Clearly, in practice the potential for bias is lower in registry-based studies and higher for studies with interviews and measurements. While some studies do in fact report response rates, accurate response rates are not available for all studies. Even for studies reporting response rates, it is frequently difficult to compare them due to non-uniform reporting.

It is hypothesized that selection bias may occur through socio-economic status (SES) or residential mobility; either because relative participation is lower for low SES controls than cases, and low SES children are more likely to be highly exposed than are high SES children; or high mobility controls are both less likely to be included and more likely to have high exposure, leaving group of controls which were included with lower exposure levels than would be in a representative group of children without leukaemia. Under these scenarios, selection bias upwardly biases the effect estimate (Mezei & Kheifets, 2006).

Some evidence supports this hypothesis. Several studies showed that higher participation tended to be related to higher socio-economic status (Hatch et al., 2000; Michaelis et al., 1997; Spinelli et al., 2001). Others showed that lower SES and higher residential mobility (Gurney et al., 1995; Jones et al., 1993) were associated with higher wire codes and perhaps higher residential exposure. However, it should also be noted that the effect of selection bias introduced by this procedure could be reduced by controlling for SES in the analyses, which most studies have done. No study was able to determine exposure among non-participants. A few studies compared, however, exposure distribution between subjects who partially participated in a study to those who fully participated. Hatch et al. (2000) found that full participants were less likely to live in homes with high wire codes (VHCC) or high measured fields (measurements at front door above 0.2 μT). Savitz et al. (1988) compared subjects with and without magnetic field measurements among those with wire code classification. They found that subjects without field measurement were more likely to live in homes with higher wire codes.

Most of the available information on SES and mobility, however, is either based on ecological studies or studies of wire code. It is unknown, at present, to what extent measured fields are correlated with participation, SES or mobility. The strongest evidence for the role of control selection bias comes from a USA study, in which exclusion of partial participants from analyses tended to increase the relative risk estimates for childhood leukaemia (Hatch et al., 2000).

Evidence against the role of selection bias comes from Ahlbom et al's (2000) pooled analysis. Taking advantage of the fact that studies conducted in the Nordic countries relied on historical calculated magnetic fields and are thus not subject to selection bias, investigators compared risk estimates in Nordic studies (OR = 2.1, 95% CI: 0.9–4.9) to the rest of the world (OR = 1.9, 95% CI:1.1–3.2) and found similar estimates. Calculated field studies, however, included only eight exposed cases, five of which were from the Swedish study. Furthermore, a sensitivity analysis which excluded from the pooling one study at a time showed that exclusion of the North American studies, for which suspicion of selection bias is strongest, did not change the overall results. Another argument against selection bias is that there is a lack of consistent association in studies of childhood brain tumours and residential magnetic fields. Many of the leukaemia studies included in the pooled analysis examined brain tumours as well and there is no reason to think that selection bias will affect one outcome and not the other. However, brain tumour studies have generally been smaller and some of lower quality; and a pooled analysis of brain tumour studies is yet to be conducted.

Pursuit of whether and how selection bias might impact effect estimates from case-control studies remains a high priority, both to understand the association between exposure to ELF magnetic fields and childhood leukaemia, and because of an impact it might have on the field of epidemiology, where similar study designs are widely used.

Misclassification bias

All of the difficulties with ELF exposure assessment are likely to have led to substantial exposure misclassification, which, in turn, is likely to interfere with detection of an association between exposure and disease. Almost certainly, measurement errors in both measured and calculated fields are not only present in all studies but they also vary considerably from study to study (Greenland & Kheifets, 2006). Target exposure, often described as the average exposure during the period prior to disease diagnosis, is not measured consistently among studies. Furthermore, because the biologically relevant exposure remains unknown, it is unknown whether, or how much, the measured exposure reflects the relevant exposure.

It is generally assumed that misclassification in ELF and leukaemia studies is non-differential, except perhaps in studies using personal exposure measurements (Green et al., 1999b; McBride et al., 1999); this means that exposure misclassification does not differ by disease status. Non-differential misclassification independent of diagnostic errors translates into a bias of the

effect estimate towards the null in most situations, although misclassification in middle categories can lead to the distortion of the dose-response curve.

Pooled analyses point to an association between ELF magnetic fields and leukaemia at levels of exposure greater than 0.3 or 0.4 μT. Since there is no established gold standard for the biologically relevant exposure, both sensitivity and specificity cannot be determined for measurements used in ELF assessment. It is known, however, that the specificity is particularly important for rare exposures; even a small decrease in specificity (less than 5%) can reduce a relative risk of 5 to the observed relative risk of approximately 2 (Schüz et al., 2001). A similar reduction in sensitivity has only a small effect on the risk estimate. For magnetic fields, identifying the unexposed as such is difficult.

It is concluded that while misclassification is likely to be ever present, it is unlikely to provide an explanation for the entire observed association. It does, however, introduce a lot of uncertainty into the potential dose response. For example, it is very possible that the apparent threshold may have resulted from smooth monotonic relation together with random measurement error.

Confounding

Since the early days of EMF research, investigators searched for possible confounding that would explain the observed association. The hypothesized confounders of the relation between ELF magnetic fields and childhood leukaemia include SES, residential mobility, residence type, viral contacts, environmental tobacco smoke, dietary agents, and traffic density (Kheifets & Shimkhada, 2005). None of these variables have been found to confound the association, although some have been identified as potential risk factors. For a factor to be a confounder it has to exert an effect considerably larger than the observed association and be strongly correlated with exposure (Kheifets & Shimkhada, 2005). Owing to limited knowledge of the etiology of childhood leukaemia and an absence of strong risk factors, it is not surprising that substantial confounding has not been identified. The same observation, however, makes it difficult to exclude a possibility of some (yet to be identified) confounder or of the combination of a number of factors. The pooled analysis by Ahlbom et al. (2000) looked at the possible effect of a number of putative risk factors. However, for none of them did adjustment move the relative risk estimate by more than 2%.

Multiple bias modeling

With such small relative risks as are seen in the context of ELF magnetic fields and childhood leukaemia, it is conceivable that a combination of the biases can explain the observed associations. In pooled analyses, where random error is not the only source of uncertainty, uncertainty from biases can be modeled using multiple-bias modeling. Multiple-bias modeling is used to systematically integrate the major sources of uncertainty into the results to provide a more unbiased estimate of an effect and can be used as a

tool to better understand the impact of the different types of biases on the effect estimate. Using multiple-bias modeling, Greenland (2005) concludes that while selection bias is present, it is unlikely to explain the association; that confounding is probably less important than selection bias; and that allowing for misclassification tends to increase the point estimate of risk, but also increases the standard deviation even more, resulting in less certainty that there is a positive association, but a higher certainty that the effect if present is larger than the observed association. In other words, misclassification greatly increases uncertainty, making both no association and a strong association more plausible. Based on one set of plausible assumptions, Greenland calculates posterior probabilities of 2–4% that the combination of misclassification, selection bias, confounding and random error (i.e. the net impact) explains the association. Other plausible assumptions would yield different results, however, and the sole point of this analysis is that, after taking account of all major uncertainty sources, due to limitations in the design, studies completed through 2003 are not decisive and further studies of similar design (such as the new English and Japanese studies) would add little information.

Possible interaction mechanisms

The absence of a clearly elucidated, robust, and reproducible mechanism of interaction of low level magnetic fields with biological systems deprives epidemiologic studies of focus in their study designs and hinders their interpretation. Based on known physical principles and a simplistic biological model, many authors have argued that average magnetic fields of 0.3–0.4 μT are orders of magnitude below levels that could interact with cells or tissues and that such interactions are thus biophysically implausible (see Chapter 4). The various mechanisms discussed include forces on magnetic particles, free radical generation, and "resonant" type interactions. Particular hypotheses directed towards childhood leukaemia include the suggestion reviewed by Kavet (2005) that contact currents generated when a person touches a conducting object at a different electrical potential to ground might be of sufficient magnitude to affect bone marrow, which is more extensively distributed in the limbs of children than in adults. In addition, Henshaw and Reiter (2005) raise the suggestion that EMF exposure may increase the risk of childhood leukaemia through the disruption of the night-time secretion of melatonin by the pineal gland (the experimental evidence for melatonin suppression by EMF exposure is discussed in Chapter 6). None of these hypotheses have however received experimental confirmation.

11.2.1.4.3 Magnetic fields as a putative factor

Epidemiologic studies of magnetic fields have consistently shown associations with childhood leukaemia, but lack of a known mechanism at such low energy levels and negative animal data suggest that the association is not causal. This section discusses some of the issues that would arise mak-

ing the "worst-case" assumption that the associations were causally related to magnetic field exposure.

Time-weighted average

In the absence of a known biophysical mechanism, which would yield a known etiologically relevant metric of exposure, the metric of choice used in most epidemiological studies has been the time-weighted average field. In many cases this has been assessed at diagnosis or over a period of, for example, one year prior to diagnosis. Further, most studies have assessed the field present over the general volume of the subject's home, or specifically in the bedroom, and used this as an estimate of the subject's exposure. This approach neglects the contribution to exposure from local sources within the home (e.g. domestic electrical appliances) and from sources outside the home. Other studies used personal dosimeters to estimate exposure from all sources, for a time interval such as a week (e.g. McBride et al., 1999).

The assessment of average personal exposure by the surrogate of average field in the home is clearly an approximation. It is, however, likely to be a better approximation for younger children, who spend more time at home, than for older children, who spend time outside the home and may have significant appliance use, and for adults, who may have significant occupational exposure as well. It is the exposure of younger children which is most relevant for studies of childhood leukaemia. Concentration on the field in the bedroom probably improves the approximation because of the time spent there sleeping. Some studies have included partial assessments of exposure from appliances believed most likely to contribute to average exposure and from schools. Others have assessed previous years and previous residences in order to approximate lifetime exposure rather than exposure at diagnosis. However, all such attempts are inevitably imperfect, particularly exposure to appliances, which so far has been only examined one at a time leading to large misclassification. The pooled analysis of Ahlbom et al. (2000) removed such extra contributions, finding its elevated risk ratio just with the 24 or 48 hour average field in the home.

The calculated-field studies calculate the field in the home from just one source, the high-voltage power line, ignoring the other sources such as low-voltage wiring, which in homes not near high-voltage power lines would be the main source. This clearly introduces an extra element of misclassification, which may be even greater if the historical loads or other data used in the calculation are imperfect. The size of the misclassification depends, however, on the relative sizes of the fields included (power line) and not included (low-voltage wiring).

It is worth mentioning that epidemiologic data appear to be not only consistent, but also specific. For cancer, the observed association seems to be limited to leukaemia, and even more specifically to childhood leukaemia. Several explanations can be advanced to explain the lack of an association with adult leukaemia. One possibility is that exposure assessment methods

used are much better in capturing exposure of children than that of adults: as mentioned, children spend more time at home and do not have occupational exposures. Another possibility is that children are more vulnerable to magnetic fields due to, for example, timing of exposure relevant to their development or predisposition due to an initiating event which occurred *in utero*.

Other correlated magnetic field exposures

The exposure most often used, implicitly or explicitly, in epidemiological studies, time-weighted average, is attractive for the pragmatic reason that it is probably the easiest to measure. However, it is also attractive because there is a class of biophysical mechanisms, those for which the effect produced is proportional to the magnitude of the field without regard to its direction, for which this indeed is the appropriate metric. Nonetheless, the metric of time-weighted average of the field has the major problem that the level of field at which an elevated risk appears, of the order of a microtesla or less, is well below the levels that can be regarded as plausible from biophysical arguments. Further, it is unlikely that any biophysical mechanism would produce an exactly linear effect over several orders of magnitude. It can also be argued that when the metric used is the average of a quantity (the field experienced by a person) which varies over, say, five orders of magnitude, it would be strange if any risk appeared in the comparatively narrow range between 0.1 and 0.3 or 0.4 μT.

The fact that the studies which have used time-weighted average field as a metric have found an elevated risk gives a particular status to this metric. Any other metric must, if it is to explain the observed association, be sufficiently correlated with time-weighted average, and the weaker the correlation, the stronger the risk with the "true" metric must be. Consideration of metrics and exposures raises a number of problems in interpretation of epidemiological studies. However, there is currently no alternative metric of exposure which is any more attractive, and the fact remains that the metric used so far, time weighted average, for all its problems, does seem to be associated with an elevated risk. Thus, the attributable fraction calculations given in the appendix are based on the arithmetic and geometric means of the time-weighted average field.

11.2.2 Adult cancer

Since the IARC (2002) review, several new studies have been published, many of which have focused on either residential or occupational exposures to ELF magnetic fields and breast cancer. This review updates the IARC evaluation by including studies published from 2001 (subsequent to the IARC monograph) through to January 2005 (for consistency studies published up to 2001 which were included in the IARC monograph are not reproduced here). The main focus is on breast cancer for which data in the previous review were considered inadequate for evaluation. Many of the issues of bias, confounding and other sources of error discussed in 11.2.1.4 in relation to studies of childhood leukaemia are also relevant to the interpretation of the studies of cancers in adults.

11.2.2.1 Breast cancer

11.2.2.1.1 Residential exposure

Table 73 lists the studies published since 2001 on residential exposure (including appliance use) to ELF electric and magnetic fields and adult cancers – seven of these studies concern breast cancer.

Table 73. Residential studies of adult cancer by exposure category subsequent to IARC (2002)

Outcome	Exposure					
	Electric blanket	Other appliances	Proximity +/- wire codes	Calculated fields	Spot measurements	Combined occupational and residential
Breast						
McElroy et al., 2001	•					
Davis, Mirick & Stevens, 2002	•	•	•		•	
Kabat et al., 2003	•					
Schoenfeld et al., 2003			•		•	
London et al., 2003			•		•	
Zhu et al., 2003	•	•				
Kliukiene, Tynes & Andersen, 2004				•		•
Acute myeloid leukaemia						
Oppenheimer & Preston-Martin, 2002	•	•				
Hematological cancers						
Tynes & Haldorsen, 2003				•		•
Malignant melanoma						
Tynes, Klaeboe & Haldorsen, 2003				•		•
Brain cancer						
Kleinerman et al., 2005	•	•				

The design and results of the studies of residential exposure and breast cancer discussed below are summarized in Table 74.

General residential exposure

Davis, Mirick & Stevens (2002) conducted a case-control study in the greater Seattle, Washington area. Eligible cases were Caucasian women aged 20 to 74 years selected from the local cancer registry, diagnosed between November 1992 and March 1995 and resident of King or Snohomish County (chosen to ensure representation of urban, suburban and rural areas). Controls were identified through random digit dialing, frequency matched to the cases by 5-year age group and county of residence. Response rate was 78% among cases and 75% among controls. Exposure to magnetic fields was estimated by both direct measurement and wire-code configuration. Continuous 48-hour measurements of magnetic field in the bedroom of each person's current residence were done using an EMDEX II meter set to record broadband (40–800 Hz) and harmonic (100–800 Hz) magnetic fields at 15-s intervals. Three variables based on broadband magnetic field measurements were constructed averaged over two nights: (1) mean nighttime (10 pm to 5 am) bedroom magnetic field; (2) proportion of nighttime bedroom magnetic field measurements $\geq$ 0.2 μT; and (3) short-term variability in the nighttime bedroom magnetic field based on grouping of measurement data into 10-min intervals. The wire-coding scheme of Wertheimer and Leeper (1979) was used to classify the participant's current residence and all previous residences occupied for at least six consecutive months within the greater Seattle metropolitan area in the 5 and 10 years prior to diagnosis. Wire codes were ordered (1–5) according to their respective in-home nighttime mean magnetic field measurements using data from the controls. In addition a questionnaire gave data on use of electrical appliances in the home. The magnetic field analyses included 744 (of 813) cases and 711 (of 793) controls. Mean nighttime broadband magnetic field levels of less than 0.16 μT were observed with 90% of both cases and controls and 76% had no measurements above 0.20 μT (mean nighttime broadband magnetic fields were 0.080 μT for cases and 0.071 μT for controls). None of the metrics of mean nighttime magnetic field exposure was associated with breast cancer risk; for the highest quartile (=58%) of the percentage of magnetic field measurements $\geq$ 0.20 μT (percentiles estimated among controls with at least one measurement $\geq$ 0.20 μT), the adjusted odds ratio was 1.1 (95% CI: 0.7–1.8). For the mean nighttime bedroom broadband magnetic field treated as a continuous variable, the adjusted odds ratio per 0.1 μT was 1.04 (95% CI: 0.97–1.12). No associations were found after stratification by age, menopausal or estrogen receptor status. There was also no association with wire codes either from current configuration or a weighted score for wire codes at residences over the previous 5 or 10 years. For wire codes at home of diagnosis (or reference date for controls), the odds ratio for very high versus very low current configuration was 0.8 (95% CI: 0.5–1.3).

Table 74. Epidemiological studies of residential exposures to magnetic fields and breast cancer and leukemia, published subsequent to IARC (2002) [a]

Study area, population	Exposure metrics	Exposure categories	OR (95% CI)	# cases	Comments	Reference
Breast cancer						
King or Snohomish County, Seattle, WA, USA *Cases*: Caucasian women aged 20–74 y identified from cancer registry (Nov 1992 – March 1995). 744 of 813 cases included. *Controls*: obtained by random-digit dialling, frequency matched on age and county of residence. 711 of 793 controls included.	48-h measurements of 40–800 Hz magnetic fields in bedroom of current residence. Estimation of magnetic fields from maps and wire coding based on current residence and residences in past 10 y. Electric appliance use from questionnaire.	% Mean nighttime bedroom magnetic field > 0.20 µT Ref.: 0% < 0.7 0.7–8.9 8.9–58 ≥ 58	Adjusted 0.6 (0.4–1.0) 1.2 (0.8–1.9) 1.1 (0.7–1.7) 1.1 (0.7–1.8)	 25 44 45 42	Data not presented for mean nighttime bedroom magnetic field > 0.20 µT. 90% of cases and controls had mean nighttime broadband magnetic field levels < 0.16 µT; 76% had no measurements > 0.20 µT, limiting statistical power to detect effects at higher exposure levels.	Davis, Mirick & Stevens, 2002
Los Angeles County, CA, USA *Cases*: Breast cancer cases from tumor registries (1993–1999), , nested within a cohort of African Americans, Latinas and Caucasians, aged 45–74 at recruitment, selected primarily licensed drivers. 743 (of 751) cases with wire configuration codes and 347 with 7-d bedroom measurements. *Controls*: Random selected by (frequency matched on ethnicity) from cohort members free of breast cancer at baseline.	7-d measurements of 40-800 Hz magnetic fields in bedroom of current residence. Wiring configuration codes in homes occupied over the previous 10 y. Electric appliance use from questionnaire (not reported).	Mean nighttime bedroom broadband magnetic field (µT) Ref.: < 0.1 0.10–0.19 0.20–0.29 0.30–0.39 0.40	Adjusted 1.3 (0.8–2.1) 1.1 (0.4–2.8) 2.1 (0.6–7.5) 1.2 (0.5–3.0)	 56 11 8 12	91% of cases and 92 % of controls had mean nighttime broadband magnetic field levels less than 0.20 µT, limiting statistical power to detect effects at higher exposure levels.	London et al., 2003

Table 74. Continued

699 (of 702) controls with wire codes and 286 with magnetic field measurements.						
Long Island, NY, *USA* *Cases*: Selected from cases aged < 75 y in the Long Island Breast Cancer Study Project (LIBCSP) (663 approached, 576 participated), with residence in same property ≥ 15 y. *Controls*: Selected from LIBCSP controls recruited by random digit dialling (< 65 y) or from Health Care Financing Administration files (≥ 65 y) (702 approached, 585 participated)	Spot and 24-h measurements of 40–800 Hz magnetic fields. Wiring maps used to classify homes according to modified method of Wertheimer and Leeper. Electric appliance use from questionnaire (reported in Kabat et al. (Kabat et al., 2003).	24-h bedroom broadband magnetic field (μT) Ref: < 0.041 0.041–0.081 0.082–0.171 ≥ 0.172	Adjusted 1.0 (0.7–1.4) 1.0 (0.7–1.4) 1.0 (0.7–1.4)	 148 140 139	Data not presented for mean 24-h or spot magnetic field measurements > 0.20 μT.	Schoenfeld et al., 2003
Norway *Cases*: All incident cancer cases (n=1830) from cancer registry (1980–96), from cohort aged ≥ 16 years living within corridor of 40 m (33 kV) to 300 m (420 kV) from power lines. *Controls*: Two controls per case from same cohort (n=3658). Matched on age and municipality.	Calculations of power line magnetic fields . Data on migration between municipalities (1967–85) and between and within municipalities (1986–96). Occupational exposure estimated from job-exposure matrix based on job title provided at decennial census.	Calculated TWA residential fields (5 most recent years) (μT) Ref.: < 0.05 All ages 0.05–0.19 ≥ 0.20 < 50 y 0.05–0.19 ≥ 0.20 *≥ 50 y* 0.05–0.19	 1.5 (1.1–1.8) 1.6 (1.3–2.0) 1.8 (1.1–2.8) 1.8 (1.2–2.8)	 121 158 37 56	Numbers of cases ≥ 0.20 μT reported at all ages, < 50 y and ≥ 50 y do not tally.	Kliukiene, Tynes & Andersen, 2004

Table 74. Continued

		≥ 0.20	1.3 (1.0–1.8)	84		
		ER+, all ages	1.6 (1.2–2.0)	112		
		0.05–0.19				
		≥ 0.20	1.2 (0.8–1.9)	38		
			1.6 (1.1–2.4)	49		
Leukaemia						
Norway *Cases:* All incident cancer cases (n=295) from cancer registry (1980–96), from cohort of Norwegian population aged ≥ 16 y living within corridor of 40 m (33 kV) to 300 m (420 kV) from high-voltage power lines. *Controls*: Two controls per case from same cohort. Matched on age, gender and municipality	See Kliukiene et al. (2004) above	Calculated TWA residential fields (10 most recent years) (μT) Ref.: < 0.05 All leukaemia 0.05–0.19 ≥ 0.20 ALL: 0.05–0.19 ≥ 0.20 CLL: 0.05–0.19 ≥ 0.20 AML: 0.05–0.19 ≥ 0.20 CML: 0.05–0.19 ≥ 0.2	 1.6 (0.8–3.1) 1.3 (0.7–2.5) 1.0 (0.1-11.0) 1.3 (0.2–8.0) 4.2 (1.0-17.9) 3.0 (0.9-10.0) 1.5 (0.4–5.0) 2.2 (0.6–8.4) 2.4 (0.4-15.0) 0.2 (0.0–2.0)	 17 19 1 3 6 7 5 5 3 1	Same cohort as Kliukiene et al. (2004) above.	Tynes & Haldorsen, 2003

[a] OR: odds ratio; CI: confidence interval; ER+: estrogen-receptor-positive; Ref.: reference group with exposure level indicated, ALL: acute lymphocytic leukaemia; CLL: chronic lymphocytic leukaemia; AML: acute myeloid leukaemia; CML: chronic myeloid leukaemia; TWA: time weighted average.

London et al. (2003) carried out a nested case-control study of residential exposure to magnetic fields among a cohort of African Americans, Latinas and Caucasians resident in Los Angeles County, aged 45–74 at recruitment, selected primarily from the file of licensed drivers. Incident breast cancer cases from 1993 to 1999 were ascertained by linkage to state tumour registries. Controls were frequency matched on ethnicity from cohort members free of breast cancer at baseline. Wiring configuration codes were derived according to the scheme of Wertheimer and Leeper (1979) in homes occupied at time of diagnosis (or reference date for controls) and over the previous 10 years. Seven-day measurements of magnetic fields in the bedroom were obtained using an EMDEX II meter, to include both broadband (40–800 Hz) and harmonic (100–800 Hz) magnetic fields sampled at 120-s intervals. The primary magnetic field measurement metric was the nighttime mean based on questionnaire response for each participant concerning usual times of going to bed, obtained separately for weekdays and weekends. Three variables based on magnetic field measurements (separately for broadband and harmonic fields) over nighttime hours for seven days were constructed: (1) mean nighttime bedroom magnetic field; (2) proportion of nighttime bedroom magnetic field measurements $\geq$ 0.4 μT; and (3) short-term variability in the nighttime bedroom magnetic field. Wire configuration codes for address at diagnosis (cases) or reference date (controls) were available for 743 (of 751) cases and 699 (of 702) controls, and 7-day measurements of magnetic fields in the bedroom for 347 cases and 286 controls. Mean nighttime broadband magnetic field levels less than 0.20 μT were found with 91% of cases and 92% of controls, and 86% of both cases and controls had no measurements above 0.40 μT (mean nighttime broadband magnetic fields were 0.097 μT for cases and 0.099 μT for controls). None of the metrics of mean nighttime magnetic field exposure (broadband or harmonic fields) was associated with breast cancer risk; adjusted odds ratios compared with mean nighttime bedroom broadband exposure < 0.10 μT were 1.1 (95% CI: 0.43–2.8) for mean nighttime bedroom broadband exposure 0.20–0.29 μT (11 cases), 2.1 (95% CI: 0.58–7.5) for 0.30–0.39 μT (8 cases), and 1.2 (95% CI: 0.50–3.0) for mean nighttime bedroom broadband exposure $\geq$ 0.40 μT. For mean nighttime bedroom broadband magnetic field treated as a continuous variable, adjusted odds ratio per 0.1 μT was 1.00 (95% CI: 0.94–1.07). No associations were found after stratification by age, menopausal or estrogen receptor status, or other potential effect modifiers. There was also no association with wire codes either from current configuration or a weighted score for wire codes at residences over the previous 10 years; for wire codes at home of diagnosis (reference), adjusted odds ratio for very high versus very low current configuration was 0.76 (95% CI: 0.49–1.18).

Schoenfeld et al. (2003) carried out a case-control study of EMF exposure (EBCLIS) within the Long Island Breast Cancer Study Project (LIBCSP) of women under 75 years at enrollment, identified between August 1996 and June 1997, who had lived in the same Long Island home for at least 15 years. Cases were selected from the 1354 LIBCSP cases (663

approached, 576 participated, response 87%). Controls were selected from 1426 LIBCSP controls (69% participation) who were recruited by random digit dialling (< 65 years) or from Health Care Financing Administration files (≥ 65 years) (702 approached, 585 participated, response 83%). Both spot (front door, bedroom and most lived-in room) and 24-hour measurements (bedroom and most lived-in room) were collected using EMDEX II meters programmed to record both broadband (40–800 Hz) and harmonic (100–800 Hz) magnetic fields sampled at 3-s intervals for the spot measurements and 15-s intervals for the 24-hour measurements. Ground-current magnetic field measurements were also obtained. Wiring maps were obtained and used to classify homes according to the modified method of Wertheimer and Leeper (Wertheimer & Leeper, 1979). Questionnaire data on electrical appliance use was reported in Kabat et al. (2003). Mean 24-hour broadband magnetic fields in the bedroom were 0.16 μT for cases and 0.14 μT for controls. None of the exposure metrics was associated with risk of breast cancer. For 24-hour measurements in the bedroom, adjusted odds ratio for highest quartile (≥ 0.172 μT) versus lowest quartile (< 0.041 μT) broadband magnetic field was 0.97 (95% CI: 0.69–1.4) and for the mean of the spot measurements it was 1.15 (95% CI: 0.82–1.6) (highest quartile ≥ 0.145 μT; lowest quartile < 0.034 μT). For estimated personal exposure ≥ 0.200 μT (based on mean 24-hour broadband measurements in bedroom and most lived-in room and test-load coefficient for most lived-in room) compared with < 0.039 μT, adjusted odds ratio was 1.08 (95% CI: 0.77–1.5). For the wire code configuration, adjusted odds ratio for very high current configuration compared with underground/very low current configuration was 0.90 (95% CI: 0.54–1.5).

Kliukiene, Tynes & Andersen (2004) carried out a nested case-control study of female breast cancer within a nationwide cohort in Norway. This comprised all women aged 16 or over who on November 1, 1980, or on January 1 of at least one of the years between 1986 and 1996 were living in a residence within a defined corridor near high-voltage power lines (corridor distances ranging from 40 m for 33 kV lines to 300 m for 420 kV lines). The cohort included around 5% of all women in Norway during 1980–1996; cases (n = 1830) with invasive breast cancer were identified for this period from the national cancer registry. Two controls per case (3658 in total) were selected randomly from the cohort according to the following criteria: born within 5 years of the case, free of breast cancer and alive at time of diagnosis, and from the same municipality as the case at entry into the cohort. Data on migration between municipalities (1967–1985) and between or within a municipality (1986–1996) were obtained. Exposure to magnetic fields from the high-voltage lines was estimated from 1967 based on residential address, utilising a computer program (Teslaw) developed at SINTEF Energy, Norway, taking account of height of the towers, distance between phases, ordering of phases, distance between power line and a house, and mean load on the power line during each year that a study participant lived in the house. Distances of houses from the power lines were checked on maps for the half of the corridor nearest the line. Time-weighted average residential exposure

to magnetic fields from the lines was estimated, both from 1967 and for the last 5 years before diagnosis of a case. Occupational exposure was estimated – on a scale from 1 (< 4 h exposure at > 0.1 μT per week) to 3 (≥ 24 h exposure at > 0.1 μT per week) – based on a job-exposure matrix from information on job title provided at decennial census, for the period January 1, 1955 (based on 1960 census) until date of diagnosis (assuming working age 18–67 years). A cumulative category x years occupational exposure measure was then calculated. For combined residential and occupational exposure (based on 1296 cases and 2597 controls with available data), women were considered exposed if time weighted average residential exposure = 0.05 μT and occupational exposure > 30 category-years. For residential exposure in most recent 5 years, odds ratio (all ages) for time weighted average exposure ≥ 0.20 μT compared with < 0.05 μT was 1.6 (95% CI: 1.3–2.0); odds ratio at < 50 years was 1.8 (95% CI: 1.2–2.8) and at 50 years 1.6 (95% CI: 1.2–2.0). Odds ratios for time weighted average exposure of 0.05–0.19 μT were similar to those for ≥ 0.20 μT (Table 74). For ≥ 0.20 μT, odds ratio for the total period (all ages) was 1.4 (95% CI: 1.0–1.8). For women with highest estimated occupational exposure compared with the lowest, odds ratio (all ages) was 1.1 (95% CI: 0.9–1.4). For combined residential and occupational exposure, odds ratio (all ages) was 1.3 (95% CI: 0.8–2.1) based on 26 cases. There was no statistically significant increase when residential and occupational exposures were considered together, but numbers were small. [No measurements of magnetic fields were undertaken for persons included in the study. Occupational data were available for 71% of cases and controls. There was only limited control for confounding: age at birth of first child, education, type of residence.]

