

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. Swanson & Kheifets, 2006

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 than 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- μ V 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- μ V 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 retina (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 $0.5 \mu\text{V m}^{-1}$ 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 periphery 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	5×10 ⁴	3 mT
	Optimised cell	10	5000	300 μT
1/f noise			1×10 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 Planck'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 $20 \text{ }\mu\text{m}$, 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 $1 \text{ }\mu\text{T}$. 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 $F=vqB$, 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 $10 \text{ }\mu\text{T}$ (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 μ T, varying from about 30 μ T near the equator to about 60 μ T 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 μ T 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 μ T 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 kilohm [k Ω]).

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 k Ω 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 μ A could enter a child's hand. Dosimetric modelling by Dawson, Potter & Stuchly (2001) estimated that a 50 μ A 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 Fewes (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 Fewes 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 $10\text{--}100 \text{ mV m}^{-1}$ 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 $50 \text{ } \mu\text{T}$ 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 $5 \text{ } \mu\text{T}$.

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.