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Review

Mechanisms for Interaction Between RF Fields and Biological Tissue

L.J. Challis*[†]

University of Nottingham, Nottingham, United Kingdom

Interaction of radiofrequency (RF) fields with biological tissue can involve either electric or magnetic fields. Many interaction mechanisms have been considered, both thermal and nonthermal, but it has not been established that any of these could result in adverse health effects at radiation levels below guidelines. The principles underlying most of these mechanisms have been well reviewed. The aim of the present study is to give a qualitative discussion of some of the more recently published work. Bioelectromagnetics Supplement 7:S98–S106, 2005. © 2005 Wiley-Liss, Inc.

Key words: radiofrequency radiation; interaction mechanisms; biophysical models

INTRODUCTION

Radiofrequency (RF) electromagnetic waves may interact with biological tissue through a number of mechanisms. It has not been established though that any of those proposed so far could result in adverse health effects at radiation levels below guidelines. Indeed Adair [2003a], in a recent review, noted that the interactions were all weak compared with the endogenous interactions and concluded that it was most unlikely that RF fields of intensity less than 100 W/m^2 incident on humans could affect physiology significantly. However, there also seems consensus that the possibility remains open that there could be health effects from exposure to RF fields below guidelines [e.g., AGNIR, 2003] and that more research is needed. This suggests a continuing need to consider new proposals for interaction mechanisms. The aim of the present study is to give a qualitative discussion of some of the more recently published work.

Interaction can take place through either thermal or nonthermal mechanisms. Thermal mechanisms are those resulting from the temperature change of the tissue caused by the RF fields. They might, for example, produce changes in the rates of biochemical reactions since these are all likely to be temperature dependent to some degree. All interactions between RF fields and biological tissue are likely to result in energy transfer to the tissue and this will ultimately lead to an increase in its temperature. But nonthermal mechanisms are those that are not directly associated with this temperature change but rather to some other change produced in the tissue by the RF electric or magnetic field.

The ICNIRP guidelines (basic restrictions) for the head or trunk for frequencies between 100 kHz and 10 GHz require the average specific energy absorption rate (SAR) in any contiguous 10 g region to be less than 10 W/kg (occupational) or 2 W/kg (public). However, to discuss mechanisms, it is usually more convenient to translate these SARs into rms RF electric fields E inside, say, the tissue of the head that gives rise to these values. For tissue of density 1×10^3 kg/m^3 and resistivity 1 $\Omega \cdot$m, an SAR of 10 W/kg corresponds to $E =$ 100 V/m and the magnetic field B accompanying such an E field would be around 0.3 μT; this assumes the relation between E and B that applies in the far field and so may be incorrect by a small factor in the near field of a mobile phone. Changes in the battery current of a mobile phone also generate ELF pulsed magnetic fields whose value 1 cm from a GSM phone can be up to about 50 μT [Jokela et al., 2004]. The frequency spectrum of the ELF fields covers the range from a few Hz up to

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[†] L.J. Challis is a Chair of Management Committee of the UK Mobile Telecommunications and Health Research Programme.

*Correspondence to: L.J. Challis, MTHR, Skipton House, 80 London Rd., London SE1 6LH, UK.
E-mail: lawriechallis@aol. com

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40 kHz. However, the currents they induce inside the head are estimated to be appreciably less than the ICNIRP guidelines.

THERMAL MECHANISMS

Thermal mechanisms are mainly associated with the absorption of the RF energy resulting from the electrical conductivity of most biological tissue. The RF electric field generates an oscillating current and the rapid transfer of the energy of this current into the molecular motion responsible for most of the heat capacity results in an increase in the local temperature. The electrical conductivity is in fact only partly due to the translational motion of charged particles—ions. The other main contribution arises from the hindered rotation of molecules, principally water. The water molecule has a large permanent dipole moment, which is randomly oriented in the absence of an applied electric field E. An electric field partially orients the dipole moments along the direction of the field. Because of the viscosity of the water, the field has to do work to rotate the dipoles resulting in energy transfer into the liquid-heat. This dissipation mechanism is most effective over a fairly broad range of frequencies, ν, close to those given by $\omega\tau = 1$, where $\omega = 2\pi\nu$ and τ is the average time the dipoles take to re-orient. Since $\tau = 4 \times 10^{-11}$ s for water, $\omega\tau \sim 0.25$ at 1 GHz, so this mechanism is very effective at the frequencies of mobile telecommunications and is comparable in fact to that provided by oscillating ions. The power dissipated is proportional to E^2 in both cases and defined as σE^2 per unit volume, where σ is referred to as the conductivity, even though associating conduction with the dipole mechanism seems less appropriate than it does for moving charges.