Use of electric blankets

Studies of electric blanket use and breast cancer are summarized in Table 75. McElroy et al. (2001) reported a case-control study of female residents of Wisconsin, Massachusetts (excluding residential Boston) and New Hampshire, aged 50–79. Cases with a new diagnosis of breast cancer reported between January 1992 and December 1994 were eligible. Data for 5685 (83%) cases were available. Controls in each state were randomly selected from two sampling frames: women aged 50–64 years were selected from lists of licensed drivers; those 65–74 years from a roster of Medicare beneficiaries; 5951 (78%) completed the study interview. The analysis was limited to 1949 cases and 2498 controls with available data who were interviewed between June 1994 and July 1995, when data on electric blanket or mattress cover use was elicited by telephone interview. The adjusted odds ratio for ever-users compared with never-users was 0.93 (95% CI: 0.82–1.1). For electric blanket or mattress cover use considered as a continuous variable, adjusted odds ratio per 12 months of use was 1.0 (95% CI: 0.98–1.0). [Although results are not separately presented by menopausal status, 93% of cases and controls were postmenopausal.]

The case-control study of residential exposure to ELF magnetic fields by Davis, Mirick & Stevens (2002) discussed above and summarized

in Table 74, included questionnaire data on use of an electric bed-warming device. For ever versus never use, the adjusted odds ratio was 1.1 (95% CI: 0.8–1.3). For hours of use included as a continuous variable, the adjusted odds ratio was 1.0 (95% CI: 1.0–1.0).

The Long Island Breast Cancer Study Project (LIBCSP) discussed above (Schoenfeld et al., 2003) also included information on electric blanket use; more detailed information on electric blanket use was included in the case-control study of EMF exposure (EBCLIS) within LIBCSP (Schoenfeld et al., 2003, summarized in Table 74) (Kabat et al., 2003). The results for LIBCSP and EBCLIS are presented separately, stratified by menopausal status; data for 1324 (out of 1354) LIBCSP cases and 1363 (out of 1426) LIBCSP controls, and 566 (out of 576) EBCLIS cases and 557 (out of 585) EBCLIS controls are included. Adjusted odds ratios for ever versus never use for pre/post menopausal women were 1.2 (95% CI: 0.9–1.6) and 1.0 (95% CI: 0.8–1.3), respectively, for LIBCSP, and 1.1 (95% CI: 0.6–1.9) and 0.9 (95% CI: 0.7–1.3), respectively, for EBCLIS. The EBCLIS study also provided data on estrogen (ER) and progesterone receptor (PR) status. For ER+/PR+, adjusted odds ratio for ever versus never use was 1.2 (95% CI: 0.9–1.5) based on 125 cases. [The EBCLIS cases are a subset of the LIBCSP cases, therefore the results are not independent of each other.]

Zhu et al. (2003) report a case-control study among African-American women aged 20–64 living in one of three Tennessee counties, with telephone service at time of the study; 304 cases (of 670 eligible women, 45%) with first histological diagnosis of breast cancer during 1995–98, identified through the Tennessee Cancer reporting system, were included. Controls were selected through random digit dialling, frequency matched to cases by 5-year age range and county; 305 women (73% of eligible women identified) were included. Information on use of electric bedding devices was obtained by telephone interview. For ever versus never use, adjusted odds ratio was 1.4 (95% CI: 0.9–2.2), and it was 1.4 (95% CI: 0.6–3.4) and 1.2 (95% CI: 0.6–2.1) for pre/post-menopausal women respectively. [Participation rate among cases was low (45%), mainly reflecting lack of physician consent. 205/304 (67%) cases and 213/305 (70%) controls provided data on use of electrical bedding devices. Overall data on only 30% of eligible cases and 51% of eligible controls was included, limiting the interpretation of the study.]

Table 75. Studies of use of electric blankets and risk of breast cancer in women, published subsequent to IARC (2002) [a]

Subjects	# cases/ controls	Ever use [b]		Use through the night [c]		Long-term use [d]		Authors
		OR (95% CI)	# cases	OR (95% CI)	# cases	OR (95% CI)	# cases	
Mostly post-menopausal	1949/ 2498	0.93 (0.82-1.1)	834	NR	NR	0.98 (0.80–1.2)	248	McElroy et al., 2001
Pre- and postmeno-pausal	720/ 725	1.1 (0.8–1.3)	302	NR	NR	NR	NR	Davis, Mirick & Stevens, 2002
LIBCSP: Premeno-pausal	472/ 503	1.2 (0.9–1.6)	171	NR	NR	1.4 (0.7–2.6)	25	Kabat et al., 2003
Postmeno-pausal	852/ 860	1.0 (0.8-1.3)	279	NR	NR	0.8 (0.5–1.3)	36	
EBCLIS: Premeno-pausal	146/ 131	1.1 (0.6–1.9)	58	1.3 (0.6–2.6)	32	1.1 (0.3–3.5)	11	
Postmeno-pausal	420/ 426	0.9 (0.7–1.3)	149	1.0 (0.7–1.5)	78	0.9 (0.5–1.7)	23	
Pre- and postmeno-pausal	205/ 213	1.4 (0.9–2.2)	73	1.7 (1.0–3.0)	56	4.9 (1.5–15.6)	16	Zhu et al., 2003

[a] OR: odds ratio; CI: confidence interval; NR: not reported.

[b] Defined as ever use by McElroy, Kabat and Zhu; any use during the last 10 years by Davis.

[c] Defined as use through the night by Kabat; on most of the time by Zhu.

[d] Defined as use for ≥ 5 years by McElroy; longer than 10 years for premenopausal women and 15 years for postmenopausal women by Kabat; longer than 10 years by Zhu.

11.2.2.1.2 Occupational exposure

Cohort studies

Pollan, Gustavsson & Floderus (2001) reported on risk of male breast cancer from an extended follow-up (to 1989) among the national

Swedish cohort study of workers, which previously had been followed up to 1984 (Floderus, Stenlund & Persson, 1999). The base population comprised 1 779 646 men aged 25–59 in 1971, who were gainfully employed at the 1970 census and who were also recorded at the 1960 census, followed through end 1989 (31 668 842 person-years). Follow up was through the national cancer registry; 250 cases of breast cancer were reported in the cohort. Occupations classified as "Services and military work" had a significant excess risk; within-cohort RR for this group was 1.8 (95% CI: 1.2–2.8). Among production workers, significant excess risks were found for "Other metal processing workers", RR = 5.3 (95% CI: 1.3–21) based on 2 cases and for "Machinery repairers", RR = 2.1 (95% CI: 1.2–3.6) based on 14 cases. Exposures to ELF magnetic fields were assessed by linking occupations to a job-exposure matrix covering the 100 most common occupations among Swedish men; for these occupations, exposure levels had been estimated based on at least four full-shift measurements. Ten further comparatively rare occupations with "definitely high" exposures but less than four measurements were added. Five exposure groups were identified based on the geometric mean of work-day mean values for an occupational group, with cutoffs at 25th, 50th, 75th and 90th centile points: $\leq$ 0.12 μT (reference group), 0.12–0.16 μT, 0.16–0.22 μT, 0.22–0.30 μT, > 0.30 μT. [Inclusion of only the 100 most common occupations for the analysis by exposure categories – with addition of 10 other occupations with "definitely high" exposures – reduced the person-years by 16%, though the number of men included in these analyses is not given.] Two hundred three cases were included in the analyses. Compared with the reference group, relative risks were 1.4 (95% CI: 0.95–2.0), 1.3 (95% CI: 0.82–1.9), 1.6 (95% CI: 1.0–2.6) and 0.92 (95% CI: 0.53–1.6) respectively. [Relative risk estimates are adjusted only for age, period and "geographical area" – counties were grouped into five classes based on their Standardised Incidence Ratio. There may be some overlap with the cases included in Håkansson et al. (2002), below, for the years 1985–89.]

Håkansson et al. (2002) reported a cohort study of cancer incidence among workers in industries using resistance welding in Sweden. All companies and workplaces where resistance welding might take place were identified for the years 1985–94; all workers ever employed at these workplaces during that period were then identified from tax returns. Information on occupation was obtained from censuses of 1980, 1985 and 1990 and from tax returns; resistance welders thus identified were assigned to the highest exposure category. Where someone changed job, the job with the highest exposure category was used; if information was missing for a particular census, that from the previous census was used. A job exposure matrix supplemented by additional information for some rare occupations and for women, was used to classify jobs into "Low" (< 0.164 μT), "Medium" (0.164–0.250 μT), "High" (0.250–0.530 μT) and "Very High" (> 0.530 μT) exposure to ELF magnetic fields based on the geometric mean of average workday mean values, with cutoffs based on 25th, 75th and 90th centile values. Seventy-five percent of people assigned to the "Very High" exposure category were

resistance welders. After exclusion of people without information on occupation or where exposure could not be estimated, data for 646 694 individuals (484 643 men and 162 051 women) were included. Cancer incidence cases from 1985–94 were obtained from the national cancer registry and mortality data from the national deaths registry. Within-cohort relative risk estimates were estimated using Cox regression with the "Low" exposure category as reference. There was no excess risk of breast cancer among women; in the "Very High" exposure category, relative risk (37 cases) was 1.1 (95% CI: 0.8–1.5). For men, numbers were small; relative risk in the "Very High" exposure category was 3.8 (95% CI: 0.3–43.5) based on 2 cases. [Classification into exposure categories was mainly on the basis of a job exposure matrix; details of the basis of measurement of workday values of average exposure to ELF magnetic fields are not provided. The results are unadjusted for potential occupational confounders other than inclusion of one dichotomous variable: blue collar workers vs. others.]

Kliukiene, Tynes & Andersen (2003) reported a follow up of breast cancer cases among Norwegian female radio and telegraph operators, based on the cohort reported in Tynes et al. (1996). These authors reported follow up of the cohort from 1961 to the end of 1991; Kliukiene, Tynes & Andersen (2003) extend the follow up to end May 2002. [The report of Tynes et al. (1996) was not included in the IARC (2002) monograph, presumably because the main focus is RF exposure rather than exposure to ELF magnetic fields. However, for completeness, Kliukiene, Tynes & Andersen (2003) is shown in Table 76, as spot measurements of ELF magnetic fields were obtained.] The cohort comprises 2619 women certified as radio and telegraph operators between 1960 and 1980 (98% of whom worked on Norwegian merchant ships). Spot measurements of ELF magnetic fields were made on two ships, when the transmitter was active and when it was shut down – they ranged from < 0.02 μT to about 6 μT, depending on the position occupied by the radio operator and whether or not the transmitter was active; normal exposure of the body was stated as about 0.1–0.2 μT (Tynes et al., 1996). Breast cancer cases were identified through the national cancer registry. There were 99 incident cases of breast cancer. Standardised Incidence Ratio (SIR) was calculated with reference to the Norwegian female population; SIR was 1.3 (95% CI: 1.1–1.6). Similar risks were observed for women < 50 years (44 cases) and ≥ 50 years (55 cases). A nested case-control study based on the same cohort is also reported in Kliukiene, Tynes & Andersen (2003), though as the focus is presumed exposure mainly to RF, results are not reported here. [Tynes et al. (1996) note that "ELF magnetic field levels at the operator's desk were comparable to those in normal working places in Norway, and the background level in the radio room was comparable to levels measured in Norwegian homes".]

Case-control studies

Band et al. (2000) report results of a case-control study in Canada focused generally on occupational risks of breast cancer, without a specific focus on ELF magnetic fields. However, they do report risks for occupations

with presumed exposure to ELF magnetic fields. [Although published in 2000, this study was not included in the IARC monograph (2002); for completeness, it is included here.] Cases, identified through the British Columbia cancer registry, were women aged < 75 years with breast cancer diagnosed between June 1, 1988 and June 30, 1989. Controls, matched by 5-year age groups, were selected randomly from the electoral roll. Information on job history and various potential confounders was obtained by questionnaire. The study included 1018 women with breast cancer (318 pre-menopausal, 700 post-menopausal) from a total of 1489 cases (68.4%), and 1025 out of 1502 (68.2%) controls; after exclusion of cases and controls with no matches or missing data there were 995 cases and 1020 controls. An excess of breast cancer was observed among electronic data-processing equipment operators; the odds ratio among all women (pre-and post-menopausal combined) was 3.1 (95% CI: 1.6–5.8) based on 24 cases. [As noted, there was no particular focus on ELF magnetic fields and no attempt was made to classify occupations by potential exposure to ELF magnetic fields.]

In a report from the Carolina Breast Cancer Study in the USA, Van Wijngaarden et al. (2001a) give results of a case-control study of occupational exposures to magnetic fields. Cases aged 20–74 years were identified through the North Carolina cancer registry, diagnosed from May 1, 1993 to September 30, 1995, and then stratified sampling was done to obtain equal numbers among younger and older black women and younger and older non-black women. Controls were sampled from lists of motor vehicle license holders (to age 65) and health care financing (above 65 years), frequency matched by race and five-year age group. Overall, response rates were 74.4% among cases and 52.8% among controls (Moorman et al., 1999); the report of Van Wijngaarden et al. (2001a) is based on 843 (of 861) cases and 773 (of 790) controls with adequate information on job history and duration. Occupational exposure to magnetic fields was estimated from the time-weighted average in six broad occupational groups and a homemaker category, based on 217 measurements done for a sample of 202 participants, using a personal average magnetic field exposure meter (AMEX 3-D). Individual exposure assignment was based on the longest and (where available) second-longest held occupation, the numbers of years worked and (where available) hours per work-week, to yield estimated μT-years of occupational exposure. Overall, risks of breast cancer by estimated cumulative exposure to magnetic fields (in comparison with 0–0.59 μT-years as reference) were > 0.59–0.90 μT-years (207 cases): OR = 1.4 (95% CI: 1.1–1.8); > 0.90–1.27 μT-years (143 cases): OR = 1.1 (95% CI: 0.8–1.5); > 1.27–2.43 μT-years (140 cases): OR = 1.0 (95% CI: 0.8–1.4); >2.43 μT-years (79 cases): OR = 1.2 (95% CI: 0.8–1.7). The risk estimates mostly showed a similar pattern by latency of exposure, whether pre- or post-menopausal and by estrogen receptor (ER) status (either ER positive or ER negative), although generally higher risks were found for pre-menopausal women, ER+, with latency > 10–20 years (in comparison with zero occupational exposure as reference): > 0–0.16 μT-years (38 cases): OR = 2.0 (95% CI: 1.1–3.9); > 0.16–0.40 μT-years (73 cases): OR = 2.0 (95% CI: 1.1–3.6); > 0.40–0.52 μT-years (28 cases): OR =

1.6 (95% CI: 0.8–3.2); > 0.52 T-years (38 cases): OR = 2.1 (95% CI: 1.1–4.0).

Labreche et al. (2003) report results of a case-control study of occupational exposure to electromagnetic fields and female breast cancer in Montreal, Canada. Cases ages 50–75 at diagnosis were identified from records of pathology departments and cancer registries from the 18 major hospitals in the greater Montreal area that treat breast cancer, between 1996 and 1997. Controls were selected from the same hospitals over the same period, with 32 different types of cancer (excluding inter alia brain and central nervous system, and leukaemia). Details on all occupations held over the working lifetime were obtained by interview. Duration of exposure to ELF magnetic fields in hours per working day was assigned by hygienists based on a four-category scale: "no exposure" (< 0.2 μT); "low exposure" (0.2–< 0.5 μT); "medium exposure" (≥ 0.5–< 1.0 μT); and "high exposure" (≥ 1.0–10 μT). Response rates were 81.1% for cases and 75.7% for controls; the report of Labreche et al. (2003) focuses on 556 (of 608) postmenopausal cases and 600 (of 667) controls. Combining time spent at "medium" and "high" exposures, across the interquartile range of exposures (6000 hours), for any period of lifetime working, the OR (adjusted for a range of potential confounders) was 1.1 (95% CI: 0.9–1.4); for a lag period of 10 years before diagnosis, the OR was 1.2 (95% CI: 1.0–1.5); and for exposures before age 35 years, the OR was 1.4 (95% CI: 1.0–2.0). The OR were around 10% larger with additional adjustment for working in the textile industry. For sub-analysis by receptor status, for exposures before age 35 years, OR were 1.6 (95% CI: 1.0–2.4) and 0.8 (95% CI: 0.4–1.5) for progesterone receptor positive (PR+) and negative (PR-) tumours respectively, and 1.5 (95% CI: 1.0–2.3) and 0.8 (95% CI: 0.3–2.1) for estrogen receptor positive (ER+) and negative (ER-) tumours respectively. [Exposure assessment was relatively crude based on job title with four classes of exposure, not supported by measurements.]

In other studies (not shown in the tables) Koc & Polat (2001) report a case series of 11 male patients with breast cancer (of a total of 196 breast cancer cases (5%)), admitted to a regional hospital in eastern Turkey from 1990–2000, four of whom worked for the Turkish Institution of Electricity. These four cases were stated to be among 13 male breast cancer cases in the records of the Turkish Institution of Electricity from 1996 to 2000; estimated male breast cancer rate among these workers was stated as 0.3%. [The report is anecdotal and no case verification data, information on possible exposures to ELF electromagnetic fields, nor data on denominators are given. However, rates for male breast cancer and among electrical workers in eastern Turkey seem very high.] Gardner et al. (2002) reported results from the Shanghai Breast Cancer Study in China, a case-control study of female breast cancer among 1458 cases and 1556 age-matched population controls, focussing on occupational risks. Although electrical occupations were not combined in the tables, it was noted that there was no increase in risk among electrical workers. In a case-control study of 1642 women with breast cancer (1494 population-controls) at ages 20–44 years in the USA, Teitelbaum et al. (2003) report breast cancer risks by occupation. Although there was no specific

focus on exposure to electromagnetic fields, no significant excess risks were reported among occupations thought to have potential exposure to electromagnetic fields.

A recent study of Forssén et al. (2005) included 20 400 cases of female breast cancer (identified through the regional cancer registry) and 116 227 controls from women gainfully employed in Stockholm or Gotland County in Sweden between 1976 and 1999. Exposure assessment was based on information about occupation obtained from the population censuses from 1960 to 1990. Information about magnetic field exposure was obtained from a job-exposure matrix derived from an electromagnetic field measurement programme performed in Stockholm County between March 2001 and October 2002. It included 49 of the most common occupations among women in Stockholm County (around 85% of the gainfully employed women in 1980 census). Measurements were made using an Emdex Lite personal monitor, carried on a belt for 24 hours; volunteers also completed a diary from which exposures at work could be estimated. Between five and 24 participants were measured in each occupation category. Exposure was estimated as the geometric mean of the time weighted average. At all ages, compared with reference (< 0.10 μT), the OR (adjusted for age, socio-economic status and year of diagnosis) was 1.0 (95% CI: 1.0–1.1) (11 369 cases) for 0.10–0.19 μT; 1.0 (95% CI: 0.9–1.1) (3243 cases) for 0.20–0.29 μT; and 1.0 (95% CI: 0.9–1.1) (814 cases) for ≥ 0.30 μT. Adjusted odds ratios were similar (all non-significant) at < 50 and ≥ 50 years, and for estrogen receptor positive and negative cases. Whereas earlier studies reported some positive results, this study was largely negative and was larger, had a better exposure matrix (based on measurements collected from women) and had more data available for female occupations than the earlier studies. [Some overlap of cases is likely with Floderus, Stenlund & Persson (1999) and possibly with Forssén et al. (2000).]

11.2.2.2 Leukaemia and brain cancer

11.2.2.2.1 Residential exposure

One residential study of haematological cancers, one study of electric blanket use and acute myeloid leukaemia, and one study of electric appliance use and brain cancer have been published since the IARC (2002) review (Table 73). Tynes & Haldorsen (2003; see Table 74) report results of risk of haematological cancers (leukaemia, lymphoma and multiple myeloma) with proximity to a high voltage power line, based on a nested case-control study from the Norwegian national cohort. This cohort was described above with respect to female breast cancer (Kliukiene, Tynes & Andersen, 2004; see Table 74), though in Tynes & Haldorsen (2003) both men and women were included. For exposure to magnetic fields during the last 10 years before diagnosis, odds ratio for time weighted average exposure 0.05–0.19 μT (compared with < 0.05 μT) was 1.6 (95% CI: 0.8–3.1) (17 cases), and for ≥ 0.20 μT it was 1.3 (95% CI: 0.7–2.5) (19 cases). For chronic lymphocytic leukaemia, there was borderline significant excess risk at 0.05–0.19 μT, OR

= 4.2 (95% CI: 1.0–17.9) (6 cases); none of the other leukaemia sub-types had significant excess (based on small numbers). For all leukaemias over all years, the OR were 1.3 (95% CI: 0.7–2.5) (18 cases) for 0.05–0.19 μT, and 1.5 (95% CI: 0.8–3.0) (15 cases) for ≥ 0.20 μT. There was no association found with occupational exposure to magnetic fields. [Limitations of the study are noted with respect to Kliukiene, Tynes & Andersen (2004) above.]

Electric blanket and electric appliance use

Oppenheimer & Preston-Martin (2002) reported results of a case-control study of acute myeloid leukaemia and electric blanket use in Los Angeles County, USA. Four hundred twelve cases (of 726 eligible, 57%) ages 30–69 years at diagnosis were identified from the local cancer registry between January 1987 and June 1994, together with neighbourhood controls (matched on birth year ± 5 years, race and gender, 55% response rate). Information on electric blanket use, use of electric waterbeds and occupation was obtained by interview of cases (or proxy respondent, 49% of cases) and controls. The OR for use of an electric blanket regularly was 0.8 (95% CI: 0.6–1.1) and it was 0.9 (95% CI: 0.7–1.2) for use of electric blanket or electrically heated waterbed regularly. [Response rates for both cases and controls were around 55%. 252 of 412 (61%) cases reported less than one year total use of electric blankets. There were proxy respondent in 49% of cases.]

Kleinerman et al. (2005) report the results of a case-control study of brain cancer and acoustic neuroma with respect to use of 14 electrical appliances. Cases (n = 782, 92% of eligible) and hospital controls (n = 799, 86% of eligible) were recruited from 1994–98 from hospitals serving as regional referral centres for the diagnosis and treatment of brain tumours, in three areas in the USA: Boston, Massachusetts; Phoenix, Arizona and Pittsburgh, Pennsylvania. Controls were selected from patients admitted to the same hospitals for a variety of conditions including injuries and non-malignant diseases. Information on residential exposure to electrical appliances was obtained by self-administered questionnaire (completion of questionnaire was aided where necessary). Response rates for the questionnaire were 86.7 % for cases (n = 678) and 85.9% for controls (n = 686), yielding overall response rates of 79.8% for cases and 73.9% for controls. For any use of hair dryers (at least three times throughout life), significantly raised odds ratios (adjusted for age, gender, income, education, race, centre, distance from centre, date of interview and help completing the questionnaire) were found for glioma among males and females combined (OR = 1.7, 95% CI: 1.1–2.5) and among males (OR = 1.7, 95% CI: 1.1–2.7). There was also a significant excess of meningioma associated with “ever” use of an electric shaver among males (OR = 10.9, 95% CI: 2.3–50), based on two non-exposed and 35 exposed cases. There were no significant findings for “ever” use of 12 other appliances, for glioma, meningioma and acoustic neuroma. Odds ratios for meningioma associated with use of an electric shaver among males were higher with increasing duration of use: compared with never users, OR were 3.9 (95% CI: 0.6–26) (1–8 years, 4 cases), 15.6 (95% CI: 2.8–85) (9–28 years, 12 cases) and 16.3 (95% CI: 3.0–89) (≥ 29 years, 15 cases).

Cohort studies

Two cohort studies giving results on leukaemia and brain cancer were published since 2001 subsequent to the IARC (2002) monograph, as well as two further studies giving results on brain cancer. In the study by Håkansson et al. (2002) described in the section on breast cancer, above (Table 76), there was no excess leukaemia risk among men; among women, numbers were small (relative risk in the "Very High" exposure category was 1.8 (95% CI: 0.4–8.5) based on 2 cases). There was no excess risk of cancers of the nervous system among men, though in men < 30 years, there was excess risk of astrocytoma grades I-II in the "High" (RR = 10, 95% CI: 1.2–83.3) and "Very High" (RR = 9.8, 95% CI: 1.1–86.2) exposure categories. For women, relative risk of nervous system tumours in the "Very High" category was 1.9 (95% CI: 0.9–3.9); for all astrocytomas, there was a significant linear trend of increasing risk across exposure categories (p = 0.004); relative risk in the "Very High" exposure category was 3.0 (95% CI: 1.1–8.6) based on 5 cases.

A retrospective cohort mortality study of personnel working in 500 kV and 750 kV power installations was carried out for the period from 1970 to 1992. The cohort consisted of 1532 cohort subjects, who contributed 24 000 person-years. At the end of the observation period, 1319 persons were alive, 141 died, and 72 were lost from the follow-up. Cause-specific standardized mortality rates (SMR) of the general population were used for the comparison. The overall SMR (reflecting all causes of death) was not elevated (SMR = 0.61). The study did not reveal any excess of either all cancers or of cardiovascular diseases, with SMRs of 0.89 and 0.54, respectively. This data have been interpreted as "a healthy worker effect" (Gurvich et al., 1999). The standardized relative mortality risk ratio (SRR) resulting from of all types of cancer was low (SRR = 0.80; 95% CI: 0.57–1.09), as it was for accidents, traumas and poisonings (SRR = 0.67; 95% CI: 0.46–0.93), and suicides (SRR = 0.45; 95% CI: 0.16–0,98). The SRRs of death from leukaemia in men (SRR = 2.03; 95% CI: 0.23–7.31) and of death from brain cancer (SRR = 1.3; 95% CI: 0.64–3.7) were non-significantly increased (Rubtsova, Tikhonova & Gurvich, 1999). These studies were published in Russian and not included in the IARC (2002) review.

Van Wijngaarden et al. (2001b) report a re-analysis of mortality among electrical utility workers in the USA, based on the cohort among five companies reported by Savitz & Loomis (1995) (not shown in Table 76; see Table 29 in IARC (IARC, 2002). For leukaemia, the previously reported association between experience as an electrician and leukaemia was no longer observed (RR = 1.2, 95% CI: 0.7–2.1, based on 15 cases). [The reported results are not directly comparable, as Savitz & Loomis (1995) give results stratified by duration of employment, whereas Van Wijngaarden et al. (2001b) give overall results only, allowing for two year lag]. Compared with the original report, occupations with presumed minimal exposure to any haz-

ardous occupational agents were included in the referent group, whereas previously, the referent group consisted of occupations with minimal exposure to magnetic fields only. This resulted, for example, in auto mechanics, heavy vehicle operators, material handlers and labourers being excluded from the referent group in Van Wijngaarden et al. (2001b), while technical workers, craft supervisors and service workers, who were considered exposed in the previous analysis, were included in the referent group in Van Wijngaarden et al. (2001b). For brain cancer, an excess was still observed among electricians in the revised analysis (RR = 1.7, 95% CI: 1.0–3.0, based on 17 cases).

Navas-Acien et al. (2002) give findings for incidence of brain cancer of an extended follow-up (to 1989) among the national Swedish cohort study of male workers, which previously had been followed up to 1984 (Floderus, Stenlund & Persson, 1999), and is described above with respect to male breast cancer (Pollan, Gustavsson & Floderus, 2001). Exposure to ELF magnetic fields was assessed by linking occupations to a job-exposure matrix covering the 100 most common occupations among Swedish men; for these occupations, exposure levels had been estimated based on at least four full-shift measurements. Ten further comparatively rare occupations with "definitely high" exposures but less than four measurements were added. Four exposure groups were identified based on the geometric mean of workday mean values for an occupational group, with lowest cut-off at 33rd centile point and highest at the 90th centile point. Navas-Acien et al. (2002) include 1 516 552 men ages 25–64 years; 2859 gliomas and 993 meningiomas were reported in the study cohort. For gliomas, compared with exposures < 0.13 μT the OR at 0.13–0.20 μT was 1.1 (95% CI: 1.0–1.2); at 0.20–0.30 μT, the OR was 1.1 (95% CI: 1.0–1.3); and at > 0.30 μT, the OR was 1.1 (95% CI: 0.9–1.2). There was no association with risk of meningioma (data not given). [This is the same base population and same period of follow-up as described above in Pollan, Gustavsson & Floderus (2001) though numbers in the cohort differ between the two reports.]

Wesseling et al. (2002) give results of a national cohort study of Finnish women born from 1906 to 1945, who reported an occupation in the 1970 census. Findings are reported for incidence of cancer of the brain and nervous system, 1971 to 1995, based on linkage to the national cancer registry (80% with histological diagnosis). Occupations were coded according to the longest held during the year. Women from the two highest social classes and farmers were excluded, giving a base population of 413 877 women, with 693 incident brain and nervous system cancers over the follow-up period. Expected numbers were based on incidence rates of the economically active female population, stratified by 5-year birth cohort, follow-up period and social class (lower two social classes only) to yield standardized incidence ratios (SIR). Occupational exposure to ELF magnetic fields was assessed using a job-exposure matrix designed by a team of exposure-assessment experts, based on job title for occupations held from 1960 to 1984 (to allow for latency), categorised as "unexposed", "low" or "medium/high" exposure. The classification was based on a cut-point of 0.8 μT, judged to be the "median of the intensity distribution of job titles with non-zero intensity".

