Biophysical Limits on Athermal Effects of RF and Microwave Radiation

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Using biophysical criteria, I show that continuous radiofrequency (RF) and microwave radiation with intensity less than 10 mW/cm² are unlikely to affect physiology significantly through athermal mechanisms. Biological systems are fundamentally noisy on the molecular scale as a consequence of thermal agitation and are noisy macroscopically as a consequence of physiological functions and animal behavior. If electromagnetic fields are to significantly affect physiology, their direct physical effect must be greater than that from the ubiquitous endogenous noise. Using that criterion, I show that none of a set of interactions of weak fields, which I argue is nearly complete on dimensional grounds, can affect biology on the molecular scale. Moreover, I conclude that such weak fields are quite unlikely to generate significant effects in their interactions with larger biological elements such as cells. In the course of that analysis, I examine important special examples of electromagnetic interactions: "direct" interactions where biology is modified simply by the motion of charged elements generated by the electric field; resonance interactions; the effects of electrostrictive forces and induced dipole moments; and modifications of radical pair recombination probabilities. In each case, I show that it is unlikely that low intensity fields can generate significant physiological consequences. Bioelectromagnetics 24:39–48, 2003. © 2002 Wiley-Liss, Inc.

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INTRODUCTION

Two extensive review studies [Michaelson and Elson, 1996; Postow and Swicord, 1996] record more than 200 papers reporting athermal biological effects of radiofrequency (RF) electromagnetic fields, that is, effects at intensity levels below that which raise the temperature of the medium significantly. However, these results do not form a coherent pattern and no single result has been accepted as valid by a consensus of scientists working in the field. Michaelson and Elson [1996] comment on concerns over "...the nonreproducibility of results and the nonrobustness of effects ...[which] seem especially vexatious." Postow and Swicord [1996] note, on a subset of the experiments, "There is no consistent repeatable pattern...of responses." They criticize the models introduced to "explain" the results as "...either incomplete or inconsistent."

Indeed, the view that *all* of the many results purporting to show athermal effects of low intensity RF electromagnetic fields are in error and that there are no such effects, is held by many. In this study, I attempt to put on a well defined biophysical basis, the reasons why some believe that athermal effects of low intensity RF and microwave radiation are highly improbable.

(Foster has reviewed athermal effects with emphasis on high intensity pulsed fields [Foster, 2000].)

INTERACTION CHARACTERISTICS

Thermal Noise

In some absolute sense, any exogenous influence on biological matter must affect physiology. However, organisms live in fundamentally noisy environments and the effects of that noise must mask very small extra influences. Thus, I classify as significant, only those exogenous influences that generate a response that is not masked by endogenous noise.

For small elements on the molecular level that noise is, for the most part, generated by thermal agitation.

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Those elements are always moving under that agitation such that the mean energy per degree of freedom is $k_bT/2$ where k_b is Boltzmann's constant and T is the absolute temperature. That energy fluctuates rapidly; for typical molecules, the fluctuation rate is of the order of 10^{11} per second and the probability at any time of the element holding an energy in one degree of freedom that is greater than w is about $P = \exp(-2w/k_bT)$. Hence, if an external signal, S, adding energy w to the element is to modify the behavior of the element in a manner not masked by noise, $N \approx k_bT$, a necessary, though not sufficient condition, is that $S/N > w/k_bT$.

If there are M independent elements acting coherently in the generation of a signal, the effective signal can be as large as S=Mw, while the total (incoherent) noise can be as small as $N=M^{1/2}k_bT$. In that case, the signal to noise, $S/N=Mw/(M^{1/2}k_bT)=wM^{1/2}/k_bT$ and the overall signal, S, will be greater than the overall noise, N, if $w>k_bT/M^{1/2}$.

Physiology is sensitive to temperature and thus to this average energy. Indeed, a deviation of more than 3% from normal is lethal. In humans, the natural secular temperature variation is about 1 °C or a change $dT/T \approx 1/300$. In many circumstances, this is equal to a change of $w \approx k_b T/300$, independent of M.

At intensities greater than about 10 mW/cm², incident RF and microwave radiations act to raise the temperature of tissues significantly and thereby generate a level of evenly distributed absorbed energy. These temperature increases affect biology in ways, which tend to mask effects of energy deposited nonuniformly at particular sites. In the following, I discuss such athermal depositions, emphasizing possible effects of radiated fields with intensities less than 10 mW/cm² (or rms electric fields less than 200 V/m), which do not change the temperature of tissues significantly.

For elements as large as cells, other sources of noise may be more important than that from simple thermal agitation. Extraneous effects can be important only if they are not masked by effects that derive from normal secular temperature changes and from the natural forces accompanying animal physiology and behavior. And, of course, that the signal be greater than noise is a necessary, but far from sufficient condition for that signal to affect physiology significantly.