In setting the occupational guidelines for the head at 10 W/kg averaged over 10 g, it is of course recognised that the power absorbed will be greater in some parts of the 10 g than in others. In general though this is thought to be of little significance since the thermal diffusivity of tissue is high enough to smooth out any resulting temperature differences. The question arises though as to whether enough high resolution modelling has been carried out to give one total confidence that this is the case in all body parts exposed significantly to mobile phone radiation. Could, for example, threads of relatively high conductivity material produce sufficiently large electric field distortions at their ends for high absorption to occur in regions of relatively low thermal diffusivity? Since temperature rises are still the only established mechanisms for health effects there would still seem to be a case for high resolution modelling within one or two structures within the head such as the inner ear.

NONTHERMAL MECHANISMS

There are some general aspects that need to be borne in mind when considering nonthermal interaction mechanisms.

Magnitude of the Energy of RF Photons

The energy of a photon of an electromagnetic wave is hν, where h is Planck's constant. At a frequency of 1 GHz, the photon energy is 4 μeV, and therefore smaller than the energy, 1eV, required to ionise a typical molecule by a factor of approximately 2×10^5. So if exposure to RF fields were to damage DNA, it could not be a result of ionization or excitation due to the absorption of single photons nor through the simultaneous absorption of 2×10^5 photons since the probability of that is immeasurably small. So if damage to DNA was to occur as the result of the exposure, it would have to be through some other process.

Excitation of Molecular Vibrations by RF Fields

A number of interaction mechanisms that have been considered are based on the excitation of molecular vibrations such as sound waves, by RF fields. For this excitation to occur, both energy and momentum have to be conserved. Energy conservation requires that the photon energy of the RF field matches the phonon energy of the vibration and, since both are equal to hν, this merely requires that the frequencies of the two are equal. Momentum conservation can be much more demanding; this is equivalent to the requirement that the RF wavelength needs to be matched to the ultrasonic wavelength. This is possible for optic modes, but these would all have frequencies appreciably greater than 1 GHz, even in very soft components like microtubules [Sirenko et al., 1996]. It is not, however, possible for acoustic modes. They have frequencies in this range but their velocities, s, of 1000 m/s or below are less than the velocity of light, c, by nearly a million. So the momentum of a photon, $\hbar k_{RF} = \hbar\nu/c$, is appreciably smaller than the momentum of an acoustic phonon, $\hbar k_s = \hbar\nu/s$; and since this should also be the case for torsional oscillations, the excitation of molecular vibrations by RF radiation is "forbidden." All this is very well known from experiment. Sound waves (1 GHz) can, of course, be generated in solids. However, they cannot be excited directly from RF waves, but are normally produced by using a thin piezoelectric film at one end of the sample or, for surface waves, using interdigital metal fingers with separation and so electric field wavelength matched to that of the sound.

The momentum conservation constraint is, however, relaxed as a result of the uncertainty principle if the molecular vibrations are very strongly attenuated (attenuation length $l < 1/k_s$ where at 1 GHz, $1/k_s$ $\sim$0.1 μm), since their momentum is then poorly defined. At room temperature, in materials like Al_2O_3 or quartz, l (1 GHz) is greater than $1/k_s$ by a thousand or more [Bömmel and Dransfeld, 1960; de Klerk, 1965], and it would seem very unlikely that $l < 1/k_s$ even in very soft biological materials. This may no longer be the case, though, if the solid is immersed in a viscous liquid. This greatly increases the attenuation to the point where molecular vibrations can be excited. However, since their energy is rapidly being transferred to the surrounding liquid, their amplitude is usually very small.

Momentum conservation can also be achieved if a photon excites 2 phonons, each of frequency $\sim\nu/2$ which travel in opposite directions to give a net momentum of $\hbar\nu/c$ although this would normally be a relatively weak process. In complex biological structures such as proteins, it might also be possible for the RF fields to excite localised centres with internal degrees of freedom, which would then relax by emitting phonons.

Voltage Across Cell Membranes at RF Frequencies

The electric field within biological tissue is very nonuniform at frequencies below about 1 MHz. If an electric field is applied across a tissue sample, most of the voltage drop occurs across the cell membranes, since they have much higher electrical resistance than most of the rest of the tissue. Calculations, in fact, suggest that the electric field within a membrane is larger than the average field by several thousand [Kotnik and Miklavčič, 2000]. So at low frequencies, even quite small *average* electric fields result in voltage drops across the membrane, which are large enough to give rise to nonlinear effects including rectification. This is, however, no longer the case at higher frequencies. Membranes also have capacity and this provides a parallel conducting path for the AC current. The conductance of this path is very small at low frequencies but it increases linearly with frequency ($G = j\omega C$) and starts to short out the membrane resistance at around 1 MHz or below. Indeed by 1 GHz, the electric field within the membrane is essentially equal to or possibly less than the average field; the voltage drop has fallen by several thousand or more. So the nonlinear effects that occur across membranes at low frequencies for quite modest average electric fields become smaller as the frequency increases and become undetectable well above 1 MHz.