For "low" exposure (≥ 0.8 μT), SIR (adjusted for year of birth, period of diagnosis and job turnover rate) was 1.1 (95% CI: 0.9–1.2); for "medium/high" exposure (> 0.8 μT) the SIR was 1.4 (95% CI: 0.9–2.1). [The exposure assessment was based on job title only, not supported by measurements. Sub-types of brain and nervous system tumours were not analysed.]

Case-control studies

Four case-control studies have reported on occupation and leukaemia risk and four on risk of brain cancer since the IARC (2002) monograph. Five of these studies (four for leukaemia and one for brain cancer) are included in Table 77. Bethwaite et al. (2001) report a case-control study of acute leukaemia among electrical workers in New Zealand. Cases ages 20–75 years at diagnosis were identified from six tertiary referral centres in New Zealand between January 1, 1989 and April 30, 1991, covering 92% of cases notified to the national cancer registry. Controls were selected at random from population registers of the catchment areas of the participating hospitals. Information on occupational history was obtained by telephone questionnaire or from next-of-kin (21 cases); exposure to ELF magnetic fields was assigned from a job-exposure matrix based on previous field measurements (using EMDEX meters) obtained from workers during their entire shifts for different occupational tasks, in an unspecified number of Los Angeles, Seattle and New Zealand workplaces. A "task-weighted" exposure estimate was then calculated based on current job tasks, and based on "historical" job tasks estimated for 15–20 years previously. Overall 100 cases and 199 controls were included with response rates of 86% and 78%, respectively. Any electrical work was associated with an OR of 1.9 (95% CI: 1.0–3.8) based on 26 cases, adjusted for age, education and gender. Among the electrical occupations, telephone line workers had adjusted OR of 5.8 (95% CI: 1.2–28) (6 cases) and welders/flame cutters an adjusted OR of 2.8 (95% CI: 1.2–6.8) (14 cases). Based on the job-exposure matrix for historical exposures, compared with < 0.21 μT (Reference): for 0.21–0.50 μT, adjusted OR was 0.5 (95% CI: 0.1–2.4) (2 cases); for 0.50–1.0 μT, OR was 2.9 (95% CI: 0.7–11.4) (5 cases); and for > 1.0 μT, OR was 3.2 (95% CI: 1.2–8.3) (15 cases) (p-value for trend = 0.002). For current exposures: for 0.21–0.50 μT, adjusted OR was 0.6 (95% CI: 0.2–2.3) (3 cases); for 0.50–1.0 μT, OR was 1.5 (95% CI: 0.2–14.6) (1 case); and for > 1.0 μT, OR was 4.0 (95% CI: 1.6–9.8) (18 cases) (p-value for trend < 0.001). For leukaemia sub-types, a significant trend was apparent only for acute non-lymphoblastic leukaemia. [The job-exposure matrix depended on measurements obtained from a previous study in the USA as well as New Zealand.]

Table 76. Cohort studies of breast cancer, leukaemia and brain cancer in occupational groups with assumed or documented exposure to ELF magnetic fields, published subsequent to IARC (2002)

Study area, population	Exposure metrics	Exposure categories	# cases	RR (95% CI) [a]	Comments	Authors
Sweden National working population of men aged 25–59 in 1971, based on employment at 1970 census (n=1 779 646). Within cohort RR, 1971–1989.	Job–exposure matrix. Geometric mean of work-day mean values for an occupational group.	*Male breast cancer* Mean exposure (μT): < 0.12 (ref) 0.12–0.16 0.16–0.22 0.22–0.30 > 0.30	203	 1.4 (1.0–2.0) 1.3 (0.8–1.9) 1.6 (1.0–2.6) 0.9 (0.5–1.6)	Extended follow up (to 1989) of cohort reported in Floderus et al. (1999). RR adjusted for age, period and geographical area.	Pollan, Gustavsson & Floderus, 2001
Sweden National working population of men aged 25-64 in 1971 based on employment at 1970 census (n=1 516 552). Within cohort RR, 1971–1989.	Job–exposure matrix. Geometric mean of work-day mean values for an occupational group.	*Glioma* Mean exposure (μT): <0.13 (ref) 0.13–0.20 0.20–0.30 > 0.30	2859	 1.1 (1.0–1.2) 1.1 (1.0–1.3) 1.1 (0.9–1.2)	Extended follow up (to 1989) of cohort reported in Floderus et al. (1999). RR adjusted for age, period, geographical area and size of town. (See Pollan et al. (2001) above)	Navas-Acien et al., 2002
Sweden Workers in industries using resistance welding. Within-cohort RR	Job exposure matrix; classification into Low (< 0.164 μT),	Men *Breast* Mean exposure: Low (ref)	 1		In men < 30 y, excess risk of astrocytoma grades I-II in High (RR=10, 95% CI 1.2–83.3) and Very high	Håkansson et al., 2002

Table 76. Continued

(n=646 694; 484 643 men and 162 051 women), 1985-94.	Medium (0.164–0.250 μT), High (0.250–0.530 μT) and Very High exposure (> 0.530 μT) based on geometric mean of average workday mean values.	Medium High Very high	7 2 2	2.9 (0.4–23.4) 3.1 (0.3–34.2) 3.8 (0.3–43.5)	(RR=9.8, 95% CI 1.1–86.2) exposure categories.
		Leukaemia Low (reference) Medium High Very high	 54 45 26 26	 0.8 (0.6–1.1) 0.8 (0.5–1.3) 0.9 (0.6–1.5)	In women, for all astrocytomas, significant linear trend of increasing risk across exposure categories (p=0.004); relative risk in Very high exposure category was 3.0 (95% CI, 1.1–8.6) (5 cases).
		Nervous system Low (reference) Medium High Very high	 105 256 90 47	 0.9 (0.7–1.1) 1.2 (0.9–1.6) 0.8 (0.5–1.1)	Unadjusted for potential occupational confounders other than dichotomous blue collar workers/others.
		Women *Breast* Low (reference) Medium High Very high	 402 492 221 37	 1.0 (0.9–1.2) 1.1 (0.9–1.3) 1.1 (0.8–1.5)	
		Leukaemia Low (reference) Medium High Very high	 11 16 12 2	 1.1 (0.5–2.4) 2.0 (0.4–12.3) 1.8 (0.4-8.5)	

Table 76. Continued

		Nervous system				
		Low (reference)	51			
		Medium	76	1.2 (0.8–1.7)		
		High	40	1.6 (1.0–2.4)		
		Very high	9	1.9 (0.9–3.9)		
Finland National working population of women aged 25-64 in 1970 based on employment at 1970 census (blue-collar occupations). SIR (n=413 877), 1971–75.	Job–exposure matrix based on expert review.	*Brain and nervous system* Low (0.8 μT) Medium/high (> 0.8 μT)	693	(SIR) 1.1 (0.9–1.2) 1.4 (0.9–2.1)	Adjusted for year of birth, period of diagnosis, job turnover rate.	Wesseling et al., 2002
Norway Female radio and telegraph operators SIR (n=2619), 1961–2002	Spot measurements on two ships (range: < 0.02 μT - about 6 μT).	*Female breast*	99	(SIR) 1.3 (1.1–1.6)	Unadjusted for potential occupational confounders.	Kliukiene, Tynes & Andersen, 2003

[a] RR: relative risk; CI: confidence interval; SIR: standardized incidence ratio.

Bjork et al. (2001) report a case-control study of 255 adult patients with chromosome positive chronic myeloid leukaemia cytogenetically analysed at a university hospital in southern Sweden between 1976–93, in relation to occupational exposure to ELF electromagnetic fields. Three population-based controls were selected per case, matched on age, gender and county (one of whom was randomly selected for interview). A lifelong occupational history (all jobs held for at least one year) was obtained by telephone interview. Two hundred twenty six cases (of 255, 89%) and 251 controls (of 349, 72%) were included; information for 182 cases (81%) and 35 controls (14%) was obtained from next-of-kin proxy respondents. Exposure to ELF magnetic fields was based on a job-exposure matrix using 8-hr arithmetic means from measurements obtained elsewhere for different occupations (Floderus, Persson & Stenlund, 1996), for jobs held 20 years or less from time of diagnosis. For the 55 cases with reported occupational exposure to ELF magnetic fields, OR was 1.7 (95% CI: 1.0–2.8). Compared with < 0.23 μT, OR at "low" exposure (0.23–0.30 μT) was 2.0 (95% CI: 1.0–4.1) (25 cases); at "moderate" exposure (> 0.30–0.50 μT), OR was 1.6 (95% CI: 0.8–3.4) (22 cases); at "high" exposure (> 0.50 μT), OR was 1.2 (95% CI: 0.4–3.1) (8 cases). People with 15–20 years occupational exposure to electromagnetic fields had OR 2.3 (95% CI: 1.2–4.5) (35 cases) compared with those with zero occupational exposure. Classification of ELF magnetic fields was uncertain for 20 cases. [Exposure assessment relied on measurements/job-exposure matrix from Floderus, Persson & Stenlund (1996), obtained for Swedish men only. No new measurements were done for this study.]

In the study of Oppenheimer & Preston-Martin (2002) discussed above with respect to use of electric blankets, having at least one of nine specified exposures in electrical occupations was associated with an OR of 1.0 (95% CI: 0.8–1.5), based on 133 cases of acute myeloid leukaemia.

Willett et al. (2003) reported results of a case-control study of people newly diagnosed with acute leukaemia at ages 16–69 years, between April 1, 1991 and December 31, 1996, in two health authorities and two counties in England. Controls matched on year of birth (±2 years), gender and ethnic group were randomly selected from the same general practitioner lists as the case. Eight hundred thirty eight cases (of 1066 eligible, 79%) were included and 1658 controls (of 3227 eligible and contacted, 51.4%). Occupational histories for all jobs held for at least six months were obtained by interview from cases (107 of 838 (13%) from proxy respondents) and controls. Willett et al. (2003) restrict analyses to Caucasians aged 20 or more two years prior to diagnosis, totalling 764 cases and their 1510 individually matched controls. A job exposure matrix was constructed based on job title to classify individuals as either "probably ever" exposed or "never" exposed, allowing for a two-year lag period before diagnosis. "Probable" exposure was associated with an OR of 1.0 (95% CI: 0.8–1.2). Excess risk among those "probably" exposed was confined to acute lymphoblastic leukaemia among women: OR = 3.5 (95% CI: 1.2–10.2) based on 13 cases. For all electrical workers, OR was 0.7 (95% CI: 0.5–1.1). [Exposure assessment was weak, based only on job title, not supported by measurements. The response

rate was only 50% among controls. There was no prior hypothesis formulated to suggest excess risk among women only, or for acute lymphoblastic leukaemia.]

Villeneuve et al. (2002) report results from the Canadian National Enhanced Cancer Surveillance System that collected data on 543 malignant brain cancer cases (63% response rate among eligible cases) among men, between January 1994 and August 1997. [Data were not collected from proxy respondents among those who had died (23%), a potential source of bias if exposure is related to survival.] Population-based controls (65% response rate) were frequency matched to the cases by age and gender; a random sample of 543 matched controls was then selected. Mailed questionnaires were used to obtain information on all jobs held for at least one year (followed up in some cases by telephone interview to clarify responses). Each occupation was assigned an exposure value (< 0.3, 0.3–< 0.6, and ≥ 0.6 μT) based on a time-weighted average magnetic flux density for full-time workers, based on expert review, and taking account of questionnaire data on job duties and employment location. Field measurements [numbers not given] were also done for some occupations that could not readily be classified, using a Drexel Corporation Magnum 310 magnetic field monitor. For all brain cancers, compared with < 0.3 μT as reference, the highest average occupational exposure ever received ≥ 0.3 μT was associated with an OR of 1.1 (95% CI: 0.8–1.5) (133 cases), and for ≥ 0.6 μT with an OR of 1.4 (95% CI: 0.8–2.4) (42 cases) [Note: the second exposure category is a subset of the first, and therefore these results are not independent.] Odds ratios were higher for the subset of glioblastoma multiforme cases: ≥ 0.3 μT: OR = 1.5 (95% CI: 0.9–2.5) (55 cases); ≥ 0.6 μT: OR = 5.5 (95% CI: 1.2–24.8) (18 cases). [Exposure assessment was based on expert review, supplemented by an unspecified number of measurements for some occupations.]

Three further case-control studies of occupation and risk of brain cancer have been reported since the IARC (2002) monograph (De Roos et al., 2003; Krishnan et al., 2003; Schlehofer et al., 2005). These are not shown in the tables as there was no specific focus on exposure to ELF electromagnetic fields, and occupations with the potential for such exposures were not separately grouped. Krishnan et al. (2003) and De Roos et al. (2003) both found a non-significant excess risk of glioma among welders and cutters (based on small numbers): OR = 3.0 (95% CI: 0.3–28.6) for longest-held occupation (Krishnan et al., 2003); OR = 2.1 (95% CI: 0.6–7.5) with > 5 years working in the occupation (De Roos et al., 2003). The latter authors also reported an excess risk among electricians and electronic equipment repairers with up to five years working in the occupation: OR = 3.3 (95% CI: 1.0–10.6) based on 10 cases; and among male (but not female) computer programmers and analysts with > 5 years working in the occupation: OR = 3.8 (95% CI: 1.2–12.3) based on 11 cases (De Roos et al., 2003). Schlehofer et al. (2005) found no significant excess risks for work in the electrical/electronics industry (OR = 0.8, 95% CI: 0.6–1.2 for males based on 54 cases, and OR = 0.9, 95% CI: 0.4–1.8 for females based on 13 cases) nor for occupational exposure to non-ionizing radiation (OR = 0.8, 95% CI: 0.6–1.0 for males based on 167 cases, and OR = 1.1, 95% CI: 0.8–1.5 for females based on 109 cases).

Table 77. Case–control studies of occupational groups with assumed or documented exposure to ELF magnetic fields, published subsequent to IARC (2002)

Study area, population	Exposure assessment	Exposure categories	# cases	RR (95% CI) [a]	Comments	Reference
Female breast cancer						
Canada Electronic data-processing equipment operators Cancer registry; electoral roll (controls) 995 cases and 1020 controls (1988-89)	Questionnaire; occupation		24	3.1 (1.6–5.8)	Matched on age.	Band et al., 2000
USA Cancer registry; population controls 843 cases and 773 controls (1993–95)	Questionnaire; job-exposure matrix	TWA [b] (μT-years): 0–0.59 (ref) > 0.59–0.90 > 0.90–1.27 > 1.27–2.43 > 2.43	 264 207 143 140 79	 1.4 (1.1–1.8) 1.1 (0.8–1.5) 1.0 (0.8–1.4) 1.2 (0.8–1.7)	Matched on age and race.	van Wijngaarden et al., 2001a
Canada 18 major hospitals; hospital-based controls 556 cases and 600 controls (1996–97)	Questionnaire; job titles graded at four levels of exposure	Time spent at "medium and high" work-time exposure (0.5–10 μT): All periods	 NR [c]	(per 6000 hours) 1.1 (0.94–1.4)	Adjusted for range of potential confounders.	Labreche et al., 2003

Table 77. Continued

		Lag of 10 years before diagnosis	NR	1.2 (0.98–1.5)		
		Before age 35 years	NR	1.4 (0.98–2.0)		
Leukaemia						
New Zealand Six major tertiary referral centers; population controls 110 cases (acute leukaemia) and 199 controls (1989–91)	Telephone interview; job-exposure matrix based on measured magnetic fields	Exposure (μT) : Past < 0.21 (ref) 0.21–0.50 0.50–1.0 > 1.0 *Current* < 0.21 (ref) 0.21–0.50 0.50–1.0 > 1.0	 88 2 5 15 88 3 1 18	 0.5 (0.1–2.4) 2.9 (0.7–11.4) 3.2 (1.2–8.3) 0.6 (0.2–2.3) 1.5 (0.2–14.6) 4.0 (1.6–9.8)	Adjusted for age, education, gender.	Bethwaite et al., 2001
Sweden University hospital in southern Sweden; population controls 226 cases (chromosome positive chronic myeloid leukaemia) and 251 matched controls (1976 –93)	Telephone interview (81% of cases proxy respondent); job-exposure matrix for jobs held within 20 y of diagnosis; 8-h arithmetic means based on Floderus et al. (1996)	Mean exposure (μT): < 0.23 (ref) 0.23–0.30 > 0.30–0.50 > 0.50	 151 25 22 8	 2.0 (1.0–4.1) 1.6 (0.8–3.4) 1.2 (0.4–3.1)	Matched on age, gender, county	Bjork et al., 2001

Table 77. Continued

USA Cancer registry; matched neighbourhood controls 412 cases with acute myeloid leukaemia and matched controls (1987–94)	Personal interview (49% of cases proxy respondent); electrical occupations	At least one of nine specified exposures in electrical occupations	133	1.0 (0.8–1.5)	Matched on age, race, gender	Oppenheimer & Preston-Martin, 2002
England Cancer registry; matched population-based controls 764 cases (acute leukaemia) and 1510 matched controls (1991–96)	Personal interview (13% of cases proxy respondent); a) occupations with "probable" exposure, b) electrical occupations	"Probable" exposure All electrical workers	120 31	1.0 (0.8–1.2) 0.7 (0.5–1.1)	Adjusted for deprivation	Willett et al., 2003
Brain cancer						
Canada Cancer registry; matched population-based controls 543 cases (malignant brain cancer) and 543 matched controls	Mailed questionnaires on all jobs held for at least one year; time-weighted average magnetic flux density for full-time workers, based on expert review	TWA exposure (μT): All brain cancers < 0.3 (ref) 0.3 0.6 Astrocytomas < 0.3 (ref) 0.3 0.6	 410 133 42 163 51 12	 1.1 (0.8–1.5) 1.4 (0.8–2.4) 0.9 (0.6–1.4) 0.6 (0.3–1.5)	Frequency matched on age and gender. 0.3 μT and 0.6 μT groups not independent	Villeneuve et al., 2002

Table 77. Continued

	Glioblastoma multiforme		
	< 0.3 (ref)	143	
	0.3	55	1.5 (0.9–2.5)
	0.6	18	5.5 (1.2–24.8)
	Other		
	< 0.3 (ref)	92	
	0.3	23	1.1 (0.6–2.1)
	0.6	9	1.5 (0.5–4.2)

[a] RR: relative risk; CI: confidence intervals.

[b] TWA: time weighted average.

[c] NR: not reported.

11.2.2.3 Other cancers

A number of studies concerning exposure to ELF electromagnetic fields in relation to other cancer sites have been published since the IARC (2002) monograph. These data are not included in the tables, but are summarized briefly here.

11.2.2.3.1 Residential exposure

McElroy et al. (2002) carried out a case-control study of endometrial cancer and electric blanket use in Wisconsin, USA. Cases diagnosed from 1991 to 1994 were identified through the statewide cancer registry; 745 cases (87% of eligible cases) participated. Controls were selected randomly from lists of licensed drivers (age < 65 years) and from Medicare beneficiary files (65–79 years); 2408 controls with intact uterus were eligible for analysis (85% response rate for controls completing the study interview). Information on use of electric blankets and mattress covers was elicited by telephone interview from June to December 1994; analysis was limited to the 148 cases and 659 controls interviewed during this period with complete information. With adjustment for possible confounders, comparing "ever" users with "never" users: OR = 1.0 (95% CI: 0.7–1.6) (68 cases). [Controls overlapped with those selected for a parallel study of electric blanket use and breast cancer discussed above (McElroy et al., 2001; see Table 75.)]

Tynes, Klaeboe & Haldorsen (2003) examined the risk of malignant melanoma with proximity to a high voltage power line, based on a nested case-control study from the Norwegian national cohort. This cohort was described above with respect to female breast cancer (Kliukiene, Tynes & Andersen, 2004; see Table 74) and leukaemia (Tynes & Haldorsen, 2003; see Table 74); in Tynes, Klaeboe & Haldorsen (2003) both men and women were included. For residential exposure in the most recent five years (men and women combined), the odds ratio for time weighted average exposure 0.05–0.19 μT (compared with < 0.05 μT) was 2.9 (95% CI: 1.9–4.4) (56 cases), and for ≥ 0.20 μT, it was 2.1 (95% CI: 1.5–3.0) (64 cases). For all years, the OR were 1.9 (95% CI: 1.2–2.8) (44 cases) and 1.9 (95% CI: 1.2–2.8) (44 cases) respectively. For exposures ≥ 0.20 μT, the estimated OR tended to be higher in women than men. For men and women with highest estimated occupational exposure to ELF electromagnetic fields compared with the lowest, the odds ratio was 1.2 (95% CI: 0.8–1.8). [No measurements of magnetic fields for persons included in the study were undertaken. There was only limited control for confounding, based on routine data: education, type of building and number of dwellings.]

Tynes & Haldorsen (2003) reported risks for lymphoma and multiple myeloma as well as leukaemia, already discussed above (Table 74). For lymphoma, for residential exposure to magnetic fields in the most recent 10 years, the odds ratio for time-weighted average exposure 0.05–0.19 μT (compared with < 0.05 μT) was 0.9 (95% CI: 0.4–1.9) (9 cases), and for ≥ 0.20 μT, it was 1.8 (95% CI: 0.7–4.6) (10 cases). For multiple myeloma, the

corresponding ORs were 2.0 (95% CI: 0.1–32.0) (2 cases) and 4.0 (95% CI: 1.0–16.0) (4 cases) respectively.

11.2.2.3.2 Occupational exposure

Three studies have reported on occupation and risk of Non-Hodgkin lymphoma (NHL). Cano & Pollan (2001) carried out an analysis of occupation and risk of NHL within the cohort of Swedish workers (followed up to 1989) discussed above with respect to male breast cancer (Pollan, Gustavsson & Floderus, 2001) and brain cancer (Navas-Acien et al., 2002). There was no specific focus on ELF magnetic fields. For workers ascribed to electrical and electronic work, relative risk for men was not reported, as the within-cohort RR was < 1.2; for women, RR was 1.3 (95% CI: 0.8–2.1). Fabbro-Peray, Daures & Rossi (2001) reported a case-control study of environmental and occupational risk factors and NHL in Languedoc-Roussillon in southern France. Four hundred forty-five cases and 1205 population controls were included. Exposure to ELF fields was not specifically investigated, though there was an excess risk associated with daily welding (occupational), with an adjusted OR of 2.6 (95% CI: 1.4–5.1). There was no excess risk associated with work as an electrician or electrical engineer. Band et al. (2004) carried out a case-control study of occupation and NHL in British Columbia, Canada, based on 782 incident cases and matched controls. There was no specific focus on exposure to ELF electromagnetic fields, and occupations with the potential for such exposures were not separately grouped. However, excess risks of NHL (among many occupations and histological subtypes examined) based on small numbers of cases were reported for electrical engineers (OR = 3.2; 95% CI: 1.2–8.0, 4 cases), systems analysts and computer programmers (OR = 3.8; 95% CI: 1.2–12.4, 3 cases) and electrical equipment installing and repairing (OR = 2.0; 95% CI: 1.1–3.5, 10 cases); welding and flame cutting was associated with excess risk of diffuse small cell cleaved tumours (OR = 3.6; 95% CI: 1.5–9.0, 4 cases).

In addition to breast cancer, leukaemia and brain cancers (Table 76), Håkansson et al. (2002) reported on risks of a number of other cancer sites among a cohort of workers in industries using resistance welding in Sweden. Borderline significant excess risk was noted for kidney cancer among men with "Very High" exposure (> 0.530 μT) compared with "Low" exposure (< 0.164 μT): OR = 1.4 (95% CI: 1.0–2.0) based on 62 cases. There was also a borderline significant excess of cancer of the urinary organs (excluding kidney) among men in the "Medium" exposure group: OR = 1.3 (95% CI: 1.0–1.5) (367 cases), but not at higher exposures. None of the other cancer sites showed a significant excess for either men or women.

Van Wijngaarden et al. (2001b) report an excess mortality from all cancers and lung cancer among electrical utility workers, consistent with previous findings from this cohort reported in Savitz & Loomis (1995) and Savitz et al. (1997). Charles et al. (2003) investigated risk of prostate cancer mortality in the same cohort, using a nested case-control design. There were 387 cases and 1935 controls [129 controls were used more than once and 32

cases were used as controls for prior cases]. Exposure to EMF was based on a job-exposure matrix that used personal EMF measurements from workers assigned to one of 28 occupational categories (Savitz & Loomis, 1995). The group average measurement was assigned to individual workers; cumulative exposure to EMFs was obtained by multiplying intensity by duration across all jobs (μT-years); exposures were categorized to < 25th percentile, 25th–< 50th percentile, 50th–< 75th percentile, 75th–< 90th percentile, and ≥ 90th percentile. Allowing for five-year lag, in comparison with the lowest exposure group, age-matched and race–adjusted OR were 1.11 (95% CI: 0.8–1.6) (94 cases) for 0.6–< 1.3 μT-years; 1.0 (95% CI: 0.7–1.3) (94 cases) for 1.2–< 2.4 μT-years; 1.2 (95% CI: 0.8–1.7) (66 cases) for 2.4–< 4.3 μT-years; and 1.6 (95% CI: 1.0–2.3) (47 cases) for ≥ 4.3 μT-years. The ORs were similar when total career exposure was considered rather than allowing for five-year lag period.

Baumgardt-Elms et al. (2002) carried out a case-control of testicular cancer study among 269 incident cases and 797 matched controls in Germany. No excess risks were found for a variety of occupations including work near high-voltage electrical transmission installations, visual display units or complex electrical environments.

Fincham et al. (2000) investigated occupational risk factors for thyroid cancer in a case-control study in Canada (1272 cases, 2666 population-based controls; response rates 80% and 60%, respectively). Occupations possibly associated with electromagnetic fields, based on self-reported job title, were included for which the OR (adjusted for age, gender and cigarette smoking) was 1.6 (95% CI: 0.8–3.2) (19 cases). [Although published in 2000, this paper was not included in the IARC (2002) monograph; it is included here for completeness. There was no external validation of EMF exposure.]

11.2.3 Epidemiology: conclusions

The IARC classification was heavily influenced by the associations observed in epidemiological studies on childhood leukaemia. The classification of this evidence as limited has not changed with addition of two childhood leaukaemia studies published after 2002. Since publication of the IARC monograph the evidence for other childhood cancers remains inadequate.

Subsequent to the IARC monograph a number of reports have been published concerning the risk of female breast cancer in adults associated with ELF magnetic field exposure. These studies are larger than the previous ones and less susceptible to bias, and overall are negative. With these studies, the evidence for an association between ELF exposure and the risk of breast cancer is weakened considerably and does not support an association of this kind.

In the case of adult brain cancer and leukaemia, the new studies published after the IARC monograph do not change the conclusion that the overall evidence for an association between ELF and the risk of these diseases remains inadequate.

For other diseases and all other cancers, the evidence remains inadequate.

11.3 Carcinogenesis in laboratory animals

A variety of animal model systems and experimental designs have been used to investigate the possibility that EMF might affect the process of carcinogenesis. The results of these studies are summarized in Table 78. Recently published reviews of these studies include those of Boorman et al. (2000c; 2000a), McCann (2000), IARC (2002) and ICNIRP (2003). Long-term rodent bioassays are suited to studying carcinogens that are effective only with chronic/long term exposure. In bioassays, large numbers of animals are exposed over most of their lifetime to several levels of the agent being tested. The animals are monitored for tumour incidence, multiplicity, type, and time of appearance. Chemically-induced or radiation-induced tumours in rodents have been widely used as models for mammary cancer, and liver tumours (e.g. Pattengale & Taylor, 1983; Russo & Russo, 1996). With some human cancers, however, such as malignant melanoma, spontaneous brain tumours and the most common form of childhood leukaemia, acute lymphoblastic leukaemia, the animal models available do not closely resemble human disease.

11.3.1 Rodent bioassays

Several studies have looked at the effect of EMF exposure alone on tumour incidence; such studies are potentially capable of revealing whether EMFs could act as a complete carcinogen or serve to increase the incidence of spontaneous tumours. Often, inbred strains of mice and rats are for genetic reasons particularly prone to certain cancers and some studies have examined EMF effects on the incidence of these particular tumours. In addition, transgenic animals – e.g. with activated oncogenes or silenced tumour suppressor genes – are being increasingly used to investigate any effects on carcinogenesis and cancer development.

11.3.1.1 Large scale, life-time studies

Four large-scale, long-term studies have been performed on the effects of power-frequency magnetic field exposure for two years on the spontaneous tumour incidences in rats and mice. Two large studies on Fischer (F344) rats (Mandeville et al., 1997; Yasui et al., 1997) investigated the effects on spontaneous cancers of bone marrow and blood cells (haematopoietic cells), mammary, brain and skin tumours. Two more recent studies on 1000 mice (male and female) (McCormick et al., 1999) and 1000 rats (male and female) (Boorman et al., 1999a) were in line with the two earlier studies. The overall results did not show any consistent increase in any type of cancer.

In the more recent study on rats (Boorman et al., 1999b), thyroid C-cell adenomas and carcinomas were significantly elevated in two groups of male animals exposed at 2 μT.

In mice, EMF exposure resulted in a slight but significant reduction in tumour incidence in some groups (McCormick et al., 1999). In two groups of female mice and in one group with male and female mice, the overall incidence of malignancies was decreased. Incidences of lymphomas and lung adenomas were found to be significantly decreased in only a few exposure groups but not in others.

The exposure of mice before and during pregnancy to power-frequency magnetic fields had no effect on mortality and the subsequent incidence of cancer in their offspring during the 78 week follow-up period (Otaka et al., 2002).

11.3.1.2 Leukaemia/lymphoma

Lymphoma and leukaemia are neoplasias of white blood cells (leukocytes) of the immune system. Neoplastic lymphocytic proliferation in the mouse may occur as a lymphoma (involving primarily lymph nodes and splenic white pulp) and/or as a leukaemia (involving primarily bone marrow, peripheral blood and splenic blood) but this distinction can be, at times, rather difficult and somewhat arbitrary (Pattengale, 1990). An overview is given in Table 78.