Equilibrium Time Constants

The different elements of a biological system have different charge distributions and are thus coupled to the electromagnetic field differently. Hence, they absorb radiated energy with different efficiencies leading to nonthermal energy distributions. However, because of the close coupling of elements of a biological system, all elements are typically brought back into thermal

equilibrium after excitation in characteristic relaxation times, τ_{rlx} , which are short compared to most biological time scales. While a detailed calculation is required for many purposes, for biological systems excited by electric fields, these time constants for specific elements will not usually be very different than that for the dissipation of the kinetic energy of a moving sphere of radius a in a fluid of viscosity η ;

$$\tau_{\eta} = \frac{\rho a^2}{9\eta} \approx 1.6 \cdot 10^5 \cdot a^2 \text{ s} \tag{1}$$

where the numerical value is that for a sphere with the density of water, $\rho = 1000 \text{ kg/m}^3$, moving through water with a viscosity, $\eta = 7 \cdot 10^{-4} \text{ N s/m}^2$.

It is interesting to compare this with the time constant for the conduction of heat from an aqueous sphere of radius *a* immersed in water [Adair, 1995],

$$\tau_{\kappa} \approx \left(\frac{1}{4\pi}\right) \frac{C\rho}{\kappa} a^2 \approx 5.6 \cdot 10^5 a^2 \text{ s}$$
 (2)

where $C\rho = 4.18 \cdot 10^6 \text{ J/m}^3$ is the heat capacity per unit volume and $\kappa = 0.6 \text{ W} \cdot \text{m}^{-1} \text{deg}^{-1} \text{ s}^{-1}$ is the thermal conductivity of water.

The similarity between the two time constants, based on different physical assumptions, suggests that relaxation times of this magnitude may be quite general. While the relaxation times so defined are derived implicitly for macroscopic systems, the results are found to be a good approximation for systems as small as individual molecules and should be useful for sectors of macromolecules.

While it is difficult to write completely general rules for the use of results that are predicated on thermal equilibrium, such use is justified for times $t \gg \tau_{\kappa}$ after singular energy disturbances and for situations such that $dT/dt \ll T/\tau_{\kappa}$ when the Kelvin temperature T is changing with time.

While most elementary systems excited through effects of electric fields have small relaxation times as described by Equations 1 and 2, systems that are excited to a higher energy through a change in magnetic moment generated by a special orientation of an electron spin or nuclear spin will usually have much longer relaxation times, even as the magnetic forces between elements in the solid state of matter are much weaker than the electric forces. States with higher, nonequilibrium energies as a consequence of a special electron spin orientations have relaxation times of the order of microseconds, while states excited by a change in nuclear spin orientation will have relaxation times measured in seconds. However, as a consequence of

the weak coupling of these magnetic fields with other matter, changes in magnetic moments through changes in nuclear or atomic spin states do not usually affect physiology.

Coupling of RF and Microwave Radiation With the Body

Often, the biological effects of external fields are of interest, although those effects must depend only on the internal fields, which will usually be smaller.

Since the body is a conductor with an average conductance of about 1 S/m^2 , there is no internal field in the presence of a DC external field. That external field generates surface charges that act to cancel the internal field. If the external field changes sign the surface charges must also reverse sign. That reversal represents an interchange of surface charge and, thus, a current through the body. That current is then a measure of an internal field, E_i , proportional to the external field, E_0 , inversely proportional to the conductivity, σ , of the body and proportional to the rate of change of the field and, thus, the frequency, $v = \omega/2\pi$.

At moderate frequencies [Foster and Schwan, 1996],

$$E_i = k \frac{E_0 \varepsilon_0 \omega}{\sigma}$$
 for $v = \frac{\omega}{2\pi}$ 100 MHz (3)

where ε_0 is the permittivity of free space. For spherical humans, k = 3/2 but k = 15 better fits more realistic models [Lin and Gandhi, 1996], and peak fields can exceed average fields by factors as great as five.

Penetration of Radiation Into Tissue

At very high frequencies, $E_i \approx E_0$; but the strong absorption of RF and microwave intensity by tissues, largely from the water in the tissues, limits the penetration of the body by that radiation. At frequencies, v < 5 GHz, typical body dimensions are not large compared to the wavelengths and relatively complex calculations are required to determine the absorption pattern in the body. For higher frequencies, it is useful to consider that the incident radiation at an intensity, I(0), is absorbed [Foster, 2000] such that the intensity at a depth, d, will be $I(d) = I(0) \exp(-d/L)$ where the absorption length $L < \lambda/10$, where the wavelength $\lambda = c/\nu$. Consequently, microwave radiation at wavelengths of 10 cm and shorter (v > 3 GHz) is absorbed largely very near the surface, and the effects of millimeter wave radiation are mainly limited to the skin. At very high frequencies, v > 10 GHz, there is significant heating of the skin from even 10 mW/cm² intensity radiation, as all of the energy is absorbed in a small region.

SET OF ELECTROMAGNETIC FIELD INTERACTIONS

Linearity of the Biological Response

Radiative electromagnetic fields act on biological elements almost solely through the electric field, E. For E < 200 V/m, the magnetic field B = E/c < 0.7 μ T, is too small to affect biology. The electric field, E, is a measure of the force on an electric charge. It has no other meaning, no other effect.