Limitations to the Effects of RF Radiation Imposed by Thermal Energies (k_BT)

The components of biological systems, like those of any other system, are constantly subjected to the random fluctuating electric and magnetic fields associated with the random motion of charges known as Brownian motion or thermal noise. These random fields impose a limit on the sensitivity of the system to respond to applied RF fields. This requirement allows us to determine the minimum size of applied field needed to produce a biological effect: the system cannot be affected by an applied field if it is less than the corresponding random field.

The condition is conveniently discussed in terms of the energy transferred to a component by the local field. This can then be compared with the energy associated with thermal noise. The thermal energy of each mode of a component has an average value of around k_BT, where k_B, Boltmann's constant, is 86 μeV per degree and T is the absolute temperature. So at body temperature, the thermal energy is around 26 meV per mode.

The approach can be simply illustrated by considering whether the oscillatory motion of an ion or other charged component in an RF field could possibly lead to biological effects. The average energy of a singly charged object of mass m and mobility μ in an rms electric field E oscillating at frequency ν is m $\mu^2E^2/2$. For a chloride ion, this is around 10^{-17} eV for $E = 100$ V/m. This is smaller than the thermal energy of 26 meV by a factor of more than 10^{15} so one can safely conclude that the oscillatory motion of ions in fields below guidelines cannot possibly cause biological effects. However, since the oscillatory energy is proportional to the mass of the charged component, energies comparable to the thermal energy might be acquired by, say, the oscillations of a large charged cell of diameter 50 μm containing 10^{15} atoms or more.

The condition should apply to all systems that are well coupled thermally to their surroundings but not necessarily to systems such as those described later in the section on free radicals, where the coupling is weak.

ELECTRIC FIELD EFFECTS

Changes in Protein Conformation

The significance of this mechanism lies in the fact that the efficiency of the protein as an enzyme depends on its conformation. Proteins consist of a sequence or chain of amino acids connected by peptide bonds. The chain can be a long straight thread but, more often, parts of the chain form loops or helices, and the whole is irregularly coiled and folded into a globule. The way in which the chain is arranged in space is called the conformation. The side chains of the amino acids are often polar. They attract or repel nearby side chains, so the conformations all have somewhat different potential energies and dipole moments.

The possibility that RF radiation may cause changes in protein conformation and hence biological properties has recently been considered by three groups [Laurence et al., 2000, 2003; Bohr and Bohr, 2000a,b; Astumian, 2003]. In a series of earlier studies, Bohr and Bohr developed a model suggesting that the conformation adopted by a protein depends on the amplitudes of the dynamic excitations within it. A large number of modes are possible, both vibrational and torsional, and their model assumes that the known changes in protein conformation with temperature are due to changes in the amplitudes of the modes. In their recent study, they suggested that the modes might also be excited by RF radiation. They calculated that the mode frequencies could go down to around 1 GHz so that, since their widths are likely to be large, they would cover the transition frequencies of interest here. The transitions would result in changes in protein folding (denaturation) and so give rise to biological effects.

The theory is, however, at an early stage and does not include an explicit calculation of the strength of interaction with the external field. Direct generation of dynamic modes would be expected to be very weak for the reasons explained earlier. Dissipative effects, such as viscous damping, have also not been considered in any detail. Hence it is not possible to estimate the size of RF field required to produce a significant effect in the presence of thermal agitation. The authors have carried out an experiment at 2.45 GHz in a modified 800 W microwave oven, which lends some support to their approach. They observed a modest but apparently significant conformational change of a protein in solution following a 5 s exposure. However, from the data provided, it would appear that the SAR was around 250 W/kg and the experiment would need to be repeated using much lower exposures and better dosimetry before one could be confident that effects would be detectable at the much lower SARs of interest.

The approach used by Laurence et al. [2000] was rather different. Their analysis suggested that conformational changes occurred on a timescale sufficiently long (around 1 μs) for the protein to remain in thermal equilibrium with its surroundings. This suggested changes could only be induced by transient increases in the local temperature. The authors argued that, at low powers, these changes could lead to biological effects but that, at somewhat higher powers, these would be suppressed by the activation of a heat shock protein. Their conclusions were, however, significantly modified in a second study [Laurence et al., 2003], which noted that the value used for the heat capacity of biological tissue in the first study was too small by a large factor and that, in fact, the local temperature rises were much too small to produce conformational changes for SARs below guidelines.

The work of Astumian [2003] concerns conformational changes in ion motive ATPases, which are proteins that span cell membranes. They act as ion pumps and are normally fuelled by ATP. Astumian proposed they might also be responsive to RF fields following experiments by Xie et al. [1997] showing ion movement across membranes during exposure to RF fields. He suggested that the coupling to the dipole moments of components in the ATPase was large enough to produce conformational changes that led to ion movement. The experiments by Xie et al. were carried out at frequencies of 1 MHz and below, and while Astumian did not suggest the mechanism would be effective at 1 GHz, it clearly needs to be considered. It seems very unlikely in fact. The effects were seen for applied electric fields of around 2000 V/m, and at frequencies of 1 MHz and below, these would generate fields in the membrane of more than 1×10^6 V/m. It seems unlikely therefore that similar effects would be seen for the 1 GHz fields in the membrane of 100 V/m or less resulting from mobile phones.