As indicated above, these animal models of childhood acute lymphoblastic leukaemia have limited direct relevance for human disease. In particular, although some phenotypic similarities have been suggested (e.g. Pattengale, 1994), the agedependent appearance of murine thymic lymphomas does not recapitulate that of childhood acute lymphoblastic leukaemia and its indirect mechanism of induction has no known human counterpart (Fry & Carnes, 1989; Hoyes, Hendry & Lord, 2000; UNSCEAR, 1993). There are various transgenic mouse models of leukaemia which develop a disease having some similarities to childhood acute lymphoblastic leukaemia: for example, BCR/ABL p190 mice (Griffiths et al., 1992), an E-BCL-2 mouse (Gibbons et al., 1999), mice incorporating the Pim-1 transgene (Kroese et al., 1997; Verbeek et al., 1991) and a TEL-JAK2 mouse model (Carron et al., 2000). Two studies (Harris et al., 1998; McCormick et al., 1998) have used the Eμ-Pim-1 transgenic model referred to above.

Fam & Mikhail (1996) reported a high incidence of lymphoma in CFW mice, reported to have a low background incidence of this disease, exposed over three successive generations to an intense (25 mT) "travelling" power-frequency magnetic field. [A travelling field is described by Fam & Mikhail (1993) as a basic principle of operation of linear synchronous motors used for example in the propulsion of magnetic levitation trains.] However, control animals, which were not sham-exposed, were exposed to stray ELF magnetic fields of up to 50 μT. There were also too few animals in the first generation to draw any rigorous conclusions. However, there was a highly significant excess of lymphomas observed in the third generation of the exposed group compared to the control group. According to some reviewers, the pathology figures presented in the paper were more indicative of age-related lymphocytic infiltrates (McCann, Kavet & Rafferty, 2000) or

hyperplasia (Boorman et al., 2000c) than neoplasia. IARC (2002) note that the study was difficult to interpret.

A lack of effect of prolonged exposure to continuous or intermittent power-frequency magnetic fields on the incidence of lymphoma was reported following the prolonged 18-month exposure of transgenic (Eμ-Pim-1) mice which are predisposed to spontaneously develop thymic lymphoblastic (T-cell) lymphoma and non-lymphoblastic (B-cell) lymphoma (Harris et al., 1998). Similarly, McCormick et al. (1998) reported a lack of effect of exposure to power-frequency magnetic fields for 23 weeks on the incidence of spontaneous lymphoma in heterozygous TSG-p53 knockout mice, which lack one copy of the p53 tumour suppressor gene and have a low incidence of spontaneous lymphoma. More recently, Sommer & Lerchl (2004) reported that prolonged exposure to power frequency magnetic fields had no effects on the incidence of thymic lymphoblastic lymphoma in a strain of mouse genetically predisposed to this disease.

11.3.1.3 Brain tumours

Several large scale studies have reported a lack of effect of ELF magnetic field exposure on brain tumour incidence (see above), but generally, the number of tumours reported has been too low to allow a meaningful conclusion to be drawn. However, a recently developed model of spontaneous medulloblastoma in Ptch-knockout mice (Hahn, Wojnowski & Miller, 1999), and more particularly, a knockout mouse model of astrocytomas (Reilly et al., 2000), a leading cause of brain cancer in humans, may prove useful in the further investigation of these effects.

Table 78. Animal cancer studies

Animal model	Exposure	Response	Comment	Reference
Large scale life-time studies				
Male and female B6C3F1 mice	60 Hz 2, 200 μT or 1 mT continuous 1 mT intermittent 2 y	No effect on incidence of most tumours; slight overall reduction in female mice exposed at higher 'doses'.	Well designed, fully described experiment.	McCormick et al., 1999
Male and female F344 rats	50 Hz 500 μT or 5 mT 2 y	No effect on tumour incidence except fibroma of subcutis.	Fibroma levels similar to historical controls.	Yasui et al., 1997
Female F344 rats	60 Hz 2, 20, 200 μT or 2 mT 2 y	No effect on tumour incidence.	Site-specific incidence close to historical controls.	Mandeville et al., 1997

Table 78. Continued

Male and female F344 rats	60 Hz 2, 200 µT or 1 mT continuous 1 mT intermittent 2 y	No effect on incidence of most tumours; significant increase in thyroid C-cell tumours in males.	Well designed, fully described experiment.	Boorman et al., 1999b
Male C3H/HeJ mice and female C57BL/6J mice	50 Hz 500 µT or 5 mT for 7 wk (males) before mating and 2 wk (both groups) during mating and up to parturition	No effect on tumour incidence in offspring over 78 wk follow-up.		Otaka et al., 2002
Leukaemia/lymphoma				
Leukaemia-prone female AKR mice for 5 generations	12 Hz or 460 Hz 6 mT, pulsed 1 h wk^{-1} until death	No effect on survival time, spleen and thymus weight.	Experiment procedures not completely described.	Bellossi, 1991
Male and female CFW mice over three generations	60 Hz 25 mT 'travelling' field continuous	Highly significant increase in lymphoma incidence in 3rd generation.	Poor experimental set up and design; possible stress; lack of age-matched controls in 2nd generation.	Fam & Mikhail, 1993; 1996
Eµ-Pim-1 transgenic mice prone to two types of lymphoma	50 Hz 1, 100, 1000 µT continuous 1000 µT intermittent 18 mo	No effect on thymic lymphoblastic or on non-lymphoblastic lymphoma.	Increase in positive control group.	Harris et al., 1998
Heterozygous TSG-p53 knockout mice prone to low incidence of lymphoma	60 Hz 1 mT continuous 18.5 h d^{-1}, 23 wk	No significant effect on lymphoma incidence.	Small numbers of mice; low incidence of tumours.	McCormick et al., 1998
AKJ/R mice, which carry the AK virus, are predisposed to lymphoma	50 Hz 1 or 100 µT 38 wk from 4–5 wk of age	No significant effect of exposure on lymphoma incidence.		Sommer & Lerchl, 2004

11.3.2 EMF exposure combined with carcinogens

A number of studies have examined the possible promotional, co-promotional or co-carcinogenic effects of ELF magnetic fields on the induction by chemicals, or by ionising or UV radiation, of pre-neoplastic lesions in the liver, leukaemia/lymphoma, mammary tumours and skin tumours.

11.3.2.1 Liver pre-neoplastic lesions

The induction of pre-neoplastic lesions (foci) in the rat liver is considered to indicate an early response to carcinogenic agents and is used as a medium term bioassay for carcinogenesis (IARC, 1992). Two studies found no promotional effect resulting from exposure to power-frequency magnetic fields on the number of chemically-initiated preneoplastic liver lesions, in contrast to the effect of a known liver tumour promoter (Rannug et al., 1993b) and a lack of any co-promotion effect on liver foci formation in rats treated with a chemical liver-tumour initiator and a promoter (Rannug, Holmberg & Mild, 1993).

11.3.2.2 Leukaemia/lymphoma

Other studies have examined promotional effects on neoplasms of the haematopoietic system.

The co-promotion study by McLean et al. (1991) of power-frequency magnetic field effects on chemically-induced skin tumours in mice (described below) reported increased numbers of exposed mice with enlarged spleens and extremely high blood mononuclear cell counts. The authors suggested that these effects might be associated with development of leukaemia.

Svedenstål & Holmberg (1993) found no effect of near life-time exposure to pulsed 20 kHz magnetic fields on the incidence of lymphomas in X-irradiated mice; unfortunately, unexpectedly high levels of X-ray-induced thymic lymphomas in the control animals rendered the study insensitive to any promotional effect. In contrast, the study of Heikkinen et al. (2001) had adequate power to detect an effect of 50 Hz magnetic fields on the incidence of lymphomas induced by X-rays in mice. Complete histopathology was done to investigate possible effects on tumours in other tissues. The incidence of lymphomas was 30% in the X-ray-exposed control animals, and was not increased by EMF exposure (22%). Furthermore, EMF exposure did not increase the incidence of any other neoplasm. Babbit et al. (2000) conducted a large study on the effect of life-time EMF exposure on X-ray induced lymphomas and other haematopoietic neoplasias in 2660 mice. This study showed no significant effect. Analyses of brain tissue from the same experiment (Kharazi, Babbitt & Hahn, 1999) also showed no effect of the EMF exposure, but the low numbers of brain tumours observed limited the power of this analysis.

Other studies reported mostly the absence of any effect of EMF exposure on chemically-induced leukaemia/lymphoma incidences. While

Shen et al. (1997) found no effect on thymic lymphoma incidences, they reported more animals with dense liver metastases in the EMF-exposed group. However, this difference was not maintained when moderate and dense metastases were combined. McCormick et al. (1998) found no effect on chemically induced lymphoblastic lymphoma in Pim-1 transgenic mice, except for a group of males that was continuously exposed to 1 mT. Notably, survival in this group was significantly increased, and the lymphoma incidence was significantly decreased.

11.3.2.3 Mammary tumours

The induction of mammary tumours in female rats has been used as a standard assay in the investigation of potential carcinogenesis, often using carcinogens such as DMBA as an initiator and promoter in the two-stage initiator/promoter model of carcinogenesis. Four groups of workers have investigated the effects of ELF magnetic field exposure on the incidence and the development of chemically-induced mammary tumours.

Beniashvili, Bilanishvili & Menabde (1991) found an increased incidence and shortened tumour latency with EMF exposure for 3 h per day, but not with 0.5 h per day. The experimental details were, however, presented very briefly, which hinders evaluation of the study. Similar results have been reported in a series of medium-term studies of magnetic field effects on DMBA-induced mammary tumour incidence carried out by Löscher and colleagues (Baum et al., 1995; Löscher et al., 1993; Löscher et al., 1994; Löscher & Mevissen, 1995; Löscher, Mevissen & Häußler, 1997; Mevissen et al., 1993a; Mevissen et al., 1993b; Mevissen et al., 1996; Mevissen & Häußler, 1998; Mevissen, Lerchl & Löscher, 1996). These authors reported significant increases by chronic EMF exposure in the incidence of palpable tumours (detected during exposure) and macroscopically visible tumours (detected during post-mortem examination) (Löscher et al., 1993; Mevissen, Lerchl & Löscher, 1996). They found a linear dose-response relationship over the flux-density range 0.3–1.0 μT up to 100 μT (Löscher & Mevissen, 1995). No significant effect on tumour incidence could be found following a full histopathalogical analysis for exposure at 100 μT (Baum et al., 1995; Löscher et al., 1994). Löscher & Mevissen (1995) argued that magnetic field exposure does not alter the incidence of neoplastic mammary lesions but accelerates tumour growth, thus enhancing the number of tumours macroscopically visible when the rats are sacrificed. In addition, Baum et al. (1995) reported that there was a statistically significant increase in the number of rats with mammary gland adenocarcinomas that had been exposed to 100 μT. However, the total number of malignant tumours in the exposed group was not significantly increased.

A replicate study at 100 μT (Mevissen & Häußler, 1998) reported that the incidence of macroscopically-visible tumours in the sham-exposed group was almost double the incidence in the earlier study. This was carried out at a different time of the year and seasonal influences were reported to occur (Mevissen & Häußler, 1998). A re-analysis of all of these data showed

a statistically significant linear correlation between increase in tumour incidence and magnetic flux density (Mevissen & Häußler, 1998). More recently, these authors (Thun-Battersby, Mevissen & Löscher, 1999) reported a significantly increased incidence of mammary tumours following 100 μT exposure for 27 weeks following initiation by a single dose of 10 mg DMBA.

In an attempted replication study of the 100 μT exposure by Löscher (1994), Anderson et al. (1999) and Boorman et al. (1999a) found no evidence that magnetic field exposure was associated with an earlier onset or an increased multiplicity or incidence of mammary tumours. There were, however, clear differences in the responsiveness to DMBA of the rats used in the replication study (Anderson et al., 1999; Boorman et al., 1999a) compared to those used by Löscher and colleagues and and there was a variety of differences in the experimental protocols (Anderson et al., 2000; Löscher, 2001). Ekström, Hansson Mild & Holmberg (1998) found no effect on DMBA-induced mammary tumour incidence in the same rat strain following prolonged exposure to intermittent power-frequency magnetic fields. There were no statistically significant differences in the number of tumour bearing animals and no differences in the total number of tumours between the different groups. In addition, the rate of tumour appearance was the same in all groups.

In their most recent study (Fedrowitz, Kamino & Löscher, 2004), the Löscher group tested the hypothesis that the different results are explained by the use of different sub-strains of Sprague Dawley rats. Exposure to a 100 μT, 50 Hz magnetic field enhanced mammary tumour development in one sub-strain, but not in another that was obtained from the same breeder. The tumour data were supported by the finding that exposure to an ELF magnetic field increased cell proliferation in the mammary gland of the sensitive sub-strain, but no such effect was seen in the insensitive sub-strain.

11.3.2.4 Skin tumours

Mouse skin models, in which repeated topical applications of single carcinogens to shaved skin on the back of mice causes the induction of epithelial tumours within 20 weeks (IARC, 1992) has been used to examine the initiating and promoting activities of a large range of chemicals. Three groups have examined the effect of magnetic fields on chemically induced skin tumours.

Exposure to ELF magnetic fields did not act as a tumour promoter on DMBA-treated mice, nor as a co-promoter on mice that were treated with DMBA followed by weekly applications of the tumour promoter tetradecanoyl phorbol acetate (TPA) (McLean et al., 1991). In the latter experiment the papilloma incidence in the sham-exposed group was very high, greatly limiting the sensitivity of the experiment. In a later study by the same group (Stuchly et al., 1992) the similar treatment, but with sub-optimal doses of TPA, increased the rate of tumour incidence, but did not affect the final number of tumours. Two replicate studies by the same authors (McLean et al.,

1997) did not confirm this increase in the rate of tumour incidence. The authors concluded that the studies did not support a role for EMFs as a strong copromoter in this mouse skin tumour model. This conclusion is supported by the work of Sasser et al. (1998) who, in an attempted replication and extension of the study by Stuchly et al. (1992), also found no effect of EMF exposure on the rate of chemically-induced skin tumour development or tumour incidence. In addition, DiGiovanni et al. (1999), expanding on the study by Sasser et al. (1998), found no evidence of exposure on early markers of skin tumour promotion using the same initiation-promotion model in SENCAR mice.

In one study, the same design was prolonged to 52 weeks (McLean et al., 1995). TPA treatment was discontinued after 24 weeks. There was no increase in total tumours or papillomas, but squamous cell carcinomas were increased in the EMF exposed animals. The authors concluded that EMF exposure may accelerate progression to malignancy.

No effect of long-term exposure to continuous or intermittent power-frequency magnetic field on chemically-induced skin tumour incidence in mice was reported by Rannug et al. (1993a; 1994). A statistically significant increase was seen in the number of skin tumour bearing animals and in the cumulative number of tumours in the pooled data from two intermittently exposed groups compared to the pooled data from animals exposed continuously (Rannug et al., 1994). Based on this comparison the authors suggested that intermittent exposure is more effective than continuous exposure. However, this interpretation is doubtful, since the results in both of these pooled groups were not significantly different from those in their respective controls.

Kumlin et al. (1998b) reported that exposure to continuous or intermittent, variable ELF magnetic fields had no significant effect on the final incidence of UV radiation-induced skin tumours in normal and transgenic mice which overexpress the human ornithine decarboxylase (ODC) gene. However, the authors reported an earlier onset of skin tumours in the animals exposed to magnetic fields and UV radiation compared to those exposed to UV radiation alone. In a more recent article, the same group (Kumlin et al., 2002) investigated the suppression of apoptosis as a possible mechanism for magnetic field effects on skin tumorigenesis and the synergy of UV radiation and magnetic field. Female mice were exposed at 50 Hz, 100 μT and to UV from lamps emitting simulated solar radiation. The authors concluded that the ELF magnetic field exposure may inhibit apoptosis caused by exposure to UV radiation.

11.3.2.5 Brain tumours

Several large-scale studies have reported no effect of exposure to ELF fields on brain tumour incidence (Boorman et al., 1999b; Kharazi, Babbitt & Hahn, 1999; Mandeville et al., 1997; Yasui et al., 1997), but generally, the number of tumours has been too low to allow a meaningful conclusion to be drawn. Mandeville et al. (2000) studied the effect of 60 Hz magnetic

fields on chemically induced tumours of the neural system in rats in which the chemical carcinogen N-ethyl-N-nitrosourea (ENU) was fed transplacentally. The authors considered that the neural tumours induced in this rat model are a reasonable model of neural tumours in humans. The number of tumour-bearing animals varied from 38% to 60%, but tended to be lower in the exposed groups. Overall, magnetic-field exposure had no statistically significant effect on the number of animals bearing neurogenic tumours or on the survival of the rats. Small changes in tumour incidence were seen in the exposed groups, but were of borderline significance ($0.1>p>0.05$). The results are consistent with the view that ELF magnetic fields do not have a promoting effect on neurogenic tumours in female rats exposed transplacentally to ENU.

Table 79 presents a summary of the results of animal cancer studies with combined exposure to EMF and carcinogens.

11.3.3 Transplanted tumours

Few studies have investigated the effect of ELF magnetic fields on the growth of transplanted tumours; the results are almost wholly negative.

No effect of life-time exposure on the development of leukaemia in mice implanted with mouse leukaemia cells was reported by Thomson, Michaelson & Nguyen (1988). Sasser et al. (1996), Morris et al. (1999), and Anderson et al. (2001) reported no effect of exposure on the development of large-granular-lymphocytic (LGL) leukaemia in rats following the injection of LGL cells derived from rats of the same strain. However, enlarged spleens appeared earlier and survival was significantly depressed in a positive-control group exposed to 5 Gy gamma radiation prior to leukaemia cell injection.

Devevey et al. (2000) examined the effect of chronic exposure to 50 Hz magnetic fields on acute myeloid leukaemia (AML) in rats, the most frequent type of leukaemia reported in studies of occupational ELF magnetic field exposure. This animal model was regarded by the authors as a reasonable model of human AML. No significant differences were seen in survival between exposed and unexposed leukaemic groups. Similarly, in the terminal stage of leukaemia when the rats were sacrificed, there were no differences in white blood cell count, the differential white blood cell count, the degree of bone marrow infiltration, or bone marrow differential cell count. Thus, exposure had no significant effect on leukaemia progression.

11.3.4 Genotoxicity in animals

Lai & Singh (2004) used the comet assay to investigate induction of DNA damage in brain cells of rats exposed to 60 Hz magnetic fields. They reported significantly increased DNA strand breaks after exposure to a 10 μT magnetic field for 24 or 48 h. The effect was seen in both the alkaline and neutral versions of the comet assay and, although the effect was small, it was seen in several separate experiments. Exposure for 48 h caused a larger increase than exposure for 24 h. The effects were blocked by treatment with

Table 79. Animal cancer studies: EMF combined with known carcinogens

Animal model	Exposure	Response	Comment	Authors
Pre-neoplastic lesions				
Partial hepatectomy plus DENA initiated liver lesions in Sprague-Dawley rats	50 Hz 0.5–500 T ~ 20 h wk^{-1}, 12 wk	No effect.	Increase in positive control group.	Rannug et al., 1993b
Partial hepatectomy plus DENA and phenobarbital induced liver lesions in Sprague-Dawley rats	50 Hz 0.5 or 500 µT ~ 20 h wk^{-1}, 12 wk	Slight inhibitory effect.	Detailed description of experimental protocol.	Rannug, Holmberg & Mild, 1993
Lymphoma/leukaemia				
Lymphoma or leukaemia in SENCAR mice painted with DMBA and TPA	60 Hz 2 mT 6 h d^{-1}, 5 d wk^{-1}, 21 wk	Larger spleens and increased mononuclear cells in spleen.	Leukaemia / lymphoma insufficiently identified.	McLean et al., 1991
X-ray induced lymphoma in CBA/S mice	20 kHz sawtooth field, 15 µT pk-pk until death	No effect of exposure.	Experiment unable to detect increase.	Svedenstål & Holmberg, 1993
X-ray induced lymphoma in CBA/S mice	50 Hz variable 1.3–130 µT 24 h d^{-1}, 1.5 y	No effect on incidence of lyphoma or other neoplasms.	Well designed, fully described experiment.	Heikkinen et al., 2001
DMBA-induced thymic lymphoma in Swiss mice	50 Hz 1 mT 3 h d^{-1}, 6 d wk^{-1}, 16 wk	No effect on tumour incidence.	Inconsistent effect on metastatic infiltration.	Shen et al., 1997
ENU-induced lymphoblastic lymphoma in Pim1 transgenic mice.	60 Hz 2, 200 µT or 1 mT continuous 1 mT intermittent (1 h on/off) 18.5 h d-1, 23 wk	No effect except decreased incidence in 1 mT continuous group.	Small numbers per group.	McCormick et al., 1998

Table 79. Continued

γ-radiation-induced lymphomas in C57BL/6 female mice	60 Hz, circularly polarised 1.42 mT 18 h d-1, up to 29 mo	No effect on incidence of haemopoietic neoplasms including lymphoma.	Large scale study (2660 mice), rigorously monitored.	Babbitt et al., 2000
Mammary tumours				
NMU-induced mammary tumours in female rats (unidentified strain)	50 Hz 20 μT 0.5 or 3 h d^{-1}, 2 y	Increased incidence in 3 h d^{-1} group, plus increased malignancy.	Experimental procedures not adequately described.	Beniashvili, Bilanishvili & Menabde, 1991
DMBA-induced mammary tumours in female Sprague-Dawley rats	50 Hz 0.3–1.0 μT 13 wk	No effect on visible or histologically identified tumour incidence.	Well designed, fully described experiment.	Mevissen et al., 1993b Löscher et al., 1994
DMBA-induced mammary tumours in female Sprague-Dawley rats	50 Hz 10 μT 13 wk	No effect on incidence of visible tumours at autopsy.	Well designed, fully described experiment.	Mevissen, Lerchl & Löscher, 1996
DMBA-induced mammary tumours in female Sprague-Dawley rats.	50 Hz 50 μT 13 wk	Increased incidence of visible tumours at autopsy.	Well designed, fully described experiment.	Mevissen et al., 1996
DMBA-induced mammary tumours in female Sprague-Dawley rats	50 Hz 100 μT 13 wk	Increased incidence of visible tumours; increased malignancy.	Well designed, fully described experiment; low incidence visible tumours in sham.	Baum et al., 1995 Löscher et al., 1993
DMBA-induced mammary tumours in female Sprague-Dawley rats	50 Hz 100 μT 13 wk	Increased incidence of visible tumours at autopsy.	Replicate of above experiment.	Mevissen & Häußler, 1998

Table 79. Continued

DMBA-induced mammary tumours in female Sprague-Dawley rats	50 Hz 30 mT 13 wk	Opposite results in replicate studies but no overall effect.	Well designed, fully described experiment; small numbers.	Mevissen et al., 1993a
DMBA-induced mammary tumours in female Sprague-Dawley rats	50 Hz 100 µT 27 wk	Increased mammary tumour incidence.	Well designed, fully described experiment.	Thun-Battersby, Mevissen & Löscher, 1999
Ornithine decarboxylase (ODC) activity in mammary glands of female Sprague-Dawley rats	50 Hz 100 µT 1 d 1, 2, 8 or 13 wk	Increased ODC activity in thoracic complex after 2 wk but not 1, 8 or 13 wk.	Well designed, fully described experiment; variable ODC data.	Mevissen, Häußler & Löscher, 1999
DMBA-induced mammary tumours in female Sprague-Dawley rats	50/60 Hz 100 or 500 µT 13 or 26 weeks	No effect.	Replication and extension of study by Löscher et al., 1993	Anderson et al., 1999 Boorman et al., 1999a
DMBA-induced mammary tumours in female Sprague-Dawley rats	50 Hz 250 or 500 µT intermittent 21 wk	No effect.	Somewhat brief description of experimental protocol, analysis and results.	Ekström, Mild & Holmberg, 1998
Skin tumours				
Sub-carcinogenic DMBA initiated or DMBA and sub-optimal (1 µg) TPA induced skin tumours in SENCAR mice	60 Hz 2 mT 6 h d^{-1}, 5 d wk^{-1}, 21 wk	No tumours in DMBA treated mice; for DMBA plus TPA, test insensitive due to 90% incidence in controls.	Detailed description of experimental protocol.	McLean et al., 1991 Stuchly, Lecuyer & McLean, 1991
DMBA and sub-optimal (0.3 µg) TPA induced skin tumours in SENCAR mice	60 Hz 2 mT 6 h d^{-1}, 5 d wk^{-1} wk 2 – wk 23 of age	No consistent effect in replicate studies.	3 replicate studies; some heterogeneity in results.	McLean et al., 1997 Stuchly et al., 1992

Table 79. Continued

DMBA and sub-optimal (0.3 µg) TPA induced skin tumours in SENCAR mice	60 Hz 2 mT 6 h d^{-1}, 5 d wk^{-1} wk 24 – wk 52 of age	Increase in malignant conversion of papillomas to carcinomas.	Continuation of study by Stuchly et al., 1992	McLean et al., 1995
DMBA and sub-optimal (0.85-3.4 nmol) TPA induced skin tumours in SENCAR mice	60 Hz 2 mT 6 h d^{-1}, 5 d wk^{-1}, 23 wk	No effect.	Repeat and extension of study by Stuchly et al., 1992	Sasser et al., 1998
Early markers of skin tumourigenesis in DMBA and sub-optimal TPA-treated SENCAR mice	60 Hz 2 mT 6 h d^{-1}, 5 d wk^{-1}, for 1, 2 and 5 wk of promotion	No effect on epidermal thickness, mitotic index, or ODC activity. No consistent effect on PKC activity.	Extension of study by Sasser et al., 1998.	DiGiovanni et al., 1999
DMBA-induced skin tumours in NMRI mice	50 Hz 50 or 500 µT ~ 20 h d^{-1}, 2 y	No effect on skin tumour incidence.	Increase in positive control group.	Rannug et al., 1993a
DMBA-induced skin tumours in SENCAR mice	50 Hz 50 or 500 µT, continuous or intermittent ~ 20 h d^{-1}, 2 y	No effect of continuous or intermittent exposure compared to control groups.	Increase in positive control group.	Rannug et al., 1994
UVR-induced skin tumours in transgenic (K2) and non-transgenic mice	50 Hz continuous at 100 µT variable 1.3–130 µT 10.5 mo	No effect on final tumour incidence but earlier appearance in exposed mice.		Kumlin et al., 1998b
Brain tumours				
ENU-induced tumours of the nervous system of female F344 rats	60 Hz 2, 20, 200 or 2000 µT 20 h d^{-1}, 65 wk	No effect of magnetic field exposure.	Exposure to ENU and magnetic fields began *in utero*.	Mandeville et al., 2000

a radical scavenger, a nitric oxide synthase inhibitor and an iron chelator, suggesting involvement of free radicals and iron in the effects of magnetic fields. The same authors have previously reported similar effects after short (2 h) exposure to much higher magnetic flux densities of 0.1 to 0.5 mT (Lai & Singh, 1997a; 1997b). Another group did not find increased DNA damage (measured by the neutral comet assay) in brain cells of mice after 2 h or 5 day exposures at 0.5 mT, but reported a significant increase after 14 days of exposure (Svedenstål et al., 1999). They also reported an increase in DNA damage in mice kept for 32 days outdoors under a power line, where the average magnetic field was approximately 8 μT (Svedenstål, Johanson & Hansson Mild, 1999). However, close control of exposure and environmental parameters is difficult under these conditions.

No effects of ELF magnetic fields have been seen after long-term exposures in other rodent genotoxicity models, such as the dominant lethal assay in mice (Kowalczuk et al., 1995), sister chromatid exchange in rats and micronuclei in mice (Abramsson-Zetterberg & Grawe, 2001; Huuskonen et al., 1998a; Huuskonen et al., 1998b).

11.3.5 Non-genotoxic studies

Only a few animal studies have investigated effects relevant to the non-genotoxic mechanisms of cancer, and the results are inconclusive. Changes in the activity of ornithine decarboxylase (ODC) have been reported in various tissues of rodents after short-term exposure to ELF magnetic fields (Kumlin et al., 1998a; Mevissen, Häußler & Löscher, 1999; Mevissen, Kietzmann & Löscher, 1995) but not after long-term exposures (Kumlin et al., 1998a; Mevissen, Häußler & Löscher, 1999; Sasser et al., 1998). Other studies have reported increases in the cell proliferation markers bromodeoxyuridine and Ki-67 in rat mammary gland (Fedrowitz, Westermann & Löscher, 2002), and inhibition of UV radiation-induced apoptosis in mouse skin (Kumlin et al., 2002).

11.3.6 Animal studies: conclusions

There is currently no adequate animal model of the most common form of childhood leukaemia, acute lymphoblastic leukaemia. Three independent large-scale studies of rats provided no evidence of an effect of ELF fields on the incidence of spontaneous mammary tumours. Most studies report no effect of ELF fields on leukaemia or lymphoma in rodent models. Several large-scale long-term studies in rodents have not shown any consistent increase in any type of cancer, including haematopoietic, mammary, brain and skin tumours.

A substantial number of studies have examined the effects of ELF fields on chemically induced mammary tumours in rats. Inconsistent results were obtained that may be due in whole or in part to differences in experimental protocols, such as the use of specific substrains. Most studies on the effects of ELF field exposure on chemically-induced or radiation-induced leukaemia/lymphoma models were negative. Studies of pre-neoplastic liver

lesions, chemically-induced skin tumours and brain tumours reported predominantly negative results. One study reported an acceleration of UV-induced skin tumourigenesis by ELF fields.

Two groups have reported increased levels of DNA strand breaks in brain tissue following in vivo exposure to ELF magnetic fields. However, other groups, using a variety of different rodent genotoxicity models, found no evidence of genotoxic effects. The results of studies investigating non-genotoxic effects relevant to cancer are inconclusive.

Overall there is no evidence that ELF exposure alone causes tumours. The evidence that ELF field exposure can enhance tumour development in combination with carcinogens is inadequate.