It is almost axiomatic that all physical systems, properly defined, including, of course, biological systems, respond nonlinearly to large stresses but vary linearly under small stresses. Of course, such a statement is empty without the definition of "properly defined" and "small." For biological systems, I have shown [Adair, 1994] that the response of the systems to the imposition of an RF field is proportional to the energy density of the field at that system, and thus to E_i^2 , if that energy, w, added to the system by the interaction of the field is small. Here, the scale is set by the requirement that $w < k_b T$ for elements that act incoherently and that $w < k_b T \cdot M^{1/2}$ for energy added to Melements that act coherently. Moreover, the final physiological consequences of the primary interaction must vary linearly with the energy density, E_i^2 , though the biological chain that leads from the primary interaction to those consequences will usually be complicated and, usually, not well understood.

If the response is linear, there can be no "windows" where the response is to be expected only for intensities above one level and below another [Postow and Swicord, 1996]. For experimental scientists, the observation of windows has long been regarded as indicating a mistake in their procedures. That view should be retained.

As a consequence of the linearity of response to weak RF fields, amplitude modulated RF fields are not rectified by biological responses. Consequently, amplitude modulated RF and microwave fields at intensities less than 10 mW/cm² (and, thus E fields of 200 V/m and B fields of $6.7 \cdot 10^{-7}$ T) cannot be expected to generate the well known biological effects of magnetic fields of a few Hz through their action on magnetosomes (biological Fe₃O₄ domains) [Walker and Bitterman, 1985; Kirschvink and Kobayashi-Kirschvink, 1991]. However, the elasmobranchs [Kalmijn, 1986; Adair et al., 1998] (sharks, skates, and rays) detect electric fields as small as 500 nV/m at frequencies of a few Hz through special sense organs (the Ampullae of Lorenzini). Since very small nonlinearities might serve to generate such weak electric fields from the rectification of an RF field of 200 V/m, these fish might well detect low intensity, amplitude modulated RF fields. Although, with no rectification, AM modulated RF will not generate low frequency E fields that modulation will generate low frequency E^2 intensity variations that could have some frequency specific affect on physiology.

If the response to the field is incremental to a natural level of response from other causes, the linearity of the incremental response with the field is even more general [Crawford and Wilson, 1996]. In some sense, we can consider that noise is that "other" cause.

Magnitudes of Energy Transfers From Dimensional Analysis

Here I argue from dimensional considerations that it is possible to define a nearly complete set of dimensionless signal to noise ratios, *A*, *B*, and *C* that describe the interactions of weak high frequency electromagnetic fields with small biological systems, i.e., molecules, organelles, and cells.

(A) The fields, E_i , acting on charges, q, held by elements, generate forces that may move the elements through a medium with a viscosity η that resists the motion. We can also expect that the mass, m, and size of the object to enter through a characteristic length, L. Using these factors, I find the simplest expression with the dimensions of energy to be,

$$w_{\eta} = \frac{(E_i q)^2 m}{(\eta L)^2} \text{ and } S/N = A(E_i^2)$$
$$= w_{\eta}/k_b T. \tag{4}$$

If we take $E_i = 200$ V/m, our postulated upper limit for athermal interactions, $q = e = 1.6 \cdot 10^{-19}$ C, the viscosity $\eta = 7 \cdot 10^{-4}$ Ns/m², the viscosity of water, $L = 10^{-10}$ m as the dimension of an atom, and $m = m_p = 1/(6 \cdot 10^{26})$ kg the mass of the proton, we have, $w \approx 10^{-33}$ J and S/N = $A = w_{\eta}k_bT \approx 2.3 \cdot 10^{-13}$. While the analysis can only be suggestive, the very small values of S/N strongly suggest that fields as weak as $E_i = 200$ V/m cannot affect physiology by simply moving charge elements.

(B) The fields acting on charges held by a system may act to switch the system from a lower to a high energy state where no significant energy is lost to dissipative processes. The energy scale for such a transition is set by the transition dipole moment, qd, where we can take $q \approx e$ and d a characteristic length. Thus,

$$w_d = E_i \cdot qd \text{ and } S/N = B(E_i^2)$$

= $(w_d/k_dT)^2$. (5)

At high frequencies, we can expect that d will be the order of magnitude of the molecular dimension. For

large molecules, this can be expected to be of the order of 10^{-8} m. Again, taking $E_i = 200$ V/m, $w_d \approx 3 \cdot 10^{-15}$ J and $w_d/k_bT \approx 7.5 \cdot 10^{-5}$. But since the average value of E_i for RF radiation is zero, the process must be second order and $S/N = B = (E_i \cdot qd/k_bT)^2 \approx 5.5 \cdot 10^{-9}$. Hence, again, we do not expect weak fields to affect physiology through this type of interaction.