Changes in Binding Ligands Such as Ca^{2+} to Cell Receptor Proteins

A mechanism that has been explored by Chiabrera et al. [2000] and others concerns the possible effect of RF fields on cell receptors. The process they investigated was the binding of light ligands such as Ca^{2+} to a protein; the binding alters the protein conformation and so controls its receptor function. Since the ligand is bound, it must be sitting in an electrostatic potential well, and Chiabrera et al. found that significant changes in the probability of ligand binding could be produced by the modulation of the well shape by RF electric fields below guideline values. This rather surprising result comes from their conclusion that the effects of the RF electric field were greatly amplified by the effects of metabolic energy. Somewhat paraphrasing their words they found that ‘‘the system takes advantage of the power supply provided by the basic metabolism of the cell much like a transistor using its power supply to amplify small signals.’’

Changes in the binding probability of Ca^{2+} have also been considered by Thompson et al. [2000] but using a very different approach. They examined the effect that the conformation of one protein might have on the conformation of its neighbours. If it were large, it would significantly change the probability that Ca^{2+} would bind to its neighbours and so could lead to the formation of an ordered array of occupied sites rather than a random distribution. They then envisaged a situation where the effect was not quite large enough for this but could be made so by an RF electric field. The RF field would then trigger a phase transition from a random to an ordered array, which could involve a large number of Ca^{2+} sites. Their analysis is statistical mechanical (Ising model), and since it does not describe the interaction mechanism in quantitative terms, it is not possible to estimate the size of RF fields that would be needed. The authors did suggest however that the mechanism could be consistent with the existence of the ‘‘power windows’’ reported in some of the early experimental work on calcium efflux from brain tissue.

Absorption by Vibrational States of Biological Components

In recent years, there has been further discussion of the role that might be played by resonant absorption of RF energy by the vibrational states of biological components such as microtubules. Fröhlich [1968] pointed out that interaction between neighbouring biological components could, in principle, broaden these vibrational states into bands, just as interaction between atoms in a solid leads to bands of electronic states. From this he developed a sophisticated model of which one suggested outcome was that relatively weak RF signals could be amplified and produce significant biological effects. The existence of bands is an essential requirement for this model, and such bands can only exist if the vibrational states have widths narrower in energy than the weak interaction between neighbouring states that leads to band formation and certainly narrower than the energy, $h\nu$, of the states.

This condition has recently been examined by two groups [Foster and Baish, 2000; Adair, 2002]. They noted that the main contribution to the width of a vibrational state in a biological component is likely to arise from the viscosity of the fluid in which it is immersed. To estimate the effect of this, Foster and Baish calculated the relaxation time of longitudinal oscillations of a cylinder immersed in water. For a cylinder with a diameter equal to that of a microtubule, the relaxation rate and hence the line width was around 1000 times larger than the frequency even at 10 MHz and would be even greater at higher frequencies. Similar conclusions were reached by Adair [2002]. Both these calculations were for rigid cylinders and so do not represent well the modes of microtubules which include interface modes with amplitudes that in the absence of damping would decay exponentially into the fluid [Sirenko et al., 1996]. However, since the fluid motion is damped in a distance less than this decay length, it seems very likely that these interface modes would also be heavily damped. It would appear then from this work that the widths of the vibrational states are far too large for the formation of the bands required by the Fröhlich model.

Adair [2002] also calculated the energy that could be transferred to a vibrational state of a biological component from an electromagnetic field. The interaction is weak and, as noted earlier, is forbidden by momentum conservation in the absence of damping. Damping progressively removes this constraint but, since it also results in power being lost to the surroundings, it limits the energy transferred into the vibrational states. For DNA molecules assumed to have vibrational frequencies around 10 GHz, Adair estimated that incident microwave power of 100 W/m^2 increased the energy of the state by 3×10^{-9} k_BT. He concluded that this was far too small to produce significant biological effects and that this would remain the case, even if the state were less strongly damped by its surroundings than expected from conventional arguments.

Enhanced Attraction Between Cells (Pearl-Chain Effect)

The aggregation or lining-up of dielectric particles in a fluid, resulting from attractive forces between them, is well known and often referred to as the pearl-chain effect. The effect can be produced by RF electric fields, and measurements of the threshold values needed at frequencies up to about 100 MHz have been made on colloidal particles and biological cells [Schwan, 1985]. In the absence of RF fields, cells are attracted to each other by dispersive forces. At any instant, the motion of the electrons is such that each cell has nonzero electric moments (dipole, quadrupole . . .). These produce an instantaneous electric field, which acts on the instantaneous moments of other cells and, when time-averaged, causes them to be attracted. The dipole–dipole attraction resulting from these processes is the Van der Waals force and varies as r^{-7}. RF electric fields produce oscillating dipole moments within cells, which enhance the attraction.