11.4 In vitro carcinogenesis studies

Experimental models used to study carcinogenesis involve both animal and cellular models. The first approach is highly pertinent in that all regulation mechanisms are present and animals are treated over their lifetime with the agent tested. In this context, human and animal studies are of greater importance than cellular models for health risk evaluation, but they cannot usually be used to investigate mechanistic events underlying the carcinogenesis processes. On the other hand, in spite of limitations linked to the absence of regulation mechanisms that exist only in vivo, cellular or in vitro models can be useful for the investigation of many of the numerous molecular aspects of carcinogenesis. Cellular models also allow for the use of either normal primary cells, immortalised cell lines, or mutant cells that can overexpress, or are silent for numerous genes, all of these being very informative. Direct and indirect effects can be studied. Genotoxicity assays are devoted to the exploration of direct damage to DNA related to initiation potential; they include the detection of immediate damage, such as DNA fragmentation, and the detection of permanent damage, mainly by means of conventional cytogenetic assays: mutation, chromosomal aberration, micronuclei, and sister chromatid exchange. Alterations in DNA repair capability of cells that can result in mutations can also be studied. In vitro models can also be helpful to study other epigenetic or physiological changes (gene expression, signal transduction pathways, proliferation, apoptosis, and production of reactive free radicals, etc.).

The characteristics of cancerous cells are mainly (i) an exaggerated growth potential resulting from non-physiological stimulation pathway (mutations resulting in the activation or overexpression of one or several actors (genes and proteins) in the signal transduction cascades, overexpression of growth (factors, receptors, etc.); (ii) the loss of responsiveness to physiological inhibitors of cell growth (inactivation of mechanisms involved in the cell cycle control, loss of responsiveness to differentiation signals, inactivation of gap-junctional intercellular communications, etc.); (iii) the capability to escape from the apoptotic process (inactivation of physiological inducers of apoptosis, autocrine secretion of growth factors, over-expression of physiological inhibitors of apoptosis, etc.); (iv) acquirement of unlimited

potential for cell division; (v) the capability for promoting neo-angiogenesis; (vi) invasiveness and metastatic capabilities. Thus not only mutagenesis but also many cross-talking processes involving numerous specific genes/proteins are involved in carcinogenesis.

In this section the main emphasis of the review is of the more recent work, especially reports published since the IARC monograph (2002).

11.4.1 Genotoxic effects

11.4.1.1 Genotoxic effects of ELF magnetic fields alone

Most studies have shown no genotoxic effects after exposure to ELF magnetic fields in several types of mammalian cells, including human cells (reviews by Murphy et al., 1993 and Cantoni et al., 1995; Cantoni et al., 1996; Fairbairn & O'Neill, 1994; ICNIRP, 2003; Livingston et al., 1991; McCann, Kheifets & Rafferty, 1998; Miyakoshi et al., 2000c; Reese, Jostes & Frazier, 1988; Simko et al., 2001). Magnetic flux densities and exposure durations studied ranged to up to 400 mT, and from 0.5 to 48 hours, respectively. However, other studies have shown genotoxicity in cellular models. Most of the studies used exposure to field strength above 1 mT and exposure prolonged to several days or weeks (Ding et al., 2001; Nordenson et al., 1992; Simko et al., 1998; Simko, Kriehuber & Lange, 1998).

Stronati et al. (2004) and Testa et al. (2004) exposed blood cells from four or five healthy donors to 50 Hz magnetic fields for 2 and 48 h, respectively. Four cytogenetic assays (chromosomal aberrations, micronucleus test, sister chromatid exchange, and comet assay, as well as the cytokinesis-blocked proliferation index) were carried out in these experiments. No damage to DNA and no alteration of lymphocyte proliferation were observed in non-mitogen-stimulated human blood cells.

In a series of papers from the Rüdiger group, it was reported that exposure to 50 Hz magnetic fields induced DNA damages in human fibroblasts, as evaluated with the comet assay. Ivancsits et al. (2002a) showed that intermittent exposure (50 Hz, 24 hours) induced not only single strand breaks and alkali damage but also double strand breaks, while continuous exposure did not. The intermittence schedule that gave rise to the highest level of damages was 5 min on/10 min off, no damage being observed with off-time greater than 20 min. Moreover, a threshold of 35 μT was found in cells from a single donor with a dose-dependent trend up to 2000 μT. In further studies, it was found that the maximum of damage was obtained in fibroblasts after 15–19 h of exposure (Ivancsits et al., 2003b), and that cells from elderly donors were found to be slightly more responsive (Ivancsits et al., 2003a). After the peak of the damage, the effect declined within the next hours and background level was almost recovered at 24h of exposure. According to another study of the same group, the maximum effect of 50 Hz magnetic fields is similar to that of exposure to 4.8 kJ m^{-2} UV, and human fibroblasts were also found to be more sensitive to vanadate treatment as compared to human lymphocytes (whole blood) and isolated lymphocytes (Ivancsits et al.,

2002b). When exposure was stopped after 15 h, the effect was found fully reversible within 6 h for both DNA single and double strand breaks (Ivancsits et al., 2003b). In those studies, cells from each donor were tested in only one to two independent experiments for each exposure conditions, which limits the statistical power of the studies. Several independent laboratories are undertaking replication studies. In the first published replication study, Scarfi et al. (2005) used the same human fibroblast cell line, the same exposure system and the same experimental protocol, but were not able to replicate the findings. The DNA strand breaks detected by the assays used have been critically re-evaluated in a subsequent publication (Crumpton & Collins, 2004). The exposure conditions producing maximum strand break levels (1 mT, 5 min on/10 min off) were also reported to induce a significant increase of micronuclei and chromosomal aberrations in fibroblasts (Winker et al., 2005).

Del Re et al. (2003; 2004) used a bacterial test system (Tn10 transposon in *E. coli*) to investigate the transposition activity (genetic rearrangement), cell proliferation, and cell viability after exposure to either continuous or pulsed 50 Hz magnetic fields at various flux densities (50, 100, 200, 500 and 1000 μT) for 58 h. No effect on proliferation (number and morphometric characters of colonies) was seen. While exposure to continuous magnetic fields decreased the transposition activity and increased the bacterial viability, square-pulsed fields had opposite effects with a 40% decrease in viability (reproductive cell death). In both cases, the effect on transposition was dependent of the intensity of the magnetic flux density with no effect observed at 50 μT and a maximum 30% decrease and 20% increase in transposition activity observed after exposure to continuous wave and pulsed fields, respectively.

Wolf et al. (2005) reported increased cell proliferation, changes in cell cycle and increased DNA damage, assessed by the comet assay, in HL-60 leukaemia cells and two fibroblast cell lines exposed to 50 Hz magnetic fields at 0.5–1 mT up to 72 hours. The increase in DNA strand breaks showed two peaks at 24 and 72 h, while no increase was seen at 48 h. A similar time-dependent pattern of oxidative DNA damage was observed by measuring 8-hydroxydeoxyguanine (8-OhdG) adducts. Involvement of magnetic field effects on free radical species was supported by changes seen in intracellular levels of reactive oxygen species measured by a fluorescent probe, and in the expression of proteins that are involved in redox-mediated signals (NFκB p65 and p50). Also, the magnetic field effects were suppressed by pre-treatment of the cells with the antioxidant α-tocopherol. The results of this study are internally consistent, and effects seen on different endpoints support each other. Independent replication of the key findings would be useful to assess their repeatability.

11.4.1.2 Combined genotoxic effects

In its 2002 evaluation on the carcinogenicity of ELF magnetic fields, IARC mentioned that “several groups have reported that ELF mag-

netic fields enhance the effects of known DNA- and chromosome-damaging agents such as ionizing radiation" (Hintenlang, 1993; Lagroye & Poncy, 1997; Miyakoshi et al., 1999; Simko et al., 2001; Walleczek, Shiu & Hahn, 1999). The effects of combined exposure to magnetic fields and either chemical or physical agents have been further investigated in a number of studies.

Three groups have investigated DNA alterations following exposure to ionising or UV radiation and 50/60 Hz magnetic fields.

Stronati et al. (2004) and Testa et al. (2004) irradiated human lymphocytes with 1 Gy of X-rays immediately after exposure to a 50 Hz magnetic field at 1 mT for 2 and 48 h, respectively. Using chromosome aberration, micronucleus, sister chromatic exchange and comet assay, they showed no alterations of X-rays-induced damage after exposure to ELF magnetic fields. In those studies, the magnetic field strength was lower and/or the schedule of exposures (pre-exposure to 50 Hz magnetic field) was different from the conditions tested by Miyakoshi et al. (2000b) who previously reported interactions between ionising radiation and high-strength 50 Hz magnetic fields (400 mT).

Lloyd and colleagues (Hone et al., 2003; Lloyd et al., 2004) also found no difference in the frequency of 2 Gy gamma-radiation-induced chromosome aberrations observed in non-mitogen-stimulated human blood lymphocytes exposed to 50 Hz magnetic fields (230, 470 or 700 μT) for 12 h, as compared with cells sham-exposed after gamma irradiation. Exposure conditions were similar to those used by Walleczek, Shiu & Hahn (1999) who previously reported that exposure to 60 Hz magnetic fields could potentiate mutations in the *hprt* gene induced by ionising radiation.

Zmyslony et al. (2004) investigated the potential interaction between UV-A irradiation (150 J m^{-2}, 5 min) and 50 Hz magnetic fields (40 μT, 5 or 60 min,) in rat lymphocytes. DNA single strand breaks and alkali labile sites were assessed using the comet assay. Exposure to 50 Hz magnetic fields alone did not cause DNA damage as compared to unexposed samples. However, a 60 min, but not a 5 min exposure to the magnetic field, significantly enhanced the damage induced by UV radiation as shown by the increased values in several parameters such as tail length (1.7-fold increase), percentage of DNA in the comet tail (2-fold increase), and tail moment (3-fold increase).

Six other papers reported on the effects on DNA damage of co-exposure to 50Hz magnetic fields and chemicals. The mutation frequency was determined by Suri et al. (1996) in cells exposed to a 60 Hz, 3 mT magnetic field, after or concurrently with one of two carcinogens, NMU (N-methylnitrosurea) and menadione (2-methyl-1,4-naphthoquinone). While menadione is known to act through a free radical mechanism, NMU does not. However, no enhancement of the mutation frequency was observed with either carcinogen.

Verheyen et al. (2003) exposed phytohemagglutinin (PHA)-stimulated human lymphocytes to 50 Hz magnetic fields and vinblastine. Lympho-

cytes were first exposed to the ELF field for 24 h at 80 or 800 μT, with or without a subsequent 48 h co-exposure to vinblastine at different doses (0–15 ng ml^{-1}). The endpoint was the frequency of micronucleated binucleated cells assessed in samples from six healthy donors per group. Based on the micronucleus assay, two additional parameters: nuclear division index (NDI) and apoptosis, were evaluated in the samples. A significant increase in the frequency of micronuclei and apoptosis, along with a significant decrease in the NDI were found at all doses of vinblastin tested. The 50 Hz magnetic fields alone did not elicit any significant effect, except on the NDI (significant 20% increase at 800 μT), nor did the ELF fields affect the vinblastine-induced responses. The small number of the samples and the lack of sham-exposed controls limit the significance of the conclusions that can be drawn from the study.

Cho & Chung (2003) exposed PHA-stimulated human lymphocytes treated with benzo(a)pyrene (BP, 0–15 μg ml^{-1}) alone or exposed to 60 Hz, 800 μT magnetic fields and BP for 24 hr. A series of samples was further treated with BP alone for an additional 48 h. The frequencies of micronuclei and sister chromatid exchanges were assessed. The proliferation and replication indexes were determined from the micronucleus and sister chromatid exchange assays, respectively. In contrast to BP, 60 Hz magnetic fields did not induce more micronuclei or sister chromatid exchanges as compared to sham-exposed cells. Co-exposure of cells to BP and an 0.8 mT magnetic field for 24 h did not affect the damage induced by BP. When co-exposure was followed by BP exposure for 48 h, significant increases in the frequency of micronuclei and sister chromatid exchanges, compared to BP treatment for 72h alone, were observed, while no effects were noted on cell proliferation.

Robison et al. (2002) exposed different cell lines, HL60, HL60R (HL60 with mutated retinoic acid receptor-alpha gene) and Raji cells to 60 Hz, 150 μT magnetic field for 24 h before treatment with 1 mM H_2O_2. Repair was assessed using the alkaline comet assay within the following 15 min. The DNA repair rate was significantly decreased (about 20% after 15 min repair time) in the magnetic-field-exposed leukaemic cell lines (HL60, HL60R cells) as compared to their non-exposed counterparts. No effect was seen in the Raji lymphoma cell line and Raji cells were also less sensitive to other stresses (see section 11.4.3).

Pasquini et al. (2003) investigated the effect of 1 or 24 h exposure of Jurkat cells to a 5 mT, 50Hz magnetic field, either alone, or with benzene, or with two genotoxic metabolites: hydroquinone (1,4-benzenediol) and 1,2,4-benzenetriol. No effect of 1 h exposure to magnetic fields alone was observed. Exposure for 24 h caused a two-fold increase in micronuclei, with no effect on proliferation. There were no additional effects of field exposure on metabolite-induced damage.

Koyama et al. (2004) investigated the mutational effects of hydrogen peroxide (H_2O_2, 1 μM for 4 h) in the presence and absence of a 60 Hz magnetic field at 5 mT, using pTN89 plasmids. Mutations were assessed in

the *supF* gene carried by these plasmids in *Escherichia coli*. Exposure to the magnetic field did not induce any mutations, but significantly increased the mutation frequency induced with H_2O_2 treatment (2.5-fold increase compared to H_2O_2 plus sham-exposure), while no difference in the mutation spectrum or the mutational hotspots could be observed between both groups. These data suggest that magnetic fields may potentiate the damage induced by H_2O_2, for instance through an enhancement in the formation of the product 8-OhdG which is known to be genotoxic.

The results of in vitro studies on genotoxic effects of ELF magnetic fields alone or in combination with genotoxic chemicals are summarized in Table 80.

11.4.2 Expression of oncogenes and cancer-related genes

Oncogene expression has been extensively investigated under exposure to ELF magnetic fields. The first reports of an effect of ELF magnetic fields on gene expression came from the Goodman group, who showed an upregulation of the c-myc proto-oncogene in human HL60 cells under exposure ranging from 0.57 to 570 μT. The effect was shown to be a "window effect" (maximum effect at 5.7 μT, no effect at lower and higher levels of exposure), dependent on Ca^{2+}. An "EMF-responsive element" (EMRE), required for the induction of c-myc expression, was identified in the c-myc promoter and corresponded to nCTCTn sequences (Goodman et al., 1989; Goodman et al., 1992; Karabakhtsian et al., 1994; Lin & Lee, 1994; Wei, Goodman & Henderson, 1990). Recently, using c-myc-EMRE expression vectors linked to luciferase or CAT (chloramphenicol transferase) in HeLa cells, the presence of EMRE was associated with a response to ELF magnetic field exposure (Lin et al., 2001).

However, over the years, several replication studies have failed to confirm these findings on c-myc at the transcriptional level in HL60 and other cells at different exposure levels (Balcer-Kubiczek et al., 1998; Balcer-Kubiczek et al., 2000; Boorman et al., 2000b; Czerska et al., 1992; Desjobert et al., 1995; Greene et al., 1993; Jahreis et al., 1998; Lacy-Hulbert et al., 1995; Loberg et al., 1999; Miyakoshi et al., 1996; Morehouse & Owen, 2000a; Owen, 1998; Parker & Winters, 1992; Saffer & Thurston, 1995).

Moreover, while sparse positive findings on the expression of diverse oncogenes either at the transcriptional or protein level have been published (Campbell-Beachler et al., 1998; Lagroye & Poncy, 1998; Phillips et al., 1993; Phillips, 1993; Rao & Henderson, 1996), a number of others studies have reported an absence of effects, including effects on a number of other cancer-related genes (Balcer-Kubiczek et al., 1998; Balcer-Kubiczek et al., 2000; Loberg et al., 1999; Miller et al., 1999).

Table 80. Genotoxic effects of magnetic fields alone or combined with genotoxic chemicals

Cells	Biological endpoint	Exposure conditions	Results	Reference
Human peripheral mononuclear cells, non proliferating 4 or 5 healthy donors	Cytogenetic assays: chromosomal aberrations (CA), micronucleus test (MN), sister chromatid exchange (SCE), alkaline comet assay (computerised analysis), cytokinesis-blocked proliferation index (CBPI)	50 Hz 1 mT 2 h	Magnetic fields: no effects. Magnetic fields plus 1 Gy of X rays: no alterations of X-ray-induced damage.	Stronati et al., 2004
Human peripheral mononuclear cells, non proliferating 4 or 5 healthy donors	Cytogenetic assays: CA, MN, SCE, comet assay (computerised analysis), CBPI	50 Hz 1 mT 48 h	Magnetic fields: no effects. Magnetic fields plus 1 Gy of X rays: no alterations of X-ray-induced damage.	Testa et al., 2004
Human diploid fibroblasts: IH-9 (28 y-old female), ES1 (6 y-old male)	Alkaline and neutral comet assay, calculation of a "comet tail factor" based on eye evaluation	50 Hz 20–2000 µT; continuous or intermittent, 11 intermittency schedules 24 h	Continuous exposure: no effects. Intermittent exposure: induction of single strand breaks, alkali damage and double strand breaks. Highest level of damage with 5 min on / 10 min off exposure, no damage with off-time greater than 20 minutes. Threshold at 35 µT, dose-dependent increase of damages up to 2000 µT (ES1 cells).	Ivancsits et al., 2002a
Human diploid fibroblasts: IH-9 (28 y-old female), ES1 cells (6 y-old male), KE1 cells (43 y-old male)	Alkaline and neutral comet assay, calculation of a "comet tail factor" based on eye evaluation	50 Hz 20–1000 µT 5 min on / 10 min off 24 h	Increase in DNA damage with exposure up to 15–19 h, then decrease in damage. When exposure was stopped at 15 h, cells recovered within the next 6 h from both single and double strand breaks.	Ivancsits et al., 2003b

Table 80. Continued

			Field strength response curve in ES1 cells: see Ivancsits et al., (2002a).	
Human diploid fibroblasts from healthy donors: IH-9 cells (28 y-old female), ES1 cells (6 y-old male), KE1 cells (43 y-old male), AN2 cells (14 y-old female), HN3 cells (56 y-old female), WW3 cells (81 y-old male)	Alkaline and neutral comet assay, calculation of a "comet tail factor" based on eye evaluation. Statistics on duplicated experiments.	50 Hz 1000 µT 5 min on / 10 min off 24 h	Cells from older donors (KE1, HN3 and WW3) exhibited higher levels of damage. Damage peaked at 15 h for youngest donors and 19 h for older ones.	Ivancsits et al., 2003a
Escherichia coli transfected with mini-Tn10 transposon	Transposition activity: count of dark clones of LacZ+ bacteria and densitometric analysis of the colour intensity. Proliferation: number, area, diameter and perimeter of clones.	50 Hz 50, 100, 200, 500, 1000 µT 58 h	No effects on proliferation. Decreased transposition frequency.	Del Re et al., 2003
Escherichia coli transfected with Tn10 transposon	Transposition activity: count of dark clones of LacZ+ bacteria and densitometric analysis of the colour intensity. Proliferation: number, area, diameter and perimeter of clones. Cell survival (CW and pulsed fields): colony-forming units (CFU) at the end of exposure.	50 Hz CW and pulsed (square-wave) 50, 100, 200, 500, 1000 µT 58 h	No effects on proliferation. Increased transposition frequency at field strength above 50 µT. Pulsed field: decreased number of CFU; continuous field: increased number of CFU.	Del Re et al., 2004

Table 80. Continued

HL-60 leukemia cells and two fibroblast cell lines	Alkaline comet assay, formation of 8-OHdG adducts, cell proliferation	50 Hz 0.5–1 mT 24, 48 or 72 h	Field strength-dependent increase in cell proliferation. Increase in DNA strand breaks and 8-OHdG adducts at 24 and 72 h. Effects blocked by α-tocopherol.	Wolf et al., 2005
Human peripheral blood from one healthy donor	Six replicate cultures, mitogenic stimulation with phytohemagglutinin Chromosomal aberrations	50 Hz 230, 470 and 700 µT 12 h Pre-irradiation with 2 Gy of gamma rays	Magnetic field alone: no effects. Gamma rays plus magnetic field: no significant effect, "borderline" significance for chromatide-type aberrations.	Hone et al., 2003 Lloyd et al., 2004
Rat lymphocytes	Alkaline comet assay (computerised analysis)	50 Hz 40 µT 5 or 60 min ± UV-A irradiation (150 J m^{-2}, 5 min)	Magnetic field alone or UV-A plus 5 min magnetic field: no effects. UV-A plus 60 min magnetic field: enhancement of DNA damages induced by UV-A.	Zmyslony et al., 2004
Human lymphocytes stimulated with phytohemagglutinin	Micronucleus assay and proliferation index Sister chromatid exchange and replication index	50 Hz 800 µT 24 h + 24 h of benzo(a)pyrene (BaP) treatment ± 48 h BaP treatment	24 h co-exposure: no effects. 24 h co-exposure + 48 hours BaP: increase in damage induced by BaP.	Cho & Chung, 2003
Transgenic rat embryo fibroblast cell line, R2 lambda LIZ	Carcinogen-induced mutation frequency	60 Hz 3 mT after or concurrently with MNU (N-methylnitrosurea) or menadione (2-methyl-1,4-naphthoquinone)	No enhancement of mutation frequency by magnetic field.	Suri et al., 1996

Table 80. Continued

Human lymphocytes stimulated with phytohemagglutinin	Cytokinesis-blocked micronucleus assay	50 Hz 80 or 800 µT 24 h ± 48 h vinblastine	Magnetic field alone: no effects. No alteration of the effect of the genotoxic agent vinblastine. No effect on proliferation and replication indexes.	Verheyen et al., 2003
Human HL60, HL60R leukaemic cells and Raji lymphoma cells	Alkaline comet assay (SCGE, computerised analysis) 15 min after treatment	60 Hz ± H_2O_2 150 µT 24 h	Raji cells: no effects. HL60, HL60R cells: decreased in the repair of H_2O_2-induced damage.	Robison et al., 2002
Human Jurkat cells	Cytokinesis-blocked micronucleus assay and proliferation index	50 Hz 5 mT 1 and 24 h ± benzene or two genotoxic metabolites: hydroquinone (1,4-benzenediol) and 1,2,4-benzenetriol	Magnetic field alone, 1 h: no effects. Magnetic field alone, 24 h: 2-fold increase in micronuclei, no effect on proliferation. Co-exposures: no additional effects on chemically-induced damage.	Pasquini et al., 2003
Escherichia coli transfected with pTN89 plasmids	Detection of mutations in the SupF gene carried by pTN89 plasmids Extraction and sequencing of mutated plasmids	60 Hz ± H_2O_2 5 mT 4 h	Magnetic field alone: no effect. Magnetic field + H_2O_2: doubling in the number of mutations induced by H_2O_2; no difference in mutation spectrum and hotspots with respect to H_2O_2 alone.	Koyama et al., 2004

Recently, Loberg et al. (2000) used arrays containing cDNAs for 588 cancer-related genes to investigate gene expression in normal (HME) and transformed (HBL-100) human mammary epithelial cells and human promyelocytic leukaemia (HL60) cells under a 24-hour exposure to a 60 Hz magnetic field (0.01 and 1.0 mT). Although some variations in gene expression could be seen (twofold increase or decrease), the high inter-experiment variability and the absence of a relationship between exposure intensity and differential gene expression led the authors to conclude that they could not identify a plausible genetic target for the action of magnetic fields.

Using yeast cells and the microarray and 2D Poly-Acrylamide Gel Electrophoresis (PAGE) high-throughput techniques, Nakasono et al. (2003) showed no differential expression in about 5900 genes and 1000 proteins, after a 24-h exposure to 50 Hz magnetic fields (10, 150 and 300 mT). By contrast, heat-shock, minimal culture medium, and aerobic conditions showed significant changes in expression profiles.

Yomori et al. (2002) exposed T98G human glioblastoma cells to 1, 20, 100, and 500 μT of 60 Hz elliptically polarized magnetic fields, typical of environmental magnetic fields polarization under overhead power lines. After 0.5 to 3 h of exposure, the level of c-myc, c-fos and c-jun (mRNA and protein) were found to be unaffected.

Wu et al. (2000) used the mRNA differential display technique to compare gene expression in human Daudi cells exposed for up to 24 h to a 0.8 mT, 50 Hz magnetic fields to that in sham-exposed cells. They identified one gene, the ceramide glucosyltransferase gene (GCS) whose expression was significantly decreased under magnetic field exposure. A biphasic drop was found at 20 min and then at 24 h of exposure. The product of this gene is known to be involved in cell growth and differentiation.

Using the same approach, Olivares-Banuelos et al. (2004) investigated gene expression in chromaffin cells during differentiation into neuron-like cells under treatment with nerve growth factor (NGF) or magnetic fields (60 Hz, 0.7 mT, 2 x 2 h per day over 7 days). The model of chromaffin cell differentiation was previously shown by the same group to be responsive to such magnetic field exposure (Drucker-Colin et al., 1994; Feria-Velasco et al., 1998; Verdugo-Diaz, Paromero-Rivero & Drucker-Colin, 1998). Amongst the 53 transcripts that showed a differential expression in cells exposed to magnetic field compared to cells treated with NGF cells, six genes were identified. These genes encoded phosphoglucomutase-1, thiamine pyrophosphokinase, neurofibromatosis-2 interacting protein and microtubule associated protein 2, while two other encode for unidentified proteins. Interestingly, not only all these genes, but also genes found unresponsive to ELF magnetic fields (actin, histone 2) contained CTCT sequences in their presumed regulatory regions. Although their density may be higher in the regulatory region of magnetic field responsive genes, those results show that the presence of CTCT sequences in the regulatory region of a gene is not sufficient to confer sensitivity to magnetic fields.

Santini et al. (2003) investigated the expression of cell adhesion molecules (CAMs), a class of proteins known to be involved in tumour growth and metastasis, in the MG-63 and Saos-2 osteosarcoma cell lines. Cells were exposed to a 5 mT, 50 Hz magnetic field for 7 and 14 days. Spikes and harmonics were present in the signal. The expression of two integrins (VLA-2 collagen receptor, and VLA-5 fibronectin receptor) and one protein from the CD-44 family (CD-44 hyaluronan receptor) was monitored, showing no effect in Saos-2 cells, while in MG-63 cells, the expression profile of VLA-5 and CD-44 was found to be weakly but significantly affected (14% decrease in CD-44 expression at day 7 and 10% increase in VLA-5 expression at day 14). The physiological significance of such data is unclear.

Another study looked at the expression of a protein suspected to be involved in invasiveness of brain tumours. When exposing MO54 human glioma cells to a 60 Hz, 5 mT magnetic field for 24 h, Ding, Nakahara & Miyakoshi (2002) showed that GAP-43 expression was transiently increased and followed a kinetic pattern similar to that observed after X-rays irradiation: GAP-43 levels plateaued between 5 and 10 h of exposure (twofold increase versus sham-exposed cells) and dropped to basal level at 24 h. No additive effect was noted after co-exposure to magnetic fields and X rays, suggesting that a similar mechanism might be involved in the cellular response to both types of exposure.

Cytokine receptors play an important role in immune cell homeostasis and altered expression of these proteins may be involved in carcinogenesis. For instance, tumour necrosis factor receptors (TNFR) are involved in the induction of apoptosis, and interleukin-6 receptor α (IL-6Rα) and transforming growth factor-β receptor 1 (TGFβR1) exert important roles in the regulation of cell differentiation and proliferation. Zhou et al. (2002) studied the effects of a 50 Hz magnetic field (0.1 and 0.8 mT) on the expression of TNFR p55 and p75, IL-6Rα and TGFβR1 cytokine receptors in HL60 cells exposed from 30 min to 72 h. Transcription levels of TNFR p75 and IL-6Rα were increased only after 72 h of exposure, at either field strength. By contrast, gene expression levels of TNFR p55 and TGFβR1 were not affected under any of the exposure conditions. The biological consequences of such a differential effect of magnetic field on the different cytokine receptors are not known.

The role of the p53 tumour suppressor gene in the biological response to ELF magnetic was investigated by Czyz et al. (2004). Mouse pluripotent embryonic stem (ES) cells bearing either a wild-type or defective p53 gene, were exposed to a 50 Hz signal simulating power-line magnetic fields (at 0.1, 1.0 or 2.3 mT). A 5 min on/ 30 min off intermittent exposure was applied for 6 or 48 h during the first stages of cell differentiation. Transcript levels of regulatory genes, such as egr-1, p21, c-jun, c-myc, hsp70 and bcl-2, were analysed immediately after exposure or after a recovery time of 18 h. p53 wild-type cells were found not to be responsive to any of the exposure conditions. By contrast p53-deficient cells elicited a response under a single exposure condition: a 6-h exposure at the highest field level tested

resulted in a transient but significant up-regulation of c-jun, p21 and egr-1 mRNA levels. The level of egr-1 after exposure in the specified conditions was similar to the basal level found in wild-type cells. It is reported that other intermittent or continuous exposures did not induce similar effects in p53-deficient ES cells. It was suggested that that the balance between positive and negative regulators of cell cycle may be transiently altered in ES cells lacking a functional p53 gene.

The effect of ELF magnetic fields on the expression of heat shock proteins (hsps) has also been investigated. Hsps are known as chaperones, in that they assist other proteins to assemble correctly, target the appropriate cellular compartment and prevent unfolding. As a superfamily of proteins, they modulate a wide range of functions such as thermotolerance, anti-apoptosis function, immunogenicity, etc. Some of the hsps are constitutively expressed, while a number of others are inducible after the cells have been exposed to a wide range of stress signals (heat, heavy metals, etc). Some hsp proteins have also been shown to be expressed at atypical levels in tumour cells or tissue. Such observations have led to suggestions that hsps could be used as biomarkers for cellular stress in general. Their use as biomarkers for carcinogenesis is not widely validated.