(C) Electrostrictive forces on an object may also generate energies that must, again, be proportional to E_i^2 , the difference in the permittivities of the object and its surroundings, $\Delta \varepsilon$, and a characteristic volume of the object, Ω . Thus,

$$w_{\varepsilon} \approx \Delta \varepsilon E_i^2 \Omega$$
 and $S/N = C(E_i^2)$
= $w_{\varepsilon}/k_b T$. (6)

At RF and microwave frequencies, we do not expect large differences between the permittivities of different regions and estimate $\Delta \epsilon \approx \epsilon_0$, the permittivity of free space. Then taking $\Omega \approx 10^{-21} \, \mathrm{m}^3$, the volume of a large molecule with a mass of $10^6 \, \mathrm{Da}$, $S/N = w_\epsilon/k_b T < 10^{-7}$. Hence, such forces cannot be expected to affect molecules.

However, for a cell with a radius of $10 \, \mu m$, we find, $w_{\varepsilon} \approx 1.5 \cdot 10^{-21} \, \text{J}$ and $S/N = w_{\varepsilon}/k_b T \approx 0.3$. Hence, such forces might well generate forces greater than from thermal fluctuations on biological elements as large as, or larger than the average cell.

Hypothesis

If the set of S/N values for the interactions of weak fields, $A(E_i^2)$, $B(E_i^2)$, and $C(E_i^2)$, were complete, then any interaction must take the form of S/N = f(A, B, C), where for the small values of the fields that concern us, from Taylor's expansion, $S/N = f(A, B, C) \approx a_1A + a_2B + a_3C$ where, the a_j are constants. I argue that the set, A, B, and C is sufficiently near to completeness to be a useful guide to the limitations on any biological effects of weak high frequency fields.

DIRECT INTERACTIONS

Rotational Motion

Many molecules have significant dipole moments, *D*. We can gain some insight into the transfer of energy to such molecules by incident microwave fields by considering the torque applied by the field to such a molecule in an aqueous environment. Hence, initially we neglect any weak couplings of the molecule to nearby molecules and any large stochastic rotations of free molecules under thermal agitation. In this approximation, the equation of motion of the molecule under

the field $E_i \cos \omega t$ at a frequency of $v = \omega/2\pi$ can be written as,

$$\beta \dot{\theta} = E_i D \cos \omega t \tag{7}$$

where for simplicity, I take the resting angle between the field and dipole moment as $\theta = \pi/2$ and use the notation $\dot{\theta} = d \dot{\theta} / dt$. To consider the magnitudes of general effects, I assume that the molecule is spherical with a radius, r, a volume $\Omega = 4/3 \cdot \pi r^3$ and the dipole moment D = 2er where e is the electronic charge. (This is in accord with or larger than the dipole moments of water, insulin, hemoglobin, or the voltage sensitive elements of voltage gated ion channels.) Then, $\beta \approx 6\eta\Omega$ where we take $\eta = 7 \cdot 10^{-4}$ Ns/m², the viscosity of water. For such a system, and, in general, for the interaction of electromagnetic fields on small elements, the inertial terms are negligible and not included.

The rate of energy transferred to such a molecule is, then,

$$\frac{dw}{dt} = \frac{E_i^2 D^2}{\beta} = \frac{E_i^2 e^2}{2\pi \eta r}.$$
 (8)

That energy transfer will be regularly interrupted by thermal agitation, and we then multiply the rate by the relaxation time τ_{κ} taken from Equation 2, and

$$S/N = w/k_b T = \frac{\tau_{\kappa} E_i^2 e^2 r}{2\pi m \cdot k_b T} \approx 3 \cdot 10^{-13}$$
 (9)

where the numerical value is calculated for a large molecule with a radius, $r = 10^{-8}$ m, and for an electric field strength, $E_i = 200$ V/m.

Although M molecules may be acted on coherently, $S/N \ll 1$ for plausible values of M.

Dimensionally, this is a Class (A) interaction.

Other Molecules, Linear Motion

For completeness, I augment the discussion of rotational motion with a simple, parallel discussion of the linear motion of an ion holding a charge q. Then,

$$\gamma \dot{x} = E_i q \cos \omega t \tag{10}$$

where, again I neglect inertial terms and assume also that restoration forces are small. From Stoke's Law, $\gamma = 6\pi\eta r$, where r is the radius of a spherical element, and I take the charge as q = e. Then,

$$\frac{dw}{dt} = \frac{E_i^2 e^2}{6\pi \eta r} \quad \text{and} \quad S/N = w/k_b T$$

$$= \frac{E_i^2 e^2 \tau_{\kappa}}{6\pi \eta r k_b T}. \quad (11)$$

For an ion with a radius, $r = 2 \cdot 10^{-10}$ m, $S/N = w/k_bT \approx 10^{-15}$ and again the energy transfer is negligible.

This is also a Class (A) interaction.

Opening of Voltage Gated Channels

It is useful to look at other direct effects of RF and microwave electromagnetic fields on molecules carrying large dipole moments. In particular, I consider interactions of a character that lead to changes in the configuration of a molecule where that configuration change modifies the biological function of the molecule. Here, I take voltage gated membrane channels as an especially important and characteristic example of such molecules.