The additional attractive potential energies have been calculated by Adair and discussed in his review of the effects of RF fields [Adair, 1994]. He considered two conducting spheres of radius 10 μm separated by their closest distance of approach and showed that, at frequencies less than about 100 MHz, an RF electric field of around 125 V/m was needed to produce an additional potential energy of k_BT, in reasonable agreement with the threshold experimental values reported by Schwan [1985]. At higher frequencies, the induced dipoles had insufficient time to change direction, so that very much bigger fields would be needed at 1 GHz to produce the same attractive energy. Adair stressed, though, that these calculations were for spherical cells and that the attractive energies could be bigger (or smaller) for other geometries, etc. So one could not totally exclude the possibility that, for some cells, attractive energies of k_BT could be produced by 1 GHz fields of 100 V/m or so.

Recent calculations of the attractive energies between cells have also been made by Krasil'nikov [1999] and Sernelius [2004]. Krasil'nikov considered the interaction between the RF electric fields and the ions attached to cell membranes. He cited data suggesting that the mobility of ions attached to membrane surfaces was higher than that of unbound ions by a factor of 20 for hydrogen ions, and 100–1000 for sodium ions. This meant that the attached ions were relatively free to move around the surface and could be treated as a two-dimensional system. Charge systems can undergo density oscillations resembling longitudinal waves whose excitations are called plasmons, and Krasil'nikov calculated that their frequency for a two-dimensional system of hydrogen ions of appropriate surface density on a membrane of radius 1 μm, was around 1 GHz. He also estimated that, although the plasmons would be fairly strongly damped, this was not enough to suppress them. The attraction of his model with regard to interaction of RF fields lies in the fact that a cell membrane has two surfaces, inner and outer. So strong coupling can be achieved with an essentially uniform electric field by creating two plasmons simultaneously, which travel in opposite directions, one on the inner surface and one on the outer.

Using this model, Krasil'nikov obtained an expression for the RF induced dipole moment. He did not extend this to determine the field needed to produce an attractive energy between cells of k_BT. However, his calculated value of the dipole moment is nearly three times larger than Adair [1994], suggesting the field would be three times smaller. Presumably larger fields would again be needed at frequencies around 1 GHz because of the time needed for the dipoles to reverse. It should also be noted that the factor of 3 is for a vesicle of radius 1 μm and, since it would appear to vary as 1/radius, the moment would in fact be smaller than Adair's value for vesicles/cells of radius greater than 3 μm.

The approach considered by Sernelius [2004] is very different. He notes that a cell at body temperature is constantly absorbing electromagnetic radiation, "black body radiation" and that the balancing emission necessary to maintain thermal equilibrium is associated with the same electronic motion responsible for the Van der Waals force between two cells. He then argues, reasonably, that the Van der Waals force should increase if the emission is increased as it would be if the temperature were raised. The basis of his next step though, which is to calculate the dipole moment induced by the incident power density from a mobile phone, seems very difficult to understand or justify. His approach is to relate the Van der Waals force to the black body radiation emitted, and it is far from clear how this can be related to incident microwave energy. A critical appraisal of his approach has been given by Adair [2004] who finds that it overestimates the interaction energy produced by an RF field by a factor of 10^{11}.

Low Frequency Electric Fields From Demodulation

In view of public concern that pulsed RF signals from mobile phones might interact differently with biological components from continuous wave RF signals, it is surprising that there has been almost no discussion of how this might arise. It is well known that pulsed RF fields can result in acoustic effects, microwave hearing. This is believed to be a thermal effect and is only detectable at much high peak powers than those of mobile phone signals. So there would need to be another mechanism if, for example, biological effects of pulsing were to occur at the power levels of GSM or TETRA handsets. One possible route would be through demodulation.

The RF fields from the mobile phones used for telecommunications are pulsed at 217 Hz (GSM) and 17.6 Hz (TETRA) so demodulation of these signals would lead to the presence of electric fields at 217 or 17.6 Hz and their harmonics, as well as fields at frequencies relating to the digital stream (tens of kHz). Now, the ICNIRP public exposure guideline for low frequency electric fields (4–1000 Hz) of 2 mV/m (for tissue of resistivity 1 Ωm) is appreciably less than the corresponding guideline at 1 GHz of around 100 V/m. So even quite weak demodulation of mobile phone signals at these fields might produce low frequency electric fields above the guidelines.

Demodulation would occur if the electrical conductivity or dielectric constant of a biological component varied significantly with electric field E, so that its electrical response was nonlinear. For example, if its conductivity $\sigma = \sigma_0 + \sigma_1 E$, there would be components of current at the modulation frequencies, which would become significant at fields at which $\sigma_1 E \sim \sigma_0$. Symmetry arguments show that these second order terms should be zero in crystals with inversion symmetry, but there are many other crystals or structures involving interfaces in which second order terms can be quite significant at high electric fields and these find useful application particularly at optical frequencies.