In a series of papers from the Goodman group, a 60 Hz, 8 μT magnetic field was shown to increase the transcription of the heat shock genes hsp70 and SSA1 in HL60 cells and the yeast *Saccharomyces cerevisiae*, respectively (1.8-fold in 20 min) (Goodman et al., 1994). This group used the same exposure conditions — with longer exposures in some papers — and different cell lines to show that ELF magnetic fields activated heat shock factor 1 (HSF1), enhanced binding of the c-myc protein to sites within the heat shock protein promoter region and enhanced the DNA binding activity of different transcription factors such as AP1 in the hsp70 promoter region by contrast to heat shock (Lin et al., 1997; 1998a; 1998b; 1999). An increase in the hsp70 protein was also observed, with a maximum increase of 40% in normal human breast cells (HTB124) (Han et al., 1998). Moreover, an electromagnetic field response element EMRE (nCTCTn sequence) was identified in the hsp70 promoter (3 sequences) as well as in the case of c-myc (8 sequences in the promoter) (Goodman & Blank, 1998).

Pipkin et al. (1999) also showed that inducible hsp70 (hsp70B) was overexpressed after ELF magnetic field exposure (60 Hz, 1 mT), but the field strength required for the effect was higher than that reported by the Goodman group.

In a recent paper, Tokalov & Gutzeit (2004) studied the expression of a number of genes from the hsp family (hsp27, 60, 70A, 70B, 70C, 75, 78, 90, 90 and hsc70) in HL60 cells under exposure to a 50 Hz magnetic field at different strengths (10–140 μT) with or without heat shock (43 °C) for 30 minutes. Only the three hsp70 genes were overexpressed after exposure to magnetic fields alone, with a maximum induction at 80 μT and almost background levels of expression at 100 and 140 μT. Moreover, when exposure to

a 100 μT magnetic field was concomitant to heat shock, the expression of the hsp70 genes was stronger than that with either treatment alone.

In contrast, other groups did not find any effects of ELF magnetic fields on hsps including hsp70 in other cell lines (Balcer-Kubiczek et al., 2000; Kang et al., 1998; Miyakoshi et al., 2000a; Parker & Winters, 1992). However, Miyakoshi et al. (2000a) showed that magnetic field exposure suppressed hsp70 expression induced by heat treatment (40–42 °C).

In a replication study of the work of the Goodman group, Morehouse & Owen (2000b) observed no significant effect on the induction of hsp70 expression and HSF-HSE binding in HL60 cells exposed to a 6.3 or 8.0 μT, 60 Hz magnetic field. Recently, Coulton et al. (2004) found no effect on the expression of hsp27, hsp70A (constitutive) and hsp70B (inducible) genes in human peripheral blood cells exposed to 50 Hz magnetic fields (20–100 μT) for 2 or 4 h. They concluded that these genes in human normal blood cells were not responsive to ELF magnetic fields

The in vitro studies on gene expression are summarized in Table 81.

11.4.3 Differentiation, proliferation and apoptosis

Only a few papers have dealt with differentiation, proliferation and apoptosis in recent years.

Ventura et al. (2005) exposed GTR1 embryonic stem cells to a 50 Hz, 0.8 mT magnetic field for 3 or 10 days, i.e. at the time of differentiation state for embryonic bodies and puromycin-selected cardiomyocytes, respectively. They showed that, under exposure, both embryonic bodies and cardiomyocytes overexpressed mRNA for two transcription factors known to be essential in cardiogenesis (GATA-4 and Nkx-2.5), as well as prodynorphin mRNA and the dynorphin protein, all involved in cardiac differentiation. This was correlated with the increased expression of two cardiac-specific mRNAs (a-myosin heavy chain and myosin light chain 2V) in magnetic field exposed cells and a significant increase in the number of beating cells within the 10 days of exposure.

Manni et al. (2004) exposed human oral keratinocytes to a 2 mT, 50 Hz magnetic field for up to 15 days. Exposure resulted in a number of changes with respect to sham-exposed samples that were correlated to cellular differentiation. The authors noted modifications in cells shape and morphology with a different actin distribution and an increased expression in involucrin and -catenin (markers of differentiation and adhesion) along with a decreased expression of epidermal growth factor receptors. These effects were accompanied by a diminished clonogenic capacity and a decreased cellular growth.

Table 81. Gene expression

Cells	Biological endpoint	Exposure conditions	Results	Reference
Hela cells	Transfected with c-myc-EMRE (nCTCTn binding sites) expression vectors linked to luciferase or chloramphenicol transferase (CAT)	60 Hz 8 µT 30 min	Increased luciferase and CAT activities in cells transfected with c-myc-EMRE expression vector. No effect when the construct does not contain nCTCTn binding sites.	Lin et al., 2001
Normal (HME) and transformed (HBL-100) human mammary epithelial cells and human promyelocytic leukaemia (HL60) cells	Gene expression using arrays containing cDNAs for 588 cancer-related genes	60 Hz 0.01, 1.0 mT 24 h	No significant effects. High inter-experiment variability and absence of a relationship between exposure intensity and differential gene expression.	Loberg et al., 2000
Yeast cells	Microarray and 2D poly-acrylamide gel electrophoresis	50 Hz 10, 150, and 300 mT 24 h	No differential expression in about 5900 genes and 1000 proteins.	Nakasono et al., 2003
T98G human glioblastoma cells	Total RNA and protein extraction ; Northern blotting	60 Hz elliptically polarized 1, 20, 100, and 500 µT 0.5–3 h	No effects on the levels of c-myc, c-fos and c-jun (mRNA and protein).	Yomori et al., 2002
Human Daudi cells	mRNA differential display technique	50 Hz 0.8 mT 24 h	Decreased expression of the ceramide glucosyltransferase gene, involved in cell growth and differentiation.	Wu et al., 2000
Chromaffin cells during differentiation in neuron-like cells	mRNA differential display technique	60 Hz 0.7 mT 2 x 2 h d^{-1}, 7 d	Induction of 53 transcripts that showed a differential expression.	Olivares-Banuelos et al., 2004
MG-63 and Saos-2 osteosarcoma cell lines	Expression of two integrins (VLA-2 collagen receptor, and VLA-5 fibronectin receptor) and CD-44 hyaluronan receptor	50 Hz 5 mT 7, 14 d	No effect in Saos-2 cells. In MG-63 cell lines: 14% decrease in CD-44 expression at day 7 and 10% increase in VLA-5 expression at day 14.	Santini et al., 2003

Table 81. Continued

MO54 human glioma cells	Protein expression of GAP 43 using immunocytochemistry and Western blot	60 Hz 5 mT 24 h	GAP 43 expression transiently increased; no synergy with X rays.	Ding, Nakahara & Miyakoshi, 2002
HL60 human cells	Expression of TNFR p55 and p75, IL-6Rα and TGFβR1 cytokine receptors	50 Hz 0.1, 0.8 mT 30 min – 72 h	Increase in transcription levels of TNFR p75 and IL-6Rα after 72 h of exposure only, at either field strength; no other effects.	Zhou et al., 2002
Mouse pluripotent embryonic stem cells with wild-type or defective p53 gene	Transcript levels of regulatory genes analysed immediately after exposure or after a recovery time of 18 h	50 Hz 0.1, 1.0, 2.3 mT 5 min on / 30 min off, 6 or 48 h	No effect on p53 wild-type cells. In p53-deficient cells, only a 6-h exposure at 2.3 mT resulted in a transient but significant up-regulation of c-jun, p21 and egr-1 mRNA levels.	Czyz et al., 2004
HL60 human cells	Expression of hsp27, 60, 70A, 70B, 70C, 75, 78, 90α, 90β and hsc70	50 Hz 10–140 µT with or without heat shock (43°C) for 30 min	Overexpression of the three hsp70 genes, maximum at 80 µT; synergy with heat shock.	Tokalov & Gutzeit, 2004
Human peripheral blood cells	Expression of hsp27, hsp70A (constitutive) and hsp70B (inducible) genes	50 Hz 20–100 µT 2 or 4 h	No effects.	Coulton et al., 2004

A number of papers have dealt with the PC12 differentiation model (formation of neurite outgrowth) giving both positive and negative outcomes. Using the PC12D model, Takatsuki et al. (2002) found that melatonin antagonized the differentiating effect observed after the cells were exposed for 22h to a 60 Hz, 33.3 µT magnetic field combined with the geomagnetic field in the presence of the differentiation-inducer forskolin. It has to be noted that melatonin is most frequently reported to have an opposite effect on cellular differentiation.

Pirozzoli et al. (2003) exposed human neuroblastoma LAN5 cells to a 50 Hz, 1 mT magnetic field in the presence of the geomagnetic field for up to 7 days. They reported that a 24-h exposure significantly increased cell proliferation (+10%) and a 72-h exposure delayed the retinoic-acid-induced

LAN5 differentiation through increased cell proliferation and decreased expression of the B-myb protein. While exposure to a magnetic field alone did not affect apoptosis as determined using the PARP-cleavage and Hoechst assays, it counteracted camptothecin-induced apoptosis and camptothecin-repressed cellular proliferation. The effect was found to be transient (it peaked at 20 h and vanished thereafter) and dependent on the dose of camptothecin (maximum effect at 12.5 and 25 ng ml^{-1}).

In other studies, apoptosis and proliferation were investigated in cells exposed to ELF magnetic fields. As reported elsewhere (see 11.4.1.2), phytohemagglutinin (PHA)-stimulated human lymphocytes exposed for 24 h to a 50 Hz magnetic field at 80 or 800 μT did not undergo apoptosis, and the effect of the genotoxic agent vinblastine was not altered in the presence of the magnetic field (Verheyen et al., 2003).

The group of Miyakoshi in Japan published two papers concerning apoptosis. Apoptosis and the expression of apoptosis-related proteins (p21, bax, and bcl-2) were determined in MCF-7 human breast carcinoma cells following a 24-h or 72-h exposure to a 60 Hz magnetic field (5 mT) alone or in combination with X-rays (Ding et al., 2001). The magnetic field alone did not induce apoptosis or expression of bax and bcl-2 proteins. However, a 24-h magnetic field exposure after 12 Gy X-irradiation significantly decreased apoptosis and bax expression, but increased bcl-2 expression. In another paper, the levels of the apoptosis-related genes p21, p53, phospho-p53 (Ser15), caspase-3 and the anti-apoptosis gene bcl-2 were determined in xrs5 (KU80-deficient) and CHO-K1 (KU80-proficient) cells following exposure to a 5 mT magnetic field and X-rays (Tian et al., 2002). A significant decrease in the induction of p53, phospho-p53, caspase-3 and p21 proteins was observed in xrs5 cells when 8 Gy X-irradiation was followed by 5, 10 or 24-h magnetic field exposure. Exposure of xrs5 cells to magnetic fields for 10 h following irradiation significantly decreased X-ray-induced apoptosis from about 1.7% to 0.7%. No apoptosis was found in CHO-K1 cells within 24 h of irradiation by X-rays alone and by X-rays combined with ELF magnetic fields. The results suggested that in some cells exposure to a 5 mT ELF magnetic field may transiently suppress X-ray-induced apoptosis.

Oda & Koike (2004) examined the effect of a 5-day exposure to a 50 Hz magnetic field at 300 mT on apoptosis in primary cerebellar granule neurons, which are known to undergo apoptosis under normal conditions (5.4 mM K^+) in vitro. While no neuronal survival was observed in sham-exposure condition, exposure to magnetic fields prevented the apoptotic death of primary neurons. The effect was found to be dependent on the induced currents in cultured flasks (1 to 4 A m^{-2}) and the magnitude of the effect was comparable to that of known survival-promoters (membrane depolarization and brain-derived neurotrophic factor).

Traitcheva et al. (2003) exposed U937 and K562 human tumour cells to 50 Hz pulsed magnetic fields (10, 39 or 55mT) for 20 min to 6 h, either alone or in combination with the pro-apoptotic agent actinomycin, with or without light illumination (which generates free radicals from actino-

mycin). They monitored the proportion of dead cells and found that pulsed magnetic fields elicited cell death (50%) immediately after exposure (10 mT for 6 h; 55 mT for 20 min), and up to 80–90% 24 h after exposure. The effect was maximized in the presence of actinomycin or actinomycin plus light. Moreover, hyperthermia (42°C) and hyperacidity (pH = 6.5) were also found to enhance the effect of the magnetic field.

Grassi et al. (2004) investigated the effect of 50 Hz magnetic fields (5–1000 μT, 1 to 5 days of exposure) on voltage-gated Ca^{2+} channels, cell proliferation and apoptosis in human neuroblastoma IMR32 and rat pituitary GH3 cells (most of the experiments being performed on IRM32 cells only). Exposure to a 50 Hz, 1 mT magnetic field significantly enhanced proliferation in both cell lines by about 40% from 24 to 72 h. In IMR32 cells, the effect was dependent on the field strength (from 0.5–1 mT). While magnetic fields did not affect apoptosis in this cell type, they were shown to inhibit puromycin- and H_2O_2-induced apoptosis (–22 and –33%, respectively). The effects on proliferation and apoptosis were found to be related to an increased Ca^{2+} influx mainly involving voltage-gated Ca^{2+} channels as determined by the use of Ca^{2+}-channel blockers and electrophysiological recordings (whole-cell and single-channel patch-clamp experiments).

Table 82 summarizes the in vitro studies into effects of ELF on differentiation, proliferation and apoptosis.

11.4.4 Gap junction intercellular communications

Gap junction intercellular communication (GJIC) operates via channels that permit the passage of ions and low molecular weight metabolites between adjacent cells, without exposure to the extracellular environment. These pathways are formed by the interaction of two hemichannels on the surface of opposing cells. These hemichannels are formed by the association of six identical subunits, named connexins (Cx), which are integral membrane proteins. GJIC is known to play an important role in cell-cell communication, cell growth and differentiation. The loss of functional GJIC or the lack of connexin expression is a common feature of cancer cells and one of the most common properties of tumour promoters, such as the phorbol ester TPA (12-0-tetradecanoylphorbol-13-acetate), is their ability to inhibit GJIC.

Three papers on the effects of ELF fields and GJIC have reported that exposure to magnetic fields (from about 0.02 to 1.6 mT, 0.5 to 24 h) modulated the effects of chemicals (TPA, chloral hydrate) and resulted in an additive loss in GJIC functionality in C3H10T1/2 mouse embryo cells (Ubeda et al., 1995), clone 9 rat liver cells (Blackman et al., 1998) and Chinese hamster lung cells (Li et al., 1999). In the later work, it was also reported that a 24-h exposure of cells to a 50 Hz, 0.8 mT magnetic field alone inhibited GJIC (while a magnetic field of 0.2 mT – but not 0.05 mT – interacted with TPA). In a attempt to reproduce the findings reported by Blackman et al. (1998), Griffin et al. (2000; 2000) did not observe any alteration in chemically-inhibited GJIC in clone 9 rat liver cells. One paper reported an increase in GJIC after exposure to a 50 Hz, 2 mT magnetic field in mouse fibroblasts (Schimmelpfeng, Stein & Dertinger, 1995).

Table 82. Differentiation, proliferation and apoptosis

Cells	Biological endpoint	Exposure conditions	Results	Reference
GTR1 embryonic stem cells: embryonic bodies (undifferentiated state) and puromycin-selected cardiomyocytes (differentiated state)	Gene expression coding for tissue-restricted transcription factors and cardiomyocyte proliferation	50 Hz 0.8 mT 3 or 10 d	Overexpression of GATA4 and Nkx-2.5 mRNA (essential in cardiogenesis) at both differentiation states. Increased expression of two cardiac-specific mRNAs. Increase in number of beating cells within 10 d of exposure.	Ventura et al., 2005
Human primary oral keratinocytes (HOK cells)	Immunofluorescent staining, confocal and scanning electron microscopy Western blotting and immunofluorescent staining Clonal proliferation	50 Hz 2 mT (field gradient: 5%) up to 15 d	Modifications in cells shape and morphology. Increased expression in two markers of differentiation and adhesion. Decreased expression of epidermal growth factor receptors. Diminished clonogenic capacity and decreased cellular growth.	Manni et al., 2004
PC12D cells	Exposure in the presence of the differentiation-inducer forskolin	60 Hz 33.3 µT combined with geomagnetic field 22 h	Melatonin antagonized the differentiating effect observed after exposure to magnetic field.	Takatsuki, Yoshikoshi & Sakanishi, 2002

Table 82. Continued

Human neuroblastoma LAN5 cells	Cell proliferation monitored colorimetrically Western blotting Apoptosis assayed by TUNEL assay, and by Hoechst staining	50 Hz 1 mT, combined with geomagnetic field up to 7 d	Cell proliferation increased at 24 h of exposure. Delay in retinoic-acid-induced LAN5 differentiation at 72 h. No effect of field alone on apoptosis. Exposure counteracted camptothecin-induced effect on apoptosis and cellular proliferation.	Pirozzoli et al., 2003
Human lymphocytes stimulated with phyto-hemagglutinin	Micronucleus, nuclear division index and apoptosis assays	50 Hz 80 or 800 µT 24 h	No induction of apoptosis. No alteration of the effect of the genotoxic agent vinblastine.	Verheyen et al., 2003
MCF-7 human breast carcinoma cells	Apoptosis and expression of apoptosis-related proteins (p21, bax, and bcl-2)	60 Hz 5 mT, alone or combined with X-rays 24, 72 h	No induction of apoptosis by magnetic field alone. Transient decrease in X-ray-induced apoptosis by 24 h exposure.	Ding et al., 2001
Chinese hamster ovary cells (CHO-K1) and xrs5 cells	Apoptosis and expression of apoptosis-related genes (p21, p53, phospho-p53, caspase-3 and bcl-2)	60 Hz 5 mT, alone or combined with X-rays 5, 10, 24 h	No induction of apoptosis by magnetic field alone in both CHO-K1 and xrs5 cells. Transient decrease in X-ray-induced apoptosis by 10 h exposure in xrs5 cells.	Tian et al., 2002
Rat primary cerebellar granule neurons	Neuronal survival assessed by staining with calcein-AM or propidium iodide.	50 Hz 300 mT 5 d	Exposure prevented apoptotic death of primary neurons. Effect dependent on induced currents (1–4 A m^{-2}). Amplitude of effect comparable to that of known survival-promoters.	Oda & Koike, 2004
U937 and K562 human tumour cells	Exposure alone or in combination with the pro-apoptotic agent actinomycin, with or without light illumination. Monitoring of the proportion of necrotic cells	50 Hz 10, 39 or 55 mT, pulsed 20 min – 6 h	Exposure caused cell death immediately and 24 h after exposure (10 mT, 6 h; 55 mT, 20 min). Stronger effect in the presence of actinomycin or actinomycin plus light. Hyperthermia (42°C) and hyper-acidity (pH = 6.5) enhanced the effect of field exposure.	Traitcheva et al., 2003

Table 82. Continued

Human neuroblastoma IMR32 and rat pituitary GH3 cells	Effect on voltage-gated Ca^{2+} channels, cell proliferation and apoptosis	50 Hz 5–1000 μT 1–5 d	1 mT exposure significantly enhanced proliferation in both cell lines. In IMR32 cells, effect dependent on field strength (from 0.5 to 1 mT). No effect on apoptosis but inhibition of puromycin- and H_2O_2-induced apoptosis. Effects on proliferation and apoptosis related to increased Ca^{2+} influx.	Grassi et al., 2004

A series of papers from the group of Li et al. have been published recently (Chiang et al., 1999; Hu et al., 2000; Hu et al., 2001; Zeng et al., 2003). When Chinese hamster lung cells were exposed as previously described (24 h, 0.8 mT) in the presence of protein kinase C (PKC) inhibitors (staurosporine and palmitoyl carnitine) during the last hour of exposure, the effect of the magnetic field was counteracted in a dose-dependent manner and almost abolished at the highest doses of PKC inhibitors tested. According to the authors, ELF magnetic fields affected GJIC via a hyper-phosphorylation of connexins (Chiang et al., 1999). The expression and localisation of Cx43 within the cell compartments was investigated, showing that under treatment to TPA or exposure to ELF magnetic field, the phosphorylation of Cx43 was enhanced and the protein was mostly located near the nucleus, in contrast to the normal location at the plasma membrane (Zeng et al., 2003). In parallel, it was shown that ELF magnetic fields (24 h, 0.8 mT) also decreased GJIC and induced Cx43 hyperphosphorylation in mouse NIH3T3 cells but did not affect the level of the Cx43 gene transcription or the expression of Cx43 protein, which is in contradiction with the previous work on Chinese hamster lung cells. It is possible however that Cx43 is stabilised via hyperphosphorylation and that hyperphosphorylated Cx43 would be in part responsible for the observed increase in Cx43. In the NIH3T3 cells the effect of the magnetic field tested was similar to a TPA dose of 3 ng ml^{-1} (Hu et al., 2000; 2001). Thus, based on this body of work, the authors conclude that ELF magnetic fields mimicked TPA in the signalling pathway leading to a decrease in GJIC, and the threshold of inhibition was 0.4 mT.

Although not related to cancer, the study of Marino, Kolomytkin & Frilot (2003) deserves to be mentioned as the effects of induced currents were investigated in HIG-82 synovial fibroblasts and 5Y neuroblastoma cells. No effects were found in nerve cells, but the authors showed a decrease in the conductance of gap junction channels under exposure to 20 mA m^{-2} at 60 Hz and a significant increase in intracellular Ca^{2+} at current densities of more than 10 mA m^{-2}. The authors hypothesised that the pain relief reported under exposure to ELF magnetic fields could be related to a drop in pro-inflammatory responses due to decreased GJIC in synovial cells. This work did not establish whether the magnetic field or the induced currents were responsible for the reported effects.

Yamaguchi et al. (2002) have also reported that pre-osteoblastic MC3T3-E1 cells elicited a decrease in GJIC after a 1-h exposure to ELF magnetic fields of up to 1.5 mT (50 % at 0.4 mT with no effect of the frequency from 30 to 120 Hz), while the well-differentiated osteoblastic ROS 17/2.8 cells did not. The effect was unrelated to Cx43 expression and distribution within the cells or intracellular Ca^{2+}.

The studies on gap junctions and intercellular communication are summarized in Table 83.

Table 83. Gap junctions and intercellular communication

Cells	Biological endpoint	Exposure conditions	Results	Reference
Chinese hamster lung cells	Gap junctional inter communications; dye transfer assay: microinjection of Lucifer Yellow, determination of the number of dye-coupled cells (DCC) per injection	50 Hz 0.05, 0.2, 0.4, 0.8 mT 24 h +/- 5 ng ml^{-1} TPA, 1 h Field perpendicular to dishes; presence of geomagnetic field	Decrease in number of DCC at 0.8 mT only, comparable to effect of TPA. Potentiation of the effect of TPA: significant decrease versus TPA alone at and above 0.2 mT.	Li et al., 1999
Chinese hamster lung cells	Gap junctional inter communications; dye transfer assay: microinjection of Lucifer Yellow, determination of the number of dye-coupled cells (DCC) per injection	50 Hz 0.8 mT 24 h Field perpendicular to dishes; presence of geomagnetic field	Magnetic fields decreased number of DCC. Use of PKC inhibitors (staurosporine or palmitoyl-DL-carnitine) restored dye transfer in a dose-dependent manner.	Chiang et al., 1999
Chinese hamster lung cells and NIH3T3 mouse fibroblasts	Level of connexin43 mRNA Northern Blot	50 Hz 0.8 mT 24 h Field perpendicular to dishes; presence of geomagnetic field	No effect.	Hu et al., 2000
NIH3T3 mouse fibroblasts	Gap junctional inter communications: fluorescence recovery after photobleaching (FRAP) analysis Connexin43 expression and phosphorylation in membrane suspensions and total protein extracts Western-blotting	50 Hz 0.8 mT 24 h +/- 3 ng ml^{-1}TPA, 2 h Field perpendicular to dishes; presence of geomagnetic field	Magnetic fields alone decreased fluorescence recovery by 50%; effect comparable to TPA. Potentiation of effect of TPA, significant decrease versus TPA alone. Hyperphosphorylation of connexin43, no change in level of Cx43. Localisation of Cx43 in the plasma membrane.	Hu et al., 2001

Table 83. Continued

Chinese hamster lung cells	Detection of Connexin43 Western blotting, confocal microscopy, immunocytochemistry	50 Hz 0.8 mT 24 h Field perpendicular to dishes; presence of geomagnetic field	Magnetic fields induced an internalisation of Cx43 from the membrane to the cytoplasm. Magnetic fields increased the level of Cx43 in the cytoplasm and the nucleus, effect similar to that of TPA (5 ng ml^{-1}; 1 h).	Zeng et al., 2003
HIG-82 fibroblats (derived from rabbit synovium) and SH-SY5Y human neuroblastoma cells	Gap junctional inter communications: registration of single gap junction channel currents Calcium influx (transmembrane calcium currents)	60 Hz currents of 2, 20 and 75 mA m^{-2}	Currents of 20 mA m^{-2} decreased conductance of gap junction channels. Currents of 10 mA m^{-2} increased flow of current through calcium channels.	Marino, Kolomytkin & Frilot, 2003
Preosteoblastic MC3T3-E1 cells and well-differentiated osteoblastic ROS 17/2.8 cells	Gap junctional inter communications; dye transfer assay: microinjection of Lucifer Yellow, determination of the number of dye-coupled cells (DCC) per injection Parachute technique: PKH26/ BCECF double staining Cytosolic calcium concentration (Fura2 staining) and Connexin43 expression (Western blotting)	30–120 Hz 0.1, 1, 3, 6 and 12.5 mT 1 and 2.5 h geomagnetic field nulled, DT< 0.6°C	No effect on ROS 17/2.8 cells. In MC3T3 cells, magnetic fields decreased the frequency of GJIC (28% of controls at 60 Hz, 1.25 mT). No effect of the frequency. No effect on intracellular Ca^{2+} and Cx43 expression and localisation.	Yamaguchi et al., 2002

11.4.5 Free radicals

The effects of exposure to electric and magnetic fields on free radical species have been studied in recent years and there are three main subdivisions to this area of research: (i) the biophysical mechanisms by which magnetic fields could affect the yield and concentration of the radicals (i.e. the radical pair mechanism, see section 4.5.4); (ii) the biological and biochemical mechanisms of increased production of radicals by exposed cells, and/or their increased availability to interact with DNA; and (iii) the potential enhancement of the effect of compounds known to increase the concentration of free radicals.

The issue of free radical involvement in bioeffects has been linked closely to the role of melatonin as a free radical scavenger, as an alteration of melatonin production under exposure had been hypothesised but not proven (see Chapter 6).

Katsir & Parola (1998) reported an enhancement of the proliferation of chick embryo fibroblasts under magnetic field exposure (100 Hz, 0.7 mT, 24 h). The increase in cell proliferation was reduced in the presence of catalase, superoxide dismutase, or vitamin E, by 79, 67, and 82%, respectively. This was interpreted by the authors as an involvement of free radicals.

The synergy with free radical generating systems was investigated by two groups. Fiorani et al. (1997) studied the effect of ELF magnetic fields on rabbit erythrocytes in combination with an oxygen-radical generating system (Fe(II)/ascorbate). Exposure at 0.5 mT (50Hz) had no effect on intact erythrocytes, but increased the damage due to the presence of the iron free radical generating system, as witnessed by a 20% decay in hexokinase activity and 100% increase in methemoglobin production, compared to the effect of the oxidant system alone.

The hypothesis of the radical pair mechanism was tested by Zmyslony et al. (2004) on rat lymphocytes exposed for 1 h to 50 Hz fields at 20, 40, or 200 μT inside a pair of Helmholtz coils with its axis along or transverse to the geomagnetic field. Iron ions (from $FeCl_2$) were used as a stimulator of the oxidation processes and oxygen radical concentration was measured using a fluorescent probe. Only in the lymphocytes exposed at 40 μT along the geomagnetic field was there a decrease of fluorescence. This finding was interpreted as evidence for the radical pair mechanism, since for this configuration the magnetic field is cancelled once per period but not for other frequency and orientation configurations.

The Simko group has studied the effects of exposure on various cellular systems and have postulated recently that some of the effects that they observed could be interpreted as due to increased free radical production. In 2001, they published data on the stimulation of phagocytosis and free radical production in mouse bone marrow-derived macrophages by 50 Hz magnetic fields (0.5–1.5mT, 45 min) (Simko et al., 2001). Under exposure, an increase was observed in superoxide radical ion production and phagocytic uptake of latex beads. Stimulation with the tumour promoter TPA showed the same

increased phagocytic activity as a 1 mT magnetic field. However, co-exposure with TPA led to no further increase of bead uptake, interpreted as ruling out a role for the protein kinase C signal transduction pathway.

The increased production of reactive oxygen species (ROS) was later reported by the same group (Rollwitz, Lupke & Simko, 2004) in bone marrow-derived promonocytes and macrophages exposed at 1 mT. TPA inhibited the exposure-induced production of ROS while the flavoprotein inhibitor DPI (diphenyleneiodonium chloride) did not, showing that the NADH-oxidase pathway, which produces the superoxide anion radicals, was affected, but not the NADPH pathway.

Simko and Mattsson have suggested in 2004 that EMFs might act as a stimulus to induce activated states of the cell such as phagocytosis, which then enhances the release of free radicals, leading possibly to genotoxic events. Exposure could lead to (i) direct activation of phagocytosis (or other cell specific responses) and thus of free radical production; (ii) direct stimulation of free radical production by some cells; and (iii) increase in the lifetime of free radicals leading to elevated free radical concentrations. Long-term exposure would lead to a chronically increased level of free radicals, subsequently causing an inhibition of the effects of melatonin. These speculations have not been substantiated but are of interest for further research on the role of free radicals in ELF magnetic field effects.

In Table 84 the in vitro studies into effects of ELF fields on free radicals are summarized.

11.4.6 In vitro conclusions

Generally, studies of the effects of ELF magnetic field exposure of cells have shown no induction of genotoxicity at fields below 50 mT. The notable exception is evidence from recent studies of DNA damage at field strengths as low as 35 μT; however, these studies are still being evaluated at this time and our understanding of these findings is incomplete. There is also increasing evidence that ELF magnetic fields may interact with DNA-damaging agents.

There is no clear evidence of the activation of genes associated with the control of the cell cycle. However, systematic studies analyzing the response of the whole genome have yet to be performed.