Such channels provide what may be the most obvious direct connection between physiology and electromagnetic fields at frequencies below that where quantum effects are important. The squid axon Na channel is closed to the passage of ions when the axon resting potential of about -60 mV is set across the channel. When the negative potential is reduced—the cell is depolarized—the channel protein changes its configuration to a form, which is open and passes ions. Then, a little later, the channel configuration changes again to a third form which stops the ion passage. The K channels, also closed at the resting potential, simply open upon depolarization, though a little more slowly.

A half century ago, Hodgkins and Huxley [1952] showed that the Na ion channels could be described accurately by a model with seven closed states and one open state. Their closely related model of the K channels had one open and four closed channels. In their models, the transitions from state to state are driven by the effects of the transmembrane electric field on dipole moments held by channel elements. With many different voltage regulated channels specifically sensitive to electric fields, I analyze a simple generic model to illustrate general characteristics of the response of these systems to fields from exogenous sources.

For our purpose of estimating effects for channels with a variety of specific characteristics, the effects of the several closed states can be simulated by an appropriately chosen single state and the transitions between open and closed states are generated by the difference in dipole moments of the two states.

If only two states, open and closed, are important, the probability of the channel being open or closed can be described by Boltzmann Gibbs' relations,

$$P_{op} = \frac{e^{-U/K_bT}}{1 + e^{-U/k_bT}}$$
 and $P_{cl} = \frac{1}{1 + e^{-U/k_bT}}$ (12)

where $U = U_{op} - U_{cl}$ is the difference between the energies of the open and closed states. Entropy factors, proportional to the logarithm of the ratio of statistical weights of the states, are included in the energy factor; thus U is properly the Gibbs energy. That energy difference can be written as,

$$U = U_0 + V_m q e. (13)$$

Here, qd_m is the difference between the dipole moments of the open and closed states, $d_m \approx 10^{-8}$ m, is the membrane thickness, $q \approx 6e$ is the gating charge [Hille, 1992], and U_0 is the energy difference when the membrane field is zero.

From these formulae, the increase in the equilibrium opening probability caused by a small change in membrane potential ΔV_m as, $U = U_0 + \Delta U$ is,

$$\Delta P_0 = \frac{e^{-U_0/k_b T}}{\left(1 + e^{-U_0/k_b T}\right)^2} \left[-\frac{\Delta U}{k_b T} + \frac{1}{2} \left(\frac{\Delta U}{k_b T}\right)^2 + \cdots \right]$$
(14)

where $\Delta U = qe \Delta V_m < k_b T$. The time constant for such a change is of the magnitude of 1 ms setting the time scale for the integration of a high frequency signal.

Then, taking $\Delta V_m \propto E_i$, low frequency (ELF) electric fields can be expected to affect the opening of the channels through their contribution to the first term in the expansion proportional to $\Delta U/k_bT$. At higher frequencies, the mean value of E_i will be zero and any effects must be proportional to E_i^2 and will be described by the second term, $(\Delta U/k_bT)^2/2$. With both the difference and the similarity as a guide, we can use a known response of systems to low frequency fields to estimate thresholds for excitement by high frequency fields.

Low frequency endogenous electric fields as small as $E_i = 1$ V/m are known to generate phosphenes [Tenforde, 1996] in the retinal visual system, presumably through effects of the fields on voltage gated channels. We can then consider the transmembrane potential difference generated by a field of 1 V/m as a marker in our efforts to understand the character of possible effects of higher frequency radiative fields. This "standard" low frequency field acts coherently on a large set of channels in the visual system neurons.

Since the resistance of the membrane is very large compared to the resistance of the cytoplasm at low frequencies when the capacitative impedance is high, almost all of the potential drop across a cell in the presence of an internal field, E_i , takes place at the cell membrane. At higher frequencies, above the characteristic β dispersion frequency of the membrane, the proportion of the potential drop across the cell taken by the membrane is reduced. For a field, E_i , in the body but

external to the membrane Foster and Schwan [1996] suggests that the incremental potential drop across the membrane from that field will be,

$$\Delta V_m = \frac{1.5E_i \cos \theta}{\sqrt{1 + (\omega \tau_{\beta})^2}} \quad \text{where} \quad \tau_{\beta} \approx 10^{-7} \text{ s}$$
 (15)

where θ is the angle between the field direction and the normal to the membrane surface and the internal field, E_i , is reduced from the external field, E_0 as per Equation 3.