However, the only known example of a biological component that is detectably nonlinear for average extracellular tissue fields less than 100 V/m is a cell membrane. The neutral lipid bilayer separates regions of opposite polarity, so that the charge distribution is similar to that of a semiconductor junction. The nonlinearity was demonstrated by the observation that membranes rectified RF signals of average field ~1 V/m frequencies below a few kHz. However, the size of the rectified signal fell rapidly at higher frequencies and at 100 kHz, was a hundred times less than the low frequency value [Montaigne and Pickard, 1984]. At lower frequencies, the field across the membrane is larger than the average field by several thousand, but as discussed earlier, this enlargement disappears at higher frequencies.

So it seems very unlikely that membranes could produce significant demodulation of the 1 GHz or so RF signals used in mobile telecommunications. It seems very probable that this is also the case for other biological components but it is desirable that this should be investigated experimentally. A sensitive technique to investigate the nonlinearity of biological components in vitro by looking for frequency doubling effects has recently been proposed by Balzano [2002, 2003a] and Balzano and Shepherd [2003]. The component is exposed to radiation of frequency at ν, and measurements are made of any signals at frequency 2ν. The proposal has led to correspondence by Adair [2003b], Balzano [2003b,c], Marino [2003], and Marinot and Frilot [2003]; and an experiment using this technique has recently been funded by the UK MTHR programme.

MAGNETIC FIELD EFFECTS

In general, the interaction of magnetic fields with tissue would be expected to be very much weaker than that of electric fields. Recent work suggests though this might not always be the case.

Magnetite (Fe_3O_4)

Tissue, including human brain tissue, may contain small particles about 50 nm across of a ferrimagnetic material, magnetite (Fe_3O_4), and particularly high concentrations occur in the meninges in the outermost part of the brain that are likely to be exposed to emissions from mobile phones. Analysis by Adair [1994] of the interaction of a magnetite particle with an RF magnetic field showed that the field required to transfer energy of k_BT is very much greater than guideline values. Kirschvink [1996] calculated that the fields would be smaller if the RF fields induced ferromagnetic resonance, although they would still seem to be appreciably greater than guideline values. It has also been proposed that the 2 Hz magnetic field pulses from a GSM mobile phone when it is switched on but not transmitting (DTX mode) produce a torgue on magnetite particles coupled mechanically to cell membranes that could activate ion channels [Dobson and Pierre, 1996].

Preliminary experimental work [Dobson et al., 2003; Cranfield et al., 2003a,b] provides some support for this latter mechanism. They looked at the effect of an 8 min exposure from a GSM 900 MHz handset in DTX mode placed above a sample of a bacterium *M. Magnetotacticum* containing magnetite [Cranfield et al., 2003a; no dosimetry information is provided] and found that the exposure significantly increased the proportion of cell deaths. This did not occur however in later experiments [Cranfield et al., 2003b] in which the sample was exposed to GSM 1800 MHz radiation in a waveguide (SARs up to 2 W/kg). Since the exposure from the RF emission from the handset would presumably have been less than 2 W/kg, the public guideline value, but did include low frequency magnetic fields, the authors suggested these might have been the cause of the increase in cell deaths seen in their first experiments. The duty cycle in DTX mode is about 1.4% so during the 8 min exposure, 2 Hz pulses of magnetic field would have been emitted for a total of 25 s.

So in summary, this work does not suggest RF magnetic fields below public guideline values produce biological effects. However it does provide some tentative evidence for biological effects from the low frequency magnetic fields generated by mobile phones and notes the existence of a mechanism, which might account for such effects.

Radical Pairs

Free radicals are molecules with an unpaired electron. They are normally highly reactive and hence short lived, and their role in disease including cancer is well established. They are usually generated in pairs, often as intermediates in chemical reactions, and free radicals are produced if the radical pair dissociates before the two radicals can recombine. Recent experiments at frequencies less than 80 MHz show that the concentration of free radicals can be increased by low intensity RF fields [Woodward et al., 2001]. So the questions of interest are how, given the limit normally set by thermal noise, can a measurable increase in concentration of free radicals be significant at such low fields and could there also be an increase at frequencies around 1 GHz? To answer these questions, we need to know the mechanism and fortunately that seems well established. The pairs formed as intermediates can be produced either with their spins antiparallel (S) or parallel (T), but oscillate between S and T at a rate determined by the hyperfine coupling. They are less likely to recombine and hence more likely to dissociate into free radicals if they are in the T state. Now RF radiation at the hyperfine splitting frequency can increase the amount of time the pairs are in the T state and hence the probability of dissociation and so the concentration of free radicals. The reason why it can occur at such low fields is that the spins are very weakly coupled to the thermal bath: Adair [1999].