Many other cellular studies, for example on cell proliferation, apoptosis, calcium signaling, intercellular communication, heat shock protein expression and malignant transformation, have produced inconsistent or inconclusive results.

11.5 Overall conclusions

New human, animal and in vitro studies, published since the 2002 IARC monograph, do not change the overall classification of ELF as a possible human carcinogen.

Table 84. Free radicals

Cells	Biological endpoint	Exposure conditions	Results	Reference
Chick embryo fibroblasts	Proliferation	100 Hz 0.7 mT 24 h	Enhancement of proliferation under exposure; this increase was reduced in the presence of catalase, superoxide dismutase, or vitamin E.	Katsir & Parola, 1998
Rabbit erythrocytes (RBCs)	Exposure with oxygen-radical generating system (Fe(II)/ascorbate)	50 Hz 0.2-0.5 mT up to 90 min	At 0.5 mT, no effect on intact RBCs; increased damage due to the presence of the iron free radical generating system.	Fiorani et al., 1997
Rat lymphocytes	Exposure with iron ions ($FeCl_2$) used as a stimulator of the oxidation processes	50 Hz 20, 40 or 200 µT, field axis along or transverse to the geomagnetic field 1 h	Decrease of fluorescence only in lymphocytes exposed at 40 µT along geomagnetic field.	Zmyslony et al., 2004
Mouse bone marrow-derived macrophages	Stimulation of phagocytosis and free radical production	50 Hz 0.5–1.5 mT 45 min	Increase in superoxide radical ion production and phagocytic uptake of latex beads. Stimulation with TPA caused same increased phagocytic activity as 1 mT. Co-exposure with TPA led to no further increase of bead uptake.	Simko et al., 2001
Mouse bone marrow-derived promonocytes and macrophages	ROS production assessed using fluorescence staining and flow cytometry; superoxide anion and nitrogen generation also assessed	50 Hz 1 mT 45 min	Increased production of ROS. Inhibition of ROS increase by TPA, but not by the flavoprotein inhibitor DPI.	Rollwitz, Lupke & Simko, 2004

12 HEALTH RISK ASSESSMENT

12.1 Introduction

The control of health risks from the exposure to any physical, chemical or biological agent is informed by a scientific, ideally quantitative, assessment of potential effects at given exposure levels (risk assessment). Based upon the results of the risk assessment and taking into consideration other factors, a decision-making process aimed at eliminating or, if this is not possible, reducing to a minimum the risk from the agent (risk management) can be started. The discussion below is based on the WHO Environmental Health Criteria 210 which describes the principles for the assessment of risks to human health from exposure to chemicals (WHO, 1999). These principles are generally applicable and have been used here for ELF electric and magnetic fields.

Risk assessment is a conceptual framework that provides the mechanism for a structured review of information relevant to estimating health or the environmental effects of exposure. The risk assessment process is divided into four distinct steps: hazard identification, exposure assessment, exposure-response assessment and risk characterization.

- The purpose of *hazard identification* is to evaluate qualitatively the weight of evidence for adverse effects in humans based on the assessment of all the available data on toxicity and modes of action. Primarily two questions are addressed: (1) whether ELF fields may pose a health hazard to human beings and (2) under what circumstances an identified hazard may occur. Hazard identification is based on analyses of a variety of data that may range from observations in humans to studies conducted in laboratories, as well as possible mechanisms of action.
- *Exposure assessment* is the determination of the nature and extent of exposure to EMF under different conditions. Multiple approaches can be used to conduct exposure assessments. These include direct techniques, such as the measurement of ambient and personal exposures, and indirect methods, for example questionnaires and computational techniques.
- *Exposure-response assessment* is the process of quantitatively characterizing the relationship between the exposure received and the occurrence of an effect. For most types of possible adverse effects (i.e. neurological, behavioural, immunological, reproductive or developmental effects), it is generally considered that there is an EMF exposure level below which adverse effects will not occur (i.e. a threshold). However, for other effects such as cancer, there may not be a threshold.
- *Risk characterization* is the final step in the risk assessment process. Its purpose is to support risk managers by providing the essential scientific evidence and rationale about risk that they need

for decision-making. In risk characterization, estimates of the risk to human health under relevant exposure scenarios are provided. Thus, a risk characterization is an evaluation and integration of the available scientific evidence and is used to estimate the nature, importance and often the magnitude of human risk, including a recognition and characterization of uncertainty that can reasonably be estimated to result from exposure to EMF under specific circumstances.

The health risk assessment can be used as an input to risk management, which encompasses (1) all the activities needed to reach decisions on whether an exposure requires any specific action(s), (2) which actions are appropriate and (3) the undertaking of these actions. Such risk management activities are further discussed in Chapter 13.

12.2 Hazard identification

12.2.1 Biological versus adverse health effects

According to the WHO Constitution, health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity. Before identifying any actual health hazards, it is useful to clarify the difference between a biological effect and an adverse health effect. A biological effect is any physiological response to, in this case, exposure to ELF fields. Some biological effects may have no influence on health, some may have beneficial consequences, while others may result in pathological conditions, i.e. adverse health effects. Annoyance or discomfort caused by ELF exposure may not be pathological per se but, if substantiated, can affect the physical and mental well-being of a person and the resultant effect may be considered to be an adverse health effect.

12.2.2 Acute effects

ELF electric and magnetic fields can affect the nervous systems of people exposed to them, resulting in adverse health consequences such as nerve stimulation, at very high exposure levels. Exposure at lower levels induces changes in the excitability of nervous tissue in the central nervous system which may affect memory, cognition and other brain functions. These acute effects on the nervous system form the basis of international guidelines. However, they are unlikely to occur at the low exposure levels in the general environment and most working environments.

Exposure to ELF electric fields also induces a surface electric charge which can lead to perceptible, but non-hazardous effects, including microshocks.

12.2.3 Chronic effects

Scientific evidence suggesting that everyday, chronic, low-intensity ELF magnetic field exposure poses a possible health risk is based on epidemiological studies demonstrating a consistent pattern of an increased risk of childhood leukaemia. Uncertainties in the hazard assessment include the role

of control selection bias and exposure misclassification. In addition, virtually all of the laboratory evidence and the mechanistic evidence fails to support a relationship between low-level ELF magnetic field exposure and changes in biological function or disease status. Thus, on balance, the evidence is not strong enough to be considered causal and therefore ELF magnetic fields remain classified as possibly carcinogenic.

A number of other diseases have been investigated for possible association with ELF magnetic field exposure. These include other types of cancers in both children and adults, depression, suicide, reproductive dysfunction, developmental disorders, immunological modifications, neurological disease and cardiovascular disease. The scientific evidence supporting a linkage between exposure to ELF magnetic fields and any of these diseases is weaker than for childhood leukaemia and in some cases (for example, for cardiovascular disease or breast cancer) the evidence is sufficient to give confidence that magnetic fields do not cause the disease.

12.3 Exposure assessment

Electric and magnetic field exposures can be expressed in terms of instantaneous or temporally averaged values. Either of these can be calculated from source parameters or measured.

12.3.1 Residential exposures

In the case of residential exposure, data from various countries show that the geometric means of ELF magnetic field strengths across homes do not vary dramatically. Mean values of ELF electric fields in the home can be up to several tens of volts per metre. In the vicinity of some appliances, the instantaneous magnetic field values can be as much as a few hundreds of microtesla. Close to power lines, magnetic fields reach as much as approximately 20 μT and electric fields can be between several hundreds and several thousands of volts per metre.

The epidemiological studies on childhood leukaemia have focused on average residential ELF magnetic fields above 0.3 to 0.4 μT as a risk factor for cancer. Results from several extensive surveys showed that approximately 0.5–7% of children had time-averaged exposures in excess of 0.3 μT and 0.4–3.3% were exposed to in excess of 0.4 μT. Calculations based on case-control studies of ELF magnetic field exposure and childhood leukaemia resulted in approximately similar ranges.

12.3.2 Occupational exposures

Occupational exposure is predominantly at power frequencies and their harmonics. Magnetic field exposure in the workplace can be up to approximately 10 mT and this is invariably associated with the presence of conductors carrying high currents. In the electrical supply industry, workers may be exposed to electric fields up to 30 kV m^{-1}, which induce electric fields in the body and lead to increased occurrence of contact currents and microshocks.

12.4 Exposure-response assessment

Exposure-response assessment is the process of characterizing the relationship between the exposure received by an individual and the occurrence of an effect. There are many ways in which exposure-response relationships can be evaluated and a number of assumptions must be used to conduct such assessments.

12.4.1 Threshold levels

For some effects there may be a continuous relation with exposure, for others a threshold may exist. There will be a certain amount of imprecision in determining these thresholds. The degree of uncertainty is reflected partly in the value of a safety factor that is incorporated in order to derive the exposure limit.

Frequency-dependent thresholds have been identified for acute effects on electrically excitable tissues, particularly those in the central nervous system. These effects result from electric fields and currents that are induced in body tissues by ELF electric or magnetic field exposure (see Chapter 5). The ICNIRP (1998a) identified a threshold current density of 100 mA m^{-2} for acute changes in functions of the central nervous system (CNS: brain and spinal cord, located in the head and trunk) and recommended basic restrictions on current density induced in these tissues of 10 mA m^{-2} for workers and 2 mA m^{-2} for members of the public. A general consideration of neural tissue physiology suggested that these restrictions should remain constant between 4 Hz and 1 kHz, rising above and below these frequencies. More recently, the IEEE (2002) identified a threshold induced electric field strength of 53 mV m^{-1} at 20 Hz for changes in brain function in 50% of healthy adults. Effects taken into account included phosphene induction and other effects on synaptic interactions. The IEEE recommended basic restrictions on induced electric field strength in the brain of 17.7 mV m^{-1} in "controlled" environments and 5.9 mV m^{-1} for members of the public. The phosphene threshold rises above 20 Hz and therefore the basic restrictions recommended by the IEEE follow a frequency-proportional law up to 760 Hz, above which restrictions are based on peripheral nerve stimulation up to 100 kHz (IEEE, 2002). The net effect is that the guidance recommended by the ICNIRP (1998a) is more restrictive than that recommended by the IEEE (2002) at power frequencies (50/60 Hz) and above (see Section 12.5.1 below). The major factor responsible for this is the difference in cut-off frequency (20 Hz for the IEEE and 1 kHz for the ICNIRP) at which thresholds for electric field strength and induced current density begin to rise (Reilly, 2005).

No thresholds have not been identified for chronic effects.

12.4.2 Epidemiological methods

The most common means of characterizing an exposure-response relationship in epidemiology is through the derivation of estimates of relative risk or the odds ratio per unit of exposure or across exposure categories.

Most epidemiological studies have used the latter method. In summary, two recent pooled analyses of the studies on ELF magnetic fields and childhood leukaemia have presented dose-response analyses. These analyses have been conducted both on the basis of exposure categories and of continuous exposure data. All these analyses show that the risk increase becomes detectable around 0.3–0.4 μT. For exposure levels above these values, the data at present do not allow further analysis because of the small numbers of cases in the high exposure category.

12.5 Risk characterization

12.5.1 Acute effects

Exposure limits based on the acute effects on electrically excitable tissues, particularly those in the CNS, have been proposed by several international organizations. The current ICNIRP (1998a) guidelines for the general public at 50 Hz are 5 kV m^{-1} for electrical fields and 100 μT for magnetic fields, and at 60 Hz are 4.2 kV m^{-1} and 83 μT. For workers, the corresponding levels are 10 kV/m and 500 μT for 50 Hz and 8.3 kV m^{-1} and 420 μT for 60 Hz. The IEEE (2002) exposure levels are 5 kV m^{-1} and 904 μT for exposure to 60 Hz EMF for the general public. For occupational groups, the IEEE levels are 20 kV m^{-1} and 2710 μT at 60 Hz. The differences in the guidelines, derived independently by the IEEE and the ICNIRP, result from the use of different adverse reaction thresholds, different safety factors and different transition frequencies, i.e. those frequencies at which the standard function changes slope (see section 12.4.1).

12.5.2 Chronic effects

The most common means of characterizing risks from epidemiological data for a single endpoint is to use the attributable fraction. The attributable fraction, based on an established exposure–disease relation, is the proportion of cases (of a disease) that are attributable to the exposure. The attributable fraction is based on the comparison between the number of cases in a population that occur when the population is exposed and the number that would occur in the same population if the population were not exposed, assuming that all the other population characteristics remain the same. The assumption of a causal relationship is critical to this evaluation. As noted in Chapter 11 and later in this chapter, an assumption of this kind is difficult to accept because of the numerous limitations on the epidemiological data on childhood leukaemia and ELF magnetic field exposure and a lack of supporting evidence from a large number of experimental studies. Nevertheless, a risk characterization has been performed in order to provide some insight into the possible public health impact assuming that the association is causal.

Attributable fractions for childhood leukaemia that may result from ELF magnetic field exposure have been calculated in a number of publications (Banks & Carpenter, 1988; Grandolfo, 1996; NBOSH - National Board of Occupational Safety and Health et al., 1996; NIEHS, 1999). Greenland & Kheifets (2006) have expanded on the analyses of two different sets of

pooled data on childhood leukaemia and ELF magnetic field exposure (Ahlbom et al., 2000; Greenland et al., 2000) to provide an updated evaluation covering estimates for attributable fractions in a larger number of countries than were included in the pooled analyses. In global terms, most of the information on exposure comes from industrialized countries. There are a number of regions of the world, such as Africa and Latin America, where no representative information on exposure is available. Although the odds ratios from the major study regions – North America, Europe, New Zealand and parts of Asia – are similar (and therefore estimates from a pooled analysis of data obtained in these regions could be used for the present calculation), there are substantial differences in the exposure distributions between these regions. Comparable or larger differences are expected to exist with and within other regions. Therefore, the estimates of attributable fractions calculated from the data of industrialized countries cannot be confidently generalized to cover developing countries.

Greenland & Kheifets (2006) also performed an analysis of the uncertainty in the estimates of attributable fractions, by varying the assumptions made (more details on this analysis can be found in the appendix). Using the exposure distribution from case-control studies, the calculated attributable fractions are generally below 1% for the European and Japanese studies and between 1.5 and 3% for the North American studies. Based upon the exposure surveys, the attributable fraction values vary between 1 and 5% for all areas. The confidence bounds on these numbers are relatively large. Moreover, since these calculations are highly dependent on assumptions about the exposure prevalence and distribution and on the effect of exposure on the disease, they are very imprecise. Thus, assuming that the association is causal, on a worldwide scale, the best point estimates of the calculated attributable numbers (rounded to the nearest hundred) range from 100 to 2400 childhood leukaemia cases per year that might be attributable to ELF magnetic field exposure (these numbers are derived from Figures A3 and A4 in the appendix; Kheifets, Afifi & Shimkhada, 2006), representing 0.2 to 4.9% of the total annual number of leukaemia cases, which was calculated to be around 49 000 worldwide in 2000 (IARC, 2000).

12.5.3 Uncertainties in the risk characterization

12.5.3.1 Biophysical mechanisms

The biophysical plausibility of various proposed direct and indirect interaction mechanisms for ELF electric and magnetic fields depends in particular on whether a “signal” generated in a biological process or entity by exposure to such a field can be discriminated from inherent random noise. There is considerable uncertainty as to which mechanism(s) might be relevant. Three mechanisms related to the direct interaction of fields with the human body stand out as potentially operating at lower field levels than the others: induced electric fields in networks of neural tissues, the prolongation of the lifetime of radical pairs and effects on magnetite.

12.5.3.2 Exposure metric

At present it is unknown which, if any, aspect of exposure might be harmful. Certain actions, while reducing one aspect of exposure, might inadvertently increase another aspect that, if it were a causal factor, would lead to increased risk. However, the assumptions are usually that less exposure is preferable and that reducing one aspect of exposure will also reduce any aspect that might be harmful. Neither of these assumptions is certain. In fact, some laboratory research has suggested that biological effects caused by EMF vary within windows of frequency and intensity of the fields. While such a complex and unusual pattern would go against some of the accepted tenets of toxicology and epidemiology, the possibility that it may be real cannot be ignored.

12.5.3.3 Epidemiology

The consistently observed association between average magnetic field exposure above 0.3–0.4 μT and childhood leukaemia can be due to chance, selection bias, misclassification and other factors which can potentially confound the association or a true causal relationship. Given that the pooled analyses were based on large numbers, chance as a possible explanation seems unlikely. Taking into account potential confounding factors has not changed the risk estimates and substantial confounding from factors that do not represent an aspect of the electric or magnetic fields is unlikely. Selection bias, particularly for the controls in case-control studies, may be partially responsible for the consistently observed association between ELF magnetic field exposure and childhood leukaemia. Difficulties with exposure assessment are likely to have led to substantial non-differential exposure misclassification, but this is unlikely to provide an explanation for the observed association and may in fact lead to an underestimation of the magnitude of risk. Exposure misclassification may also introduce uncertainty into the potential dose-response relation. Because the estimates of the attributable fraction are calculated from the relative risks and exposure prevalence, and since both are affected by exposure misclassification, the attributable fraction may also be affected by exposure misclassification. However, the effect on the relative risk and on the exposure misclassification tends to work in opposite directions.

12.6 Conclusions

Acute biological effects have been established for exposure to ELF electric and magnetic fields in the frequency range up to 100 kHz that may have adverse consequences on health. Therefore, exposure limits are needed. International guidelines exist that have addressed this issue. Compliance with these guidelines provides adequate protection.

Consistent epidemiological evidence suggests that chronic low-intensity ELF magnetic field exposure is associated with an increased risk of childhood leukaemia. However, the evidence for a causal relationship is lim-

ited, therefore exposure limits based upon epidemiological evidence are not recommended, but some precautionary measures are warranted.

13 PROTECTIVE MEASURES

13.1 Introduction

With 25 years of research into possible health risks from ELF fields, much knowledge and understanding have been gained, but important scientific uncertainties still remain. Acute effects on the nervous systems have been identified and these form the basis of international guidelines. Regarding possible long-term effects, epidemiological studies suggest that everyday, low-intensity ELF magnetic field exposure poses a possible increased risk of childhood leukaemia, but the evidence is not strong enough to be considered causal and therefore ELF magnetic fields remain classified as possibly carcinogenic. The evidence is weaker for other studied effects, including other types of cancers in both children and adults, depression, suicide, reproductive dysfunction, developmental disorders, immunological modifications, neurological disease and cardiovascular disease.

Given the lack of conclusive data on possible long-term adverse health effcts decision-makers are faced with a range of possible measures to protect public health. The choices to be made depend not only on the assessment of the scientific data, but also on the local public health context and the level of concern and pressure from various stakeholders.

This chapter describes public health measures for the management of ELF risks. The scientific basis for current international EMF standards and guidelines is reviewed, followed by a summary of existing EMF policies. The use of precautionary-based approaches is discussed and recommendations are provided for protective measures considered to be appropriate given the degree of scientific uncertainty.

In the context of this chapter the collective term "policy-makers" refers to national and local governmental authorities, regulators and other stakeholders who are responsible for the development of policies, strategies, regulations, technical standards and operational procedures.

13.2 General issues in health policy

13.2.1 Dealing with environmental health risks

Most risk analysis approaches that deal with the impacts on health of a particular agent include three basic steps.

The first step is to identify the health risk and establish a risk profile or risk framing. This entails a brief description of the health context, the values expected to be placed at risk and the potential consequences. It also includes prioritizing the risk factor within the overall national public and occupational health context. This step would also comprise committing resources and commissioning a risk assessment.

The second step is to perform a risk assessment (hazard identification, exposure assessment, exposure-response assessment and risk characterization), involving a scientific evaluation of the effects of the risk factor as

carried out in this document (see Chapter 12). Some countries have the resources to undertake their own scientific evaluation of EMF health-related effects through a formal health risk assessment process (for example, the EMF RAPID programme in the United States, NIEHS, 1999) or through an independent advisory committee (for example, the Independent Advisory Group on Non-Ionizing Radiation in the United Kingdom, AGNIR, 2001b). Other countries may go through a less formal process to develop science-based guidelines or a variation on these.

Finally, risk management strategies need to be considered, taking into account that there is more than one way of managing all health risks. Specifically, appropriate management procedures need to be devised for complex, controversial and uncertain risks. The aim in these cases is to identify ways of coping with uncertainty and inadequate information by developing sound decision-making procedures, applying appropriate levels of precaution and seeking consensus in society. The term "risk management" encompasses all of those activities required to reach decisions on whether a risk requires elimination or reduction. Risk management strategies can be broadly classified as regulatory, economic, advisory or technological, but these categories are not mutually exclusive. Thus a broad collection of elements can be factored into the final policy-making or rule-making process, such as legislative mandates (statutory guidance), political considerations, socio-economic values, costs, technical feasibility, the population at risk, the duration and magnitude of the risk, risk comparisons and the possible impact on trade between countries. Key decision-making factors such as the size of the population, resources, the costs of meeting targets, the scientific quality of the risk assessment and subsequent managerial decisions vary enormously from one decision context to another. It is also recognized that risk management is a complex multidisciplinary procedure which is seldom codified or uniform, is frequently unstructured and can respond to evolving input from a wide variety of sources. Increasingly, risk perception and risk communication are recognized as important elements that must be considered for the broadest possible public acceptance of risk management decisions.

The process of identifying, assessing and managing risks can helpfully be described in terms of distinct steps, as described in a report of the US Presidential/Congressional Commission on Risk Assessment and Risk Management (1997) which emphasizes the analysis of possible options, clarification of all stakeholders' interests and openness in the way decisions are reached. In reality, however, these steps overlap and merge into one other, and should ideally be defined as an iterative process that includes two-way feedback and stakeholder involvement at all stages (Figure 10).

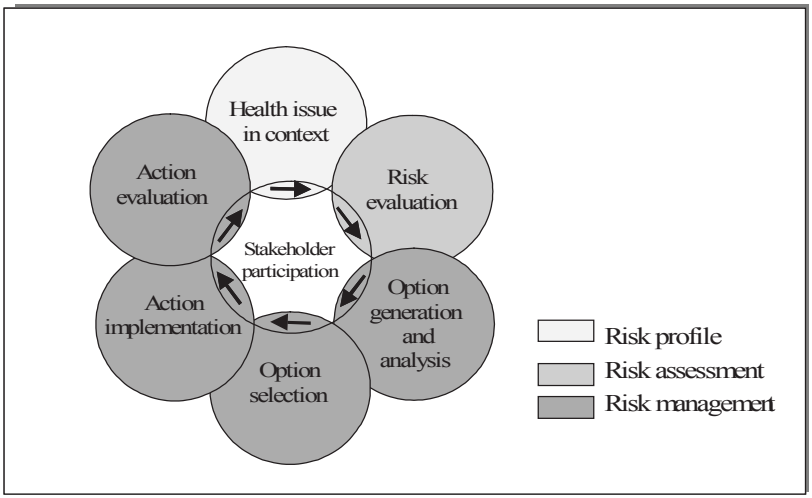

Figure 10. Dealing with risk: A risk analysis process that includes identifying, assessing and managing risks.

13.2.2 Factors affecting health policy

For policy-makers, scientific evidence carries substantial weight, but is not the exclusive criterion. Final decisions will also incorporate social values, such as the acceptability of risks, costs and benefits and cultural preferences. The question policy-makers strive to answer is "What is the best course of action to protect and promote health?"

Governmental health policies are based on a balance of "equity", i.e. the right of each citizen to an equitable level of protection and "efficiency", where cost-benefit or cost-effectiveness is important. The level of risk deemed acceptable by society depends on a number of factors. Where there is an identified risk, the value that society places on the reduction of risk or disease arising from a particular agent, technology or intervention is based on the assumption that the reduction will actually occur. For involuntary exposures a notional (*de minimis*) value of lifetime mortality risk of 1 in 100 000 is accepted as a general threshold (with 1 in a million as an ideal goal) below which the risk is considered to be acceptable or impractical to improve on (WHO, 2002). For example, the risk of ionizing radiation exposure from radon is reasonably well-characterized and the exposure should be reduced so that it does not cause radiation-induced cancer in more than one per 100 000 individuals over their lifetime.

In developing policy, regulators try to maximize the benefits and minimize societal costs. The following issues are considered to be part of this process.

- *Public health/safety* – A major objective of policy is to reduce or eliminate harm to the population. Harmful effects on health are

usually measured in terms of morbidity caused by the exposure and the probability that an effect would occur. They could also be measured in terms of extra cases of disease or death due to exposure, or of the number of cases avoided by reducing exposure.

- *Net cost of the policy* – The cost, referring to more than simply the monetary expense, of the policy for society as a whole, without considering any distribution of the cost, consists of several components: (a) the direct cost imposed on the entire society for any measures taken; (b) the indirect cost to society, for example, resulting from less than optimal use of the technology; and (c) cost reduction created by the policy, for example, faster implementation of a beneficial technology.
- *Public trust* – The degree of public trust in the policy and the degree of its acceptance as an effective means to adequately protect public health is an important objective in many countries. Moreover, the public's feeling of safety is important in itself, since the WHO definition of health addresses social well-being and not only the absence of disease or infirmity (WHO, 1946).
- *Stakeholder involvement* – A fair, open and transparent process is essential to good policy-making. Stakeholder involvement includes participation at each stage of policy development and opportunities to review and comment on a proposed policy prior to its implementation. Such a process may legitimately result in outcomes different from those that would be chosen by scientific experts or decision-makers alone.
- *Non-discriminatory treatment of sources* – All sources should receive the same attention when considering exposure (for example, for ELF fields, when reducing magnetic fields that result from grounding practices in the home, household appliances, power lines and transformers). The policy should focus on the most cost-effective option for reducing exposure. The policy-maker must determine whether (a) different consideration should be given to new or existing facilities and (b) there is justification for a different policy for non-voluntary and voluntary exposure. For further information, see the statement of the European Commission on the precautionary principle (EC, 2000).
- *Ethical, moral, cultural and religious constraints* – Notwithstanding stakeholder consultation, individuals and groups may differ in their views regarding whether a policy is ethical, moral and culturally acceptable or in agreement with religious beliefs. These issues can affect the implementation of a policy and need to be considered.
- *Reversibility* – The consequences of implementing a policy must be carefully considered. Policies need to be balanced and based on

current information and include sufficient flexibility to be modified as new information becomes available.

13.3 Scientific input

Science-based evaluations of any hazards caused by EMF exposure form the basis of international guidelines on exposure limits and provide an essential input to public policy response. Criteria and procedures for determining limit values are outlined in the WHO Framework for Developing Health-based EMF Standards (WHO, 2006a).

13.3.1 Emission and exposure standards

Standards contain technical specifications or other precise criteria that are used consistently as rules, guidelines or definitions of characteristics to ensure that materials, products, processes and services are fit for their purpose. In the context of EMF they can be emission standards, which specify limits of emissions from a device, measurement standards, which describe how compliance with exposure or emission standards may be ensured, or exposure standards, which specify the limits of human exposure from all devices that emit EMF into a living or working environment.

Emission standards set various specifications for EMF-emitting devices and are generally based on engineering considerations, for example to minimize electromagnetic interference with other equipment and/or to optimize the efficiency of the device. Emission standards are usually developed by the International Electrotechnical Commission (IEC), the Institute of Electrical and Electronic Engineers (IEEE), the International Telecommunications Union (ITU), the Comité Européen de Normalisation Electrotechnique / European Committee for Electrotechnical Standardization (CENELEC), as well as other independent organizations and national standardization authorities.

While emission standards are aimed at ensuring, inter alia, compliance with exposure limits, they are not explicitly based on health considerations. In general, emission standards are intended to ensure that exposure to the emission from a device will be sufficiently low that its use, even in proximity to other EMF-emitting devices, will not cause exposure limits to be exceeded.

Exposure standards that limit human EMF exposure are based on studies that provide information on the health effects of EMF, as well as the physical characteristics and the sources in use, the resulting levels of exposure and the people at risk. Exposure standards generally refer to maximum levels to which whole or partial body exposure is permitted from any number of sources. This type of standard normally incorporates safety factors and provides the basic guide for limiting personal exposure. Guidelines for such standards have been issued by the International Commission on Non-Ionizing Radiation Protection (ICNIRP, 1998a), the Institute of Electrical and Electronic Engineers (IEEE, 2002) and many national authorities. These have been discussed in Chapter 12. While some countries have adopted the

ICNIRP guidelines, others use them as the de facto standard without giving them a legal basis (WHO, 2006b).

13.3.2 Risk in perspective

There is scientific uncertainty as to whether chronic exposure to ELF magnetic fields causes an increased risk of childhood leukaemia. In addition, given the small estimated effect resulting from such a risk, the rarity of childhood leukaemia, the rarity of average exposures higher than 0.4 μT and the uncertainty in determining the relevant exposure metric (see section 12.5.3), it is unlikely that the implementation of an exposure limit based on the childhood leukaemia data and aimed at reducing average exposure to ELF magnetic fields to below 0.4 μT, would be of overall benefit to society.

The actual exposures of the general public to ELF magnetic fields are usually considerably lower than the international exposure guidelines. However, the public's concern often focuses on the possibility of long-term effects caused by low-level environmental exposure. The classification of ELF magnetic fields as a possible carcinogen has triggered a reappraisal by some countries of whether the exposure limits for ELF provide sufficient protection. These reappraisals have led a number of countries and local governments to develop precautionary measures as discussed below.

13.4 Precautionary-based policy approaches

Since protecting populations is part of the political process, it is expected that different countries may choose to provide different levels of protection against environmental hazards, responding to the factors affecting health policy (see section 13.2.2). Various approaches to protection have been suggested to deal with scientific uncertainty. In recent years, increased reference has been made to precautionary policies, and in particular the Precautionary Principle.

The Precautionary Principle is a risk management tool applied in situations of scientific uncertainty where there may be need to act before there is strong proof of harm. It is intended to justify drafting provisional responses to potentially serious health threats until adequate data are available to develop more scientifically based responses. The Precautionary Principle is mentioned in international law (EU, 1992; United Nations, 1992) and is the basis for European environmental legislation (EC, 2000). It has also been referred to in some national legislation, for example in Canada (Government of Canada, 2003), and Israel (Government of Israel, 2006). The Precautionary Principle and its relationship to science and the development of standards have been discussed in several publications (Foster, Vecchia & Repacholi, 2000; Kheifets, Hester & Banerjee, 2001).