If we take $r \approx 10 \, \mu m$ as the radius of a typical cell, a field of $E_i \approx 1 \, V/m$ can be expected to generate maximum transmembrane potentials of the order of 0.015 mV. Since, over a whole cell, effects proportional to the electric field E_i , the first term in the expansion of Equation 14, can be expected to be reduced by symmetry considerations. Hence, as the average value of $\cos \theta$ is zero over a sphere, fields somewhat smaller than 1 V/m may affect physiology in some circumstances. Aligned cell systems such as those near the retina supporting vision, probably are quite asymmetric, hence the low threshold for phosphine production

Taking the gating charge for a channel [Hille, 1992] as 6e and $\Delta E_i = 1$ V/m, then S/N = 1 for $\Delta U/k_bT \approx 0.003$ at low frequencies, a value that suggests that something of the order of $M = 10^5$ channels are affected coherently. Equating the value of the second term in the expansion of Equation 17, we might then reasonably expect to see biological effects (and S/N = 1) for $(\Delta U/k_bT)^2/2 \approx 0.003$ for RF and microwaves. That corresponds to values of $\Delta V_m \approx 0.08$ mV.

Setting the external field at $E_0 = 200$ V/m (corresponding to 10 mW/m^2), I determined the internal field, E_i , as a function of frequency from Equation 3. Then, knowing E_i , I used Equation 15 to find ΔV_m . The largest resultant value of ΔV_m was only $8 \cdot 10^{-4}$ mV, about two orders of magnitude too small to generate physiological effects.

I have noted that the low frequency field must act coherently on as many as 10^5 channels. Since some of the low frequency fields must reduce the firing probabilities for those channels, where $\cos\theta < 0$; more channels may be available for the high frequency interactions somewhat increasing the relative sensitivity to the high frequency fields. However, such an increase would not be very large.

Thus it seems unlikely that RF intensities of the order of 200 V/m would affect biology through the direct excitation of voltage gated ion channels.

This is a Class (B) interaction.

ELECTROSTRICTIVE FORCES AND INDUCED DIPOLE MOMENTS

For the dimensional Class C interactions, the energy added by the electric field is proportional to the volume of the element. Hence, for very large elements, the energies added by even very weak fields, will exceed thermal fluctuations in that very large energy. We should then expect that variations in those energies from other sources would provide the most significant limit on the effects of weak electric fields.

Schwan [1985] has summarized a wide variety of interactions between electromagnetic fields and cells that follow from electrostrictive forces, which, in turn, derive from the electric dipole moments induced by the fields. The effects of these interactions seem to divisible into two sets: (1) forces on the surfaces of the elements that follow from the induced dipole moments tend to distort the elements; and (2) forces develop between elements that arise from forces between the dipole moments induced in the elements. While other relatively large elements are subject to these effects, I consider cells especially, as they are both ubiquitous and possibly vulnerable.

Electrostrictive Forces on Cells

The time average electrostrictive pressure, P, generated by the effects of an electric field, $E_i \cos \omega t$, on a sphere (cell) containing a liquid (cytoplasm) with a permittivity ϵ' , immersed in a liquid (tissue plasma) with a permittivity ϵ , is approximately,

$$P \approx (\varepsilon - \varepsilon') \frac{E_i^2}{2}.$$
 (16)

We can take $\epsilon' - \epsilon = \epsilon_0$ for illustration, where ϵ_0 is the permittivity of free space, since the tissue plasma and cytoplasm, both water based, should not have radically different permittivities. In that approximation, the electrostrictive pressure from radiation with an intensity of $10 \text{ mW/cm}^2 \, \mu\text{W/cm}^2$, is about $2 \cdot 10^{-7} \, \text{N/m}^2$ or about 10^{-12} of the differences in the distolic and systolic blood pressures during a heart beat. The electrostrictive pressures from the weak fields are about ten times smaller than the pressures from the absorption or reflection of incident sun light.

If $\epsilon' > \epsilon$, the electrostrictive forces will tend to generate a prolate distortion of an otherwise spherical cell; if $\epsilon' < \epsilon$, the forces will tend to generate an oblate form.

The energy, $w = P\Omega$, transferred from the electric field, E_i , to a cell with a volume Ω , as given by Equation 6, for Class C interactions, then exceeds k_bT for large cells. But the electrostrictive forces are so minute compared to the variations in the natural forces on cells

in a living animal that it is difficult to believe that the small electrical forces can significantly affect animal biology.

Dipole-Dipole Interactions Between Cells

We can estimate the magnitude of the dipole moment, p, induced in a spherical cell with a volume Ω by the internal field as $p \approx 3\epsilon_0 \Omega E_i$. The interaction energy between two adjacent cells separated by their diameter will then be, roughly, $w \approx p^2/(32\pi\epsilon_0 r^3) \approx (3/8)$ $\epsilon_0 \Omega E_i^2$, a result in accord with Equation 6 for Class (C) interactions.

Limitations on Induced Dipole Effects

From Equation 3, internal fields, E_i , nearly as great as the external field $E_0 = 200$ V/m at an intensity of 10 mW/cm^2 , are only to be found at frequencies, v > 1 GHz, and then, because of the strong absorption in tissue, largely near the surface or in the skin. There are also upper limits on the effective frequencies. The dipole moments oscillate at the frequency of the imposed field. That oscillation will be damped when the RC time constant of the cell capacitor, $\tau_{rc} = RC \approx \rho \epsilon$, is not much longer than the oscillation period. Hence, the electrostrictive forces and the related dipole effects can be expected only at frequencies less than $v \approx (1/2\pi)(1/\epsilon_0 \rho) \approx 20 \text{ GHz}$, a wavelength of about 1.5 cm, where $\rho \approx 1 \Omega$.