It seems unlikely though that RF radiation at frequencies of 1 GHz or so could lead to a significant increase in the concentration of free radicals. The hyperfine splittings in most biomolecules are less than 100 MHz, and while molecules containing transition metal ions such as iron can have hyperfine splittings of 1 GHz or more, in most cases, the randomisation of the orientations of the electron spins (spin relaxation) is expected to be too fast for RF fields to have a significant effect on the dissociation of the radical pairs. However, in view of the clear link between disease and free radical concentration, it would seem desirable to establish this more firmly.

SUMMARY

A wide variety of RF interaction mechanisms have been considered over the years and recent reviews include those by Foster [2000], Pickard and Moros [2001], and Adair [2003a]. Thermal mechanisms are well established and reasonably well understood and it is generally accepted that the temperature rises that result from exposures at or below guideline levels are normally far too small to cause adverse health effects. It is less clear though that this is the case for locally heated regions that are thermally insulated from the bulk tissue, and there is a case for further experimental and modelling work in this area. All thermal effects depend on the size of the electrical parameters of the exposed tissue, in particular, its electrical conductivity. So, should these turn out to be age dependent, this could be relevant to the issue of whether children are at greater risk from exposure to RF fields than adults. However, one might expect the age-dependence of the electrical parameters to be modest. If so, and since the guidelines for the public offer a considerable measure of protection against thermal effects, it seems unlikely that any small increase in SAR in children would lead to significant additional risk to health. This, of course, assumes that any local heating effects will not turn out to be significant.

The position is less clear for nonthermal processes and it is certainly not possible to say whether any of them might be more effective in children than adults. Some mechanisms seem most unlikely to lead to biological effects, let alone adverse health effects at frequencies around 1 GHz and exposures below guidelines. For a few others, their complexity and the consequent difficulty of providing quantitative estimates of the SARs needed to produce significant effects mean that it is not possible to say whether they might give rise to biological effects. However, we recall Adair's general conclusion cited in the Introduction that this is unlikely for exposures below guidelines. One mechanism involving the opening of ion channels by the torque on nearby magnetite particles has tentative experimental support and might be worth further exploring further with better dosimetry.

The need for high resolution modelling of particular structures in the head where local temperature rises might possibly be significant has already been mentioned, and further work on two nonthermal mechanisms would also seem desirable. Since there is a proven link between free radicals and disease, there is a need to establish more clearly whether the spin relaxation of any biomolecules with large hyperfine splittings might be slow enough for RF fields to increase the free radical concentration. Also, since the guidelines for ELF electric fields are as small as 2 mV/m, we need to determine whether any biological components might demodulate mobile phone signals, even though this seems improbable. A project to investigate this has recently been funded by the UK MTHR programme.

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REFERENCES

Adair RK. 1994. Effects of weak high-frequency electromagnetic fields on biological systems. In: Klauenberg BJ, Grandolfo M, Erwin DN, editors. Radiofrequency standards. New York: Plenum Press. pp 207–222.

Adair RK. 1999. Effects of very weak magnetic fields on radical pair reformation. Bioelectromagnetics 20:255–263.

Adair RK. 2002. Vibrational resonances in biological systems at microwave frequencies. Biophysical J 82:1147–1152.

Adair RK. 2003a. Biophysical limits on athermal effects of RF and microwave radiation. Bioelectromagnetics 24:39–48.

Adair RK. 2003b. Comment on the comment of Marino and Frilot on ‘‘Proposed test for detection of nonlinear responses in biological preparations exposed to RF energy.’’ Bioelectromagnetics 24:440–441.

Adair RK. 2004. Comment on ‘‘Possible induced enhancement of dispersion forces by cellular phones.’’ Phys Chem Chem Phys 6:3915.

AGNIR. 2003. Health effects from radiofrequency electromagnetic fields. Report of an advisory group on non-ionising radiation. Doc NRPB 14(2):1–177.

Astumian RD. 2003. Adiabatic pumping mechanism for ion motive ATPases. Phys Rev Letts 91: 118102 1–4.

Balzano Q. 2002. Proposed test for detection of nonlinear responses in biological preparations exposed to RF energy. Bioelectromagnetics 23:278–287.

Balzano Q. 2003a. Reply to the comment of Marino and Frilot on ‘‘Proposed test for detection of nonlinear responses in biological preparations exposed to RF energy.’’ Bioelectromagnetics 24:73.

Balzano Q. 2003b. Reply to Dr Adair’s comment on the comment of Marino and Frilot on ‘‘Proposed test for detection of nonlinear responses in biological preparations exposed to RF energy.’’ Bioelectromagnetics 24:443.

Balzano Q. 2003c. RF non-linear interactions in living cells-II: Detection methods for spectral signatures. Bioelectromagnetics 24:483–488.

Balzano Q, Shepherd A. 2003. RF non-linear interactions in living cells—I: Nonequilibrium thermodynamic theory. Bioelectromagnetics 24:473–482.

Bohr H, Bohr J. 2000a. Microwave enhanced kinetics observed in ORD studies of a protein. Bioelectromagnetics 21:68–72.

Bohr H, Bohr J. 2000b. Microwave-enhanced folding and denaturation of globular proteins. Phys Rev E61:4310–4314.