13.4.1 Existing precautionary ELF policies

With regard to possible effects from chronic ELF exposure, policymakers have responded by using a wide variety of precautionary policies based on cultural, social, and legal considerations. These include the impor-

tance given to avoiding a disease that affects mostly children, the acceptability of involuntary, as opposed to voluntary, exposures and the different importance given to uncertainties in the decision-making process. Some measures are mandatory and required by law, whereas others are voluntary guidelines. Several examples are presented below.

- *Prudent avoidance* – This precautionary-based policy was developed for power-frequency EMF. It is defined as taking steps to lower human exposure to ELF fields by redirecting facilities and redesigning electrical systems and appliances at low to modest costs (Nair, Morgan & Florig, 1989). Prudent avoidance has been adopted as part of policy in several countries, including Australia, New Zealand and Sweden (see Table 85). Low-cost measures that can be taken include routing new power lines away from schools and phasing and configuring power line conductors to reduce magnetic fields near rights-of-way.
- *Passive regulatory action* – This recommendation, introduced in the USA for the ELF issue (NIEHS, 1999), advocates educating the public on ways to reduce personal exposure, rather than setting up actual measures to reduce exposure.
- *Precautionary emission control* – This policy, implemented in Switzerland, is used to reduce ELF exposure by keeping emission levels as low as "technically and operationally feasible". Measures to minimize emissions should also be "financially viable" (Swiss Federal Council, 1999). The emission levels from a device or class of devices are controlled, while the international exposure limits (ICNIRP, 1998a) are adopted as the maximum level of human exposure from all sources of EMF.
- *Precautionary exposure limits* – As a precautionary measure, some countries have reduced limits on exposure. For example, in 2003, Italy adopted ICNIRP standards but introduced two further limits for EMF exposure (Government of Italy, 2003): (a) "attention values" of one tenth of the ICNIRP reference levels for specific locations, such as children's playgrounds, residential dwellings and school premises, and (b) further restrictive "quality goals" which only apply to new sources and new homes. The chosen values for 50 Hz, 10 μT and 3 μT respectively, are arbitrary. There is no evidence of possible acute effects at that level nor evidence from epidemiological studies of leukaemia which suggests that an exposure of 3 μT is safer than an exposure of 10 or 100 μT.

Other examples of various types of precautionary policies applied to power-frequency field exposure are given in Table 86 (Kheifets et al., 2005). A complete database of EMF standards worldwide is provided on the website of the WHO International EMF Project (WHO, 2006b).

Table 85. Examples of precautionary approaches

Precautionary approach	Country	Measures
Prudent avoidance	New Zealand Australia Sweden	Adopt ICNIRP guidelines and add low-cost voluntary measures to reduce exposure
Passive regulatory action	USA	Educate the public on measures to reduce exposure
Precautionary emission control	Switzerland	Adopt ICNIRP guidelines and set emission limits
Precautionary exposure limits	Italy	Decrease exposure limits using arbitrary reduction factors

Table 86. Various approaches to EMF exposure limitation for the general public [a]

Agency / country	Limits	Comments
Precautionary policies based on exposure limits		
Israel, 2001	1 μT	Newly constructed facilities
Italy, 2003	100 μT	
	10 μT	Attention value applies to exposures that occur for more than 4 hours per day
	3 μT	Quality target that only applies to new lines and new homes
USA	15–25 μT	Under maximum load conditions. Established by regulations in some states (e.g. Florida) and by informal guidelines in others (e.g. Minnesota)
	0.2–0.4 μT	Adopted in some local ordinances (e.g. Irvine, California)

Table 86. Continued

Precautionary policies based on separation of people from sources of exposure		
Ireland, 1998	No new transmission lines or substations closer than 22 metres to an existing school or building	Local government will not grant construction permits for electrical power installations in the vicinity of schools and daycare centres
The Netherlands, 2005	Increased distance between power lines and places were children can spend significant amounts of time to ensure that their mean exposure will not exceed 0.4 μT	For new buildings near existing power lines, or new power lines near existing buildings
USA	Restrictions on sitting new schools close to existing electric transmission lines	Adopted by the California Department of Education
	New lines must be buried unless technically infeasible and there must be buffer zones near residential areas, schools, day care facilities and youth camps	Adopted by the State of Connecticut
Precautionary policies based on costs		
USA	No- or low-cost alterations to the design or routing if substantial field reduction (more than 15%) can be achieved; 4% used as benchmark of project cost	Adopted by the Public Utilities Commission for the State of California
Precautionary policies based on non-quantitative objectives		
Australia, 2003	Reduction of exposure where it is easily achievable	
Sweden, 1996	Reduction of exposure with no recommendations regarding levels	Includes taking into account EMF when designing new transmission and distribution facilities and siting them away from sensitive areas

[a] Source: Kheifets et al., 2005.

13.4.2 Cost and feasibility

The problem faced by the regulator is how to determine and evaluate the trade-off between various objectives and constraints. If zero tolerance to risk is desired, then it implies that cost is of no importance, which is problematic in a world with limited resources. On the other hand, accepting the use and introduction of technologies, provided that they have not been proven hazardous, disregards any potential health effects and may have a cost that society is not willing to pay.

From a utilitarian perspective, policy decisions cannot be made without a consideration of costs and these costs must be placed in context with the benefits. The costs and benefits of policy options should be considered at the broadest level and also presented in such a way that the costs and possible benefits to various stakeholders can be understood. All costs should be included, whether borne by industry, consumers or others. Even when allowing for the legitimate desire of society to err on the side of safety, it is likely that it will be difficult to justify more than very low-cost measures to reduce exposure to ELF fields.

Examples of approaches to considering the costs and benefits of precautionary actions on EMFs can be found in various countries. One example of an assessment of the costs of possible actions to reduce fields from power lines is in the Netherlands (Kelfkens et al., 2002). Here national geographical records were used to identify homes close to power lines, and hence to calculate the numbers of homes exposed to various levels of ELF magnetic fields. Four possible interventions were then considered: vector-sequence rearrangement, phase conductor splitting, line relocation and undergrounding, and each of these were costed for those lines where people live nearby. The effect of each of these measures on the change in distance of various field levels to the line was also calculated. Dividing the cost by the number of homes removed from exposure to the given field level provided an "average cost per dwelling gained". For 0.4 μT, this cost per dwelling for vector-sequence rearrangement, phase conductor splitting, line relocation and undergrounding was €18,000, €55,000, €128,000 and €655,000, respectively. An analysis of this kind is useful to policy-makers as it allows for the consideration and comparison of technical measures with other measures, for example, the relocation of power lines or dwellings.

Extensive "what if" policy analyses relating to EMFs from power lines and in schools were carried out in California in the late 1990s. The authors considered both a utilitarian and duty ethic approach to the question: "How certain do we need to be of the extent of the disease impact from EMFs before we would take low-cost or expensive EMF avoidance measures?" The results are summarized in a "Policy Options" document. Computer models were developed which allow users to investigate the impact of several variables, such as costs, probability of disease and extent of disease (von Winterfeldt et al., 2004). The cost–benefit analysis tended to suggest that avoidance measures at modest cost could be justified from a cost–benefit viewpoint below a "beyond a reasonable doubt" level of scientific certainty.

This approach has not been formally implemented in California, where the no- or low-cost policy has been recently reaffirmed.

Five Swedish governmental authorities published "Guidance for Decision-makers" in 1996, in which caution was recommended at reasonable expense. Examples of costing estimates were provided for several case studies. Based on their definition of the precautionary principle, measures should be considered when the fields deviate strongly from what can be deemed normal in the environment concerned (NBOSH, 1996).

When attempting to place a notional value on the benefit of preventing fatalities or cases of disease, extensive literature is available from areas other than EMFs. The two main approaches to obtaining a financial value are "human capital" and "willingness to pay". "Human capital" attempts to calculate the loss to society of a fatality, for example, by estimating the lost wages that would have been earned by that person during the rest of their life and in more sophisticated analyses including, for example, the cost to society of treating disease etc. "Willingness to pay" attempts to observe what individuals or society as a whole are willing to pay to prevent ill health or fatality, e.g. by looking at the extra salary paid to people in high-risk occupations or the amount that people are willing to pay to avoid living in an earthquake zone.

Both the "human capital" and "willingness to pay"-approaches are society-specific. For example, a WHO analysis of "The cost of diabetes in Latin America and Caribbean" (Alberto et al., 2003) used the human capital approach, calculating lost earings resulting from premature death and disability, and valued premature death in Latin America and the Caribbean at $37,000 per person. But a WHO analysis (Adams et al., 1999) of the economic value of premature death attributed to environmental tobacco smoke cites an EPA study from the USA which placed the "willingness"to pay" value of human life lost at $4.8 million per person and another study that places the value of human life lost at $5 million per person. The wage-risk trade-off method was used to determine this amount.

These examples provide an insight into how some researchers and national or local authorities have analysed several scenarios, assuming the potential health risk from ELF exposure to be important enough to implement precautionary measures. For countries without the resources to conduct such an exercise, recommendations are provided below that the Task Group considers appropriate, based on all the evidence considered.

13.5 Discussion and recommendations

Countries are encouraged to adopt international science-based guidelines. In the case of EMF, the international harmonization of standard-setting is a goal that countries should aim for (WHO, 2006a).

If precautionary measures are considered to complement the standards, they should be applied in such a way that they do not undermine the science-based guidelines.

Table 87. Factors relevant to the analysis of each policy option [a]

Option	Relevant factors in considering benefits	Relevant factors in considering costs
Do nothing	Childhood leukaemia is a relatively rare disease, and only a small proportion of the population is exposed to levels mentioned in epidemiological studies (i.e. estimated time-weighted average above 0.3 or 0.4 μT). There are many uncertainties regarding the effectiveness of policies, which could be reduced with scientific progres. When the only available options are costly it may be more appropriate not to take formal action. Allows for the adaptation of policy as evidence emerges.	No possibility of reducing burden of disease. No progress towards removal of uncertainties and better knowledge in future. Undermines trust in authorities. Concerned citizens may take matters into their own hands.
Research	Reduces uncertainty and facilitates better decision-making. Contributes to the scientific base. Helps in developing solutions.	Diversion of resources from higher priority areas. May delay actions awaiting research results.

Table 87. Continued

Option		Relevant factors in considering benefits	Relevant factors in considering costs
Communication		A knowledgeable public - can better evaluate the acceptability of different levels of ELF risks - can reduce public concern due to misperceived ELF risks - can increase trust in those providing the information. A knowledgeable public and workers - can be involved in the decision-making process regarding ELF sources - can make informed decisions on what appliances to purchase or how to place them so as to minimize exposure - can influence market forces to design sources in order to minimize exposure (e.g. electric blankets).	Possibility of giving rise to unjustified alarm or concern. May have limited effectiveness where the understanding of exposure is difficult or where exposure is involuntary and hard to avoid.
Mitigation	Changes to planning of new facilities	Reassessment of the need for new facilities. Avoid unnecessary exposure by comparing different planning scenarios so as to minimize exposure. Use of best available technology. Lower cost since options are dealt with in planning stage of new installations.	Requires alternative technical designs be presented for the construction of new facilities. Costs may include sterilization of land, devaluation of property, and compensation payments. Possibility of setting a precedent for future projects regardless of future circumstances.

Table 87. Continued

Option		Relevant factors in considering benefits	Relevant factors in considering costs
Mitigation	Engineering changes of existing facilities	Reduction of exposure by taking protective measures such as installing shielding, changing wiring practices in houses and in distribution or transmission systems (split phasing, raising ground clearances, undergrounding etc.).	A significant part of the cost may be in identifying the instances rather than remediation. Changes introduced to existing installations involve a higher cost. Costs may include sterilization of land, devaluation of property and compensation payments.
	Engineering changes to appliances	Reduction of exposure to magnetic fields.	Increased cost (or increased size or weight) of appliances.
National standards	Exposure limits	May increase public confidence in the authority's action to protect health.	May undermine science-based guidelines. May give false sense of security. May hinder incentives for further reduction of undue exposure. Cost of compliance. Difficult to move towards less stringent standards if justified by new scientific evidence.

[a] With the exception of the first option, all the options are evaluated in relation to "doing nothing" rather than adopting international guidelines.

As a result of considering the various options, policy makers will select and implement appropriate, country-specific measures for the protection of the general public and workers from exposure to ELF fields. Factors relevant to the evaluation of each policy option are given in Table 87. Precautionary measures are generally implemented through voluntary codes, encouragement and collaborative programmes rather than through mandatory enforcement, and should be seen as interim policy tools.

Risk perception and communication

The lack of policy harmonization worldwide is one of many factors that may exacerbate public anxiety. People's perceptions of a risk depend on personal factors, external factors and the nature of the risk (Slovic, 1987). Personal factors include age, sex, and cultural or educational backgrounds, while external factors comprise the media and other forms of information dissemination, the current political and economic situation, opinion movements and the structure of the regulatory process and political decision-making in the community.

The nature of the risk can also lead to different perceptions depending on the degree of control the public has over a situation, fairness and equity aspects in locating EMF sources and fear of specific diseases (for example, cancer versus headache). The greater the number of factors that contribute to the public's perception of risk, the greater the potential for public concern. Public concern can be reduced through information and communication between the public, scientists, governments and industry. Effective risk communication is not only a presentation of the scientific calculation of risk, but also a forum for discussion on broader issues of ethical and moral concern (WHO, 2002).

Consultation

The acceptability of the risks of ELF fields, relative to other environmental health risks, is ultimately at least as much about political and societal values and judgements as it is about scientific information. To establish public trust and confidence, stakeholders need to be involved in decision-making at the appropriate time. ELF stakeholders include government agencies, scientific and medical communities, advocacy groups, consumer protection organizations, environmental protection organizations, other affected professionals such as planners and property professionals, and industry including the electricity industry and appliance manufacturers. While there will not always be consensus on such issues, the position taken should be transparent, evidence-based and able to withstand critical scrutiny.

Need for periodic evaluation

As new scientific information becomes available, exposure guidelines and standards should be updated. Certain studies may be more likely than others to prompt a re-evaluation of the scientific basis of the guidelines and standards because of the strength of the evidence or because of the sever-

ity of the health outcome under study. Changes to standards or policy should only be made after a proper assessment of the science base as a whole, to ensure that the conclusions of the research in a given area are consistent.

Exposure reduction

In recommending precautionary approaches, an overriding principle is that any actions taken should not compromise the essential health, social and economic benefits of electric power. In the light of the current scientific evidence and given the important remaining uncertainties, it is recommended that an assessment be conducted of the impact of any precautionary approach on the health, social and economic benefits of electric power. Provided that these benefits are not compromised, implementing precautionary procedures to reduce exposures is reasonable and warranted. The costs of implementing exposure reductions will vary from one country to another, making it very difficult to provide a general recommendation for balancing the costs against the risk from ELF fields. Given the weakness of the evidence for a link between exposure to ELF magnetic fields and childhood leukaemia and the limited potential impact on public health, the benefits of exposure reduction on health are unclear and thus the cost of reducing exposure should be very low.

13.5.1 Recommendations

In view of the above, the following recommendations are given.

- Policy-makers should establish guidelines for ELF field exposure for both the general public and workers. The best source of guidance for both exposure levels and the principles of scientific review are the international guidelines.
- Policy-makers should establish an ELF EMF protection programme that includes measurements of fields from all sources to ensure that the exposure limits are not exceeded either for the general public or workers.
- Provided that the health, social and economic benefits of electric power are not compromised, implementing very low-cost precautionary procedures to reduce exposures is reasonable and warranted.
- Policy-makers and community planners should implement very low-cost measures when constructing new facilities and designing new equipment including appliances.
- Changes to engineering practice to reduce ELF exposure from equipment or devices should be considered, provided that they yield other additional benefits, such as greater safety, or involve little or no cost.

- When changes to existing ELF sources are contemplated, ELF field reduction should be considered alongside safety, reliability and economic aspects.
- Local authorities should enforce wiring regulations to reduce unintentional ground currents when building new or rewiring existing facilities, while maintaining safety. Proactive measures to identify violations or existing problems in wiring would be expensive and unlikely to be justified.
- National authorities should implement an effective and open communication strategy to enable informed decision-making by all stakeholders; this should include information on how individuals can reduce their own exposure.
- Local authorities should improve planning of ELF EMF-emitting facilities, including better consultation between industry, local government, and citizens when siting major ELF EMF-emitting sources.
- Government and industry should promote research programmes to reduce the uncertainty of the scientific evidence on the health effects of ELF field exposure.

APPENDIX: QUANTITATIVE RISK ASSESSMENT FOR CHILDHOOD LEUKAEMIA

Although a causal relationship between magnetic fields and childhood leukaemia has not been established, estimates of the possible public health impact which assume causality are presented below in order to provide a potentially useful input into policy analysis under different scenarios (Kheifets, Afifi & Shimkhada, 2006).

The public health impact of exposure to an agent can be based on calculations of attributable fractions. The attributable fraction, based on an established exposure-disease relation, is the proportion of the case load (of disease) that is attributable to the exposure assuming there is a causal relationship. The attributable fraction is based on the difference between the number of cases in a population that occur when the population is subject to a given exposure distribution, and the number that would occur in the same population if that distribution were changed (e.g. if exposure was reduced or eliminated by an intervention). In this calculation, it is assumed that all other population characteristics remain the same. Hence, the attributable fraction can be used to estimate the degree of incidence reduction that would be expected if exposure were reduced. Since the epidemiological literature has consistently found elevated risk of childhood leukaemia at ELF magnetic field exposure levels above 0.3 μT for the arithmetic mean and above 0.4 μT for the geometric mean, attributable-fraction estimates for these (relatively) high-level exposures allow the estimated impact on disease incidence of eliminating or reducing exposure above these levels, assuming the relation between exposure and leukaemia incidence is causal.

There are two basic pieces of information needed to make a crude estimate of the attributable fraction: (1) an estimate of the exposure effect on the disease and (2) the prevalence of exposure in the population.

A.1 Exposure distribution

In evaluating the risks from exposure to any biologically active agent, physical, biological, or chemical, it is important to understand the distribution and magnitudes of the exposures in the general population. In order to effectively quantify the risks of childhood leukaemia, if any, from exposure to ELF magnetic fields, we must first get some estimate of the degree of exposure in children. As noted in Chapter 2, these exposures will different from country to country due to a number of factors, most notably the frequency and voltage used for power distribution.

There are two types of studies from which the exposure distribution is extracted: (1) exposure surveys to provide estimates of the exposure prevalence in children (P_0), and (2) case series from case-control studies to provide estimates of P_0 and P_1 where P_1 is the exposure prevalence in children with childhood leukaemia. Use of each of these sources provides some advantage. Case-control studies provide most relevant measurements of exposure, but may be biased, if for example, restrictions on the population (e.g. to live within a certain distance of power lines) make the case exposure

prevalence in the study different from the population prevalence P_1; this renders unusable the case and control prevalences from studies with exposure-related restrictions. Even if the cases are representative, the controls will not be if matching has been done and the matching factors are associated with exposure; in that case the P_0 estimate from the study will be biased upward, toward P_1; fortunately, the most common matching factors were child's age and sex, which appear to be almost independent of exposure in the studies (Greenland, 2001; 2005). Exposure surveys, on the other hand, included both children and adults, as well as personal measurements throughout the day, that are thus only tangentially related to the exposure in the child's bedroom. At the very least the use of both of these sources provides a range of relevant exposures and subsequently a range of attributable fractions and numbers for consideration.

In contrast, in the case-control studies, the exposure distributions of the cases were used. For those case-control studies included in each pooled analysis, the exposure distribution reported in the pooled analysis was used. For studies not included in either pooled analysis, the exposure distribution was extracted directly from the study. (See Tables A.1 and A.2 for details of all the exposure distributions used.) It is assumed that there are no significant difference in the exposure distributions based on exposure surveys and on case-control studies. Furthermore, it is assumed that exposures obtained using personal measures are equivalent to those from household measurements, regardless of length of time of measurement.

Globally, there is disproportionately more information on exposure from industrialized countries; and among these countries, the majority of the studies have been in the USA and, to a lesser extent, in Europe. There are a number of regions of the world, such as Africa and Latin America, where no representative information on exposure is available. Furthermore, there can be substantial differences in the exposure distributions within a region; for example, exposures in Korea are probably very different from those in China and India. This poses a difficulty for a global estimation of attributable fractions and numbers since these are highly dependent on the exposure distribution, hence emphasizing the need for more data on exposure levels worldwide.

A.2 Exposure-response analysis using attributable fraction estimates for EMF and childhood leukaemia

If no adjustment for covariates is needed, the values of the estimates of (1) the exposure effect on the disease and (2) the prevalence of exposure in the population are simply entered into the unadjusted (crude) attributable fraction formula (Levin, 1953):

$$AF_p = P_0(RR - 1)/[P_0 (RR - 1) + 1]$$

where AF_p is the estimated attributable fraction and RR is the risk ratio estimate. If confounding is present, both RR and P_0 should be adjusted (Rothman & Greenland, 1998), but in practice only an adjusted estimate for

RR is usually available. To make this calculation for the ELF-childhood leukaemia relation, as leukaemia is a rare disease, the odds ratio is assumed to estimate the risk ratio. It is also assumed that the risk ratio estimates the effect in the target population, that there is no bias, and no change in the effect estimate moving from the study to the target population (Greenland, 2004). Performing analyses that incorporate uncertainty from biases and other sources of uncertainty beyond random error are highly informative and require sophisticated techniques.

The attributable number is defined as the excess number of cases attributable to exposure. For example, the attributable number associated with high exposures is interpreted as the number of cases that would be averted if these exposures were eliminated. The attributable number is obtained by multiplying the attributable fraction by the total number of cases:

$$AN = AF_p \times m_1$$

where AN is the attributable number and m_1 is the number of cases.

For case-control studies with adjusted odds ratios, a less biased formula than that given by Levin is:

$$AF_p = P_1(RR_a - 1) / RR_a$$

where RR_a is the adjusted rate ratio estimate (study odds ratio) and P_1 is the exposure prevalence among the cases in the target population (Rothman & Greenland, 1998). This formula has the advantage of requiring no adjustment of P_1 to be valid, and is unaffected by matching controls to cases. Furthermore, assuming that exposure is independent of the adjustment factors (which appears to be approximately true in studies that did not match at all or matched on age and sex only) allows one to estimate P_0 from P_1 and RR_a via the (rare-disease) formula:

$$P_0 / (1 - P_0) = P_1 / (1 - P_1)RR_a.$$

It is also possible to make the calculations using continuous exposure data as does Greenland et al. (2001) for 11 studies. It is not possible to do that here because such data were not available from all the sources used in this analysis, and the results in Greenland et al. (2001) indicate that results from continuous exposure would differ little from the categorical results.

Dose response functions from two pooled analyses were used for estimating the RRs. One of the differences between the two pooled analyses is in the exposure metric used: Ahlbom et al. (2000) looked at the association between the geometric mean magnetic field level and childhood leukaemia in nine epidemiologic studies, Greenland et al. (2000), however, used the arithmetic mean to examine this association in twelve studies; Greenland (2005) extended this analysis to include 14 studies using a dichotomy at

0.3 μT. The other difference in these two analyses relates to the categories used for classifying exposures. In Ahlbom et al. (2000), four categories were used relating to < 0.1 μT, 0.1–< 0.2 μT, 0.2–< 0.4 μT, and ≥ 0.4 μT. In contrast, Greenland et al. (2000) used ≤ 0.1 μT, > 0.1–≤ 0.2 μT, > 0.2 –≤ 0.3 μT, and > 0.3 μT. To address the sensitivity of attributable fraction estimates to the choice of data sets and exposure categorization, two sets of attributable fraction estimates are presented relating to these two methods for developing RRs.

In the pooled analysis by Ahlbom et al. (2000), risk for childhood leukaemia with mean residential magnetic field exposure is: OR = 1.08, (95% CI = 0.891.31) for 0.1–0.2 μT, OR = 1.11 (0.89–1.47) for 0.2–0.4 μT, OR = 2.00 (1.27–3.13) for above 0.4 μT relative to exposure below 0.1 μT. In the pooled analysis by Greenland et al. (2000) OR = 1.01 (0.84–1.21) for 0.1–0.2 μT, OR = 1.06 (0.78–1.44) for 0.2–0.3 μT, and OR = 1.68 (1.24–2.31) for exposures greater than 0.3 μT, all compared to less than 0.1 μT (both the point estimate and confidence limits remain virtually unchanged by adding 2 studies). Incorporating, in addition to the random error, all sources of bias increases the last estimate to an OR = 2.7 (0.99–32.5) (Greenland, 2005) (Note: this estimate will be used later to incorporate additional uncertainty into the attributable fraction calculations.) .

A.3 Risk characterization

Attributable fraction (AF) estimates were made for all countries with an exposure distribution (see Figures A.1 and A.2). For the US and Germany, where there were multiple distributions, the largest of the case-control studies and the largest of the exposure surveys were used for the AF calculation used in Figure A.1. The AF estimates are divided into different exposure categories to enable a comparison of high exposures to overall exposure.

The attributable numbers (AN) of leukaemia cases were calculated for regions around the world and then added to obtain a global estimate. To compute these regional estimates, the lowest and highest exposure levels estimated in Tables A.1 and A.2 from the countries in that region were used to come up with a regional range. Where there was no information from any country in the region, the lowest and highest exposure prevalences from Tables A.1 and A.2 were used. The range of exposure prevalences for the arithmetic mean being > 0.3 μT used was 0.47% and 10.49% (Table A.1); that for the geometric mean being 0.4 μT was 0.37% and 4.78% (Table A.2). Yang's study (Yang, Ju & Myung, 2004), which is based on a larger sample and considered as more representative for non-Western regions, was used to calculate an upper range for regions with unknown levels (Latin America, Africa, Oceania). These low and high estimates were each added together to come up with a range for the entire world (Figures A.3 and A.4).

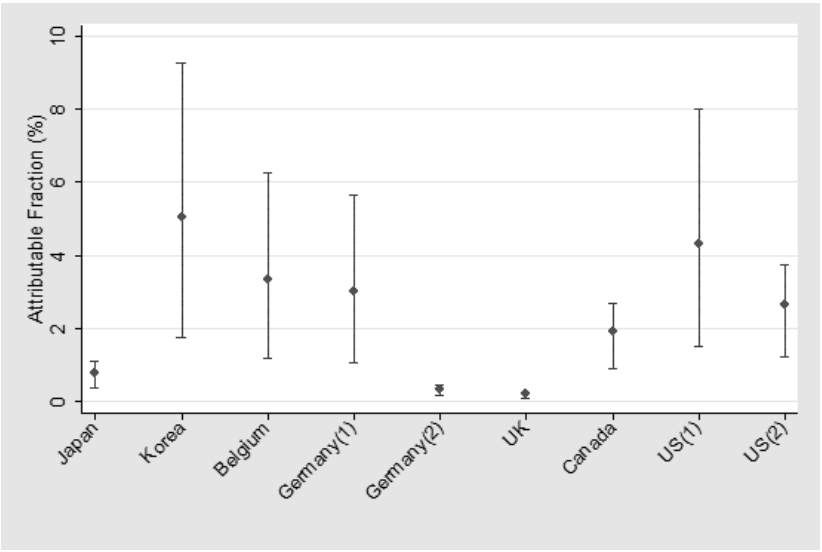

Figure A.1. Upper, lower and point estimates for attributable fractions, based on arithmetic mean exposure using exposure distributions for specific countries and estimate of effect from the pooled analysis by Greenland et al., 2000. (Japan: Kabuto et al., 2006; Korea: Yang, Ju & Myung, 2004; Belgium: Decat, Van den Heuvel & Mulpas, 2005; Germany(1): Brix et al., 2001; Germany(2): Schüz et al., 2001; UK: UKCCSI, 1999; Canada: McBride et al., 1999; US(1): Zaffanella & Kalton, 1998; US(2): Linet et al., 1997.)

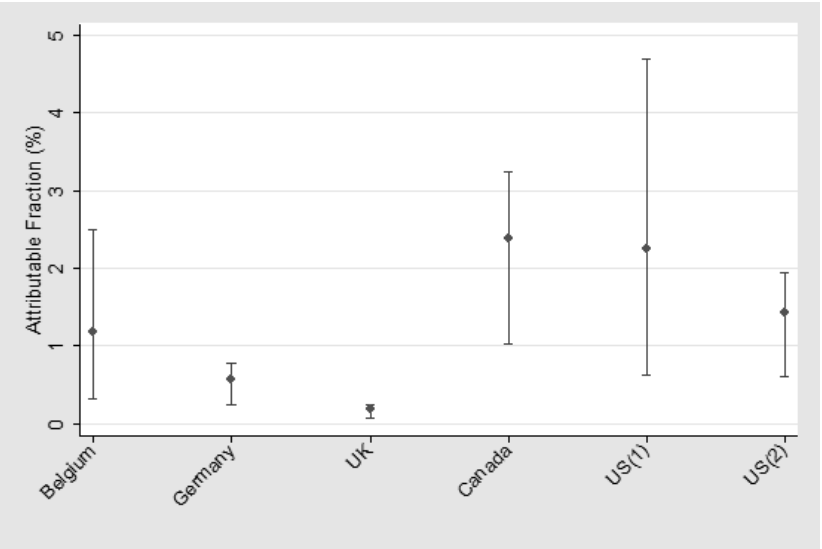

Figure A.2. Upper, lower and point estimates for attributable fractions, based on geometric mean exposure using exposure distributions for specific countries and estimate of effect from the pooled analysis by Ahlbom et al., 2000. (Belgium: Decat, Van den Heuvel & Mulpas, 2005; Germany: Michaelis et al., 1998; UK: UKCCSI, 1999; Canada: McBride et al., 1999; US(1): Zaffanella & Kalton, 1998; US(2): Linet et al., 1997.)