Within that range, 1 GHz < v < 20 GHz, any effects of the weak fields can be expected to vary only weakly with the frequency of the endogenous field as the permittivities vary with those frequencies.

While I do not expect large numbers of very large cells to act with complete coherence—cells are always somewhat autonomous—since there may be some level of coherence in their operations, the true signal to thermal noise values calculated here could be somewhat larger than that calculated above.

More important, the effects are only greater than that from thermal agitation for rather large structures, where thermal effects average out. Then the electrostrictive forces on those structures are so very much smaller than the expected transitory changes in the normal forces that it seems most unlikely that the electrostrictive forces generate significant physiological responses.

RESONANCES

A molecule made up of M nuclei will have M-1 normal vibrational modes. The frequencies of these modes are usually centered in the infrared but extend down into microwave frequencies. Excepting those modes with frequencies such that $hv > k_bT$ and are thus

"frozen out" quantum mechanically, each mode will oscillate with amplitudes corresponding to mean energies of k_bT . Thus, the total thermal energy of the molecule will be near $w_{kT} \approx (M-1)k_bT$. In general, the modes will couple to the electromagnetic field through charges held by the atoms hence, oscillating electromagnetic fields might excite resonances in many biologically interesting molecules. However, there are strong couplings between modes, so that energies absorbed in any resonant mode are transferred to other modes in very short relaxation times.

Some of these systems will be coupled to the electromagnetic field by the dipole moment charge distributions they carry, thus admitting the possibility that microwave exposures may generate physiological effects in man and other species. However, such microwave excitable resonances are expected to be strongly damped by internal conduction to other vibrational modes and with their external aqueous biological environment. Moreover, the coupling of the field to elements that are very much smaller than the microwave wavelengths, and hence have very small dipole moments, must generally be very small. Consequently, the absorbed energy is so strongly limited that such resonances cannot affect biology significantly even if the systems are much less strongly damped than expected from basic dissipation models.

We can describe the absorption of energy from an incident wave, with a wavelength λ , in terms of an absorption cross section [Blatt and Weiskopf, 1952; Marion and Heald, 1980],

$$\sigma_a(\nu) = 3 \frac{\lambda^2}{\pi} \frac{\Gamma_s \Gamma_a}{(\nu - \nu_r)^2 + \Gamma^2/4}.$$
 (17)

The cross section, σ_a , is the power absorption area. The widths, $\Gamma_j = 1/\tau_j$, where τ_j are the effective lifetimes for decay through the processes j. Thus, τ_a is the lifetime of the state dictated by the absorptive effects and $\tau_s \gg \tau_a$ is the lifetime if the only energy loss mechanism were the reradiation of electromagnetic energy through the oscillating dipole moment.

The maximum energy of the oscillating system will be.

$$\Delta w = I \left[\frac{12\lambda^2}{\pi} \right] \tau_a \times \left[\frac{\tau_a}{\tau_s} \right]. \tag{18}$$

Hence, the energy, Δw , is the product of four terms, the power density, I, an area proportional to the square of the wave length, the lifetime of the resonance, τ_a , and then a coupling factor τ_a/τ_s .

The area is that part of the incident beam that has the proper angular momentum to interact with a small dipole element.

We estimate the values of the widths and lifetimes. Using classical electrodynamics and a simple mechanical model,

$$\Gamma_s = \frac{1}{\tau_s} \approx \frac{q^2 \omega^2}{6\pi \varepsilon_0 mc^3}.$$
 (19)

For v = 100 GHz, q = e, $m = m_p = 1.67 \cdot 10^{-27}$ kg, $\Gamma_s = 1.34 \cdot 10^{-8}$ s⁻¹, and $\tau_s = 1/\Gamma = 7.5 \cdot 10^7$ s. Even as the lifetime of such states by radiative decay is very long, the radiative width and, thus, the coupling to the electromagnetic field is very small.

From Equation 19 and the evaluation of the radiative width, $\Gamma_s = 1/\tau_s$, we are able to calculate the maximum energy storage of the oscillator when excited by an incident microwave beam with an intensity, $I=10~\text{mW/cm}^2$ in terms of the lifetime of the state τ_a . We conventionally express that lifetime in terms of the Q value of the resonance, where $Q=\omega\tau_a$. Only if we take $Q=2\pi\cdot 100\approx 630$ and $\tau_a=Q/(2\pi v)=10^{-8}$ s, do we have $S/N=\Delta w/k_bT\approx 1$, and a significant resonance effect. But that lifetime is far greater than typical relaxation times (Eqs. 2 and 3) that are of the order of $\tau_a\approx 10^{-11}$ s, which leads to very small energy storage and $S/N=w/k_bT\approx 10^{-6}$.

Hence, resonance effects can be important biologically only if the dipole moment of the resonant system is much larger than one might expect from general principles and if the damping of the system is much less than seems plausible.

These are Class B interactions.

Coherent Processes; Cell Membranes

Frölich [1968] has emphasized the possible importance of the oscillations of systems, where many dipole moments act coherently. In particular, he has suggested that such oscillations may be generated in the cell membranes that may affect biology. Following the specific example he describes, we consider a membrane section with an area of about 10^{-10} m² normal to the electric field where internal and external electric charges that account for the normal $V_{mem} \approx 60$ mV polarization potential across the membrane form dipole moments. The alternating electric field will induce alternating compressive and expansive (tension) forces on the membrane through their action on the charges that bound the membrane.

We can expect a resonance frequency such that $v_{res} = v_{mem}/d_{mem} \approx 2 \cdot 10^{11}$ Hz, where we take v_{mem} , the speed of sound in the membrane, as 1500 m/s, the speed of sound in water. The wavelength is then $\lambda = 1.5$ mm,

corresponding to a frequency of 200 GHz. This is close enough to 100 GHz, so that within the uncertainties of our calculations, the results can be considered to pertain to our situation.

Taking the specific capacity of the membrane as $c_m = 0.01 \text{ F/m}^2$ (1 $\mu\text{F/cm}^2$) and the resting potential as $V_m = -60 \text{ mV}$, the charge density $Q = V_m c_m \approx 7 \cdot 10^{-4} \text{ C/m}^2$. Thus the charge on a characteristic sector of membrane with an area, $A = L^2 = 10^{-10} \text{ m}^2$ will be $q \approx 7 \cdot 10^{-14} \text{ C}$.

We can estimate the mass of the sector as $m = L^2$ $d_{mem}\rho \approx 7 \cdot 10^{-16}$ kg by taking the membrane element as an area L^2 , where L = 10 µm, a thickness as $d_{mem} = 7$ nm and $\rho = 1000$ kg/m³, the density of water.

With these values we find,

$$\Gamma_s = \frac{q^2 \omega^2}{6\pi \epsilon_0 (m/4)c^3} \approx 5 \cdot 10^{-8} \,\mathrm{s}^{-1}.$$
 (20)

With $\tau_s \approx 2 \cdot 10^7$ s, and an incident beam with an intensity of 10 mW/m², $S/N = \Delta w/k_bT \approx 5 \cdot 10^{-9}$, assuming a Q value of $2\pi \cdot 1000$. Hence, even if the resonance is only weakly damped, it cannot be expected to affect biology. A better estimate of the damping [Adair, 2002] puts $Q = \tau_a/(2\pi \cdot v) \approx 0.2$, and the resonance can be expected to be over damped.

The failure of the coherence of many elementary elements, to increase the effective signal to noise over that from one resonant element, is found in the strong coupling of the individual elements. Even as the coupling to the radiative field is greatly increased, so is the viscous damping.

These are also Class B interactions.

MAGNETIC FIELD EFFECTS: RADICAL PAIR RECOMBINATION

Radicals are free parts of molecules with an unpaired valence electron or hole and are, therefore, highly reactive chemically. Certain molecules break up into pairs of radicals, each of which holds an unpaired electron where the two electrons were in a singlet state before the break up [Brocklehorst, 1976; Adair, 1999]. The pairs, held close together by the viscosity of the local medium and sometimes by micelle structures, may join to reform the molecule eliminating their contribution to biologically important chemistry. But that will only occur of the spins of the unpaired electrons attached to the two radicals are in a singlet state. Generally, the precession rate of the two electrons, acted on by different nuclear magnetic fields, will differ; hence, after time apart, they will not be precisely aligned in singlet states, thus reducing the recombination probability. External fields can modify that differential precession, thus modifying the recombination probability and the probability of the radicals affecting biology through their chemical activity.

The effects are roughly proportional to the product of the average external magnetic field strength times the mean time the radicals are separated but physically close. For our canonical maximum intensity of 10 mW/cm^2 , the magnetic field strength is only $6.67 \cdot 10^{-7}$ T which is much smaller than smallest fields, $B > 0^{-4}$ T, that have been known to affect chemistry by modifying radical pairs recombination probabilities. Moreover, if such weak fields are to be effective, they must act over separation times $\tau \gg 10 \text{ ns}$. Hence, the maximum frequency, $\nu \ll \tau/2\pi \approx 10 \text{ MHz}$. Aside from the high frequency limitation, any effects should be largely independent of frequency.

These magnetic field induced effects do not fall into the classes of electrically driven interactions, Classes A, B, and C, but form a separate category.

SUMMARY

In considering possible athermal effects of low intensity radio frequency and microwave electromagnetic fields on human physiology, I have used dimensional analyses to attempt to define a complete set of possible biological interactions of weak high frequency electromagnetic fields with intensities less than 10 mW/cm^2 . I then examined specific characteristic interactions belonging to that set. From the general criteria, as illuminated by the specific examples, I found it quite unlikely that any mechanism