Bömmel HE, Dransfeld K. 1960. Excitation and attenuation of hypersonic waves in quartz. Phys Rev 117:1245–1252.

Chiabrera A, Bianco B, Moggia E, Kaufman JJ. 2000. Zeeman-Stark modelling of the RF EMF interaction with ligand binding. Bioelectromagnetics 21:312–324.

Cranfield CG, Wieser HG, Al Maddam J, Dobson J. 2003a. Preliminary evaluation of nanoscale biogenic magnetite-based ferromagnetic transduction mechanisms for mobile phone bio-effects. IEEE Trans NanoBioscience 2:40–43.

Cranfield CG, Wieser HG, Dobson J. 2003b. Exposure of magnetic bacteria to simulated mobile phone-type RF radiation has no impact on mortality. IEEE Trans NanoBioscience 2:146–149.

de Klerk J. 1965. Behaviour of coherent microwave phonons at low temperatures in Al_2O_3 using vapor-deposited thin-film piezoelectric transducers. Phys Rev 139:A1635–A1639.

Dobson J, Pierre TG. 1996. Application of the ferromagnetic transduction model to D.C. and pulsed magnetic fields: Effects on epileptogenic tissue and implications for cellular phone safety. Biochem Biophys Res Commun 227:718–723.

Dobson J, Cranfield CG, Al Maddam J, Wieser HG. 2003. Cell mortality in magnetite-producing bacteria exposed to GSM radiation. In: Meyer G, editor. Electromagnetic compatibility (supplement). Zurich: Communication Technology Laboratory Publishers. pp 293–296.

Foster KR. 2000. Thermal and nonthermal mechanisms of interaction of radio-frquency energy with biological systems. IEEE Trans Plasma Science 28:15–23.

Foster KR, Baish JW. 2000. Viscous damping of vibrations in microtubules. J Biolog Phys 26:255–260.

Fröhlich H. 1968. Long range coherence and energy storage in biological systems. Int J Quantum Chem 2:641–649.

Jokela K, Puranen L, Sihvonen A-P. 2004. Assessment of the magnetic field exposure due to the battery current of digital mobile phones. Health Physics 86:56–66.

Kirschvink JL. 1996. Microwave absorption by magnetite: A possible mechanism. Bioelectromagnetics 17:187–194.

Kotnik T, Miklavčič D. 2000. Second-order model of membrane electric field induced by alternating external electric fields. IEEE Trans Biomed Engineering 47:1074–1081.

Krasil’nikov PM. 1999. Resonance interaction of surface-charged lipid vesicles with the microwave electromagnetic field. Biofizika 44:1078–1082 (English Translation in Biophysics 1999; 44: 1041–1045).

Laurence JA, French PW, Lindner RA, McKenzie DR. 2000. Biological effects of electromagnetic fields-mechanisms for the effects of pulsed microwave radiation on protein conformation. J Theor Bio 206:291–298.

Laurence JA, McKenzie DR, Foster KR. 2003. Application of the heat equation to the calculation of temperature rises from pulsed microwave exposure. J Theor Biol 222:403–405.

Marino AA. 2003. Reply to Dr Adair’s comment. Bioelectromagnetics 24:442.

Marinot AA, Frilot C. 2003. Comment on ‘‘Proposed test for detection of nonlinear responses in biological preparations exposed to RF energy.‘‘ Bioelectromagnetics 24:70–72.

Montaigne K, Pickard WF. 1984. Offset of the vacuolar potential of characean cells in response to electromagnetic radiation over the range 250 Hz to 250 kHz. Bioelectromagnetics 5:31–38.

Pickard WF, Moros EG. 2001. Energy deposition processes in biological tissue: Nonthermal biohazards seem unlikely in the ultra-high frequency range. Bioelectromagnetics 22:97–105.

Schwan HP. 1985. EM-field induced effects. In: Chiabrera A, Nicolini C, Schwan HP, editors. Interactions between electromagnetic fields and cells. New York: Plenum Press. pp 371–390.

Sernelius BoE. 2004. Possible induced enhancement of dispersion forces by cellular phones. Phys Chem Chem Phys 6:1363–1368.

Sirenko YM, Stroscio MA, Kim KW. 1996. Elastic vibrations of microtubules in a fluid. Phys Rev E53:1003–1010.

Thompson CJ, Yang YS, Anderson V, Wood AW. 2000. A cooperative model for Ca^{++} efflux windowing from cell membranes exposed to electromagnetic radiation. Bioelectromagnetics 21:455–464.

Woodward JR, Timmel CR, McLaughlan KA, Hore PJ. 2001. Radio frequency magnetic field effects on electron-hole recombination. Phys Rev Letts 87: 077602 1–4.

Xie TD, Chen YD, Marszalek P, Tsong TY. 1997. Fluctuation-driven directional flow in biochemical cycle: Further study of electric activation of Na, K pumps. Biophysics J 72:2496–2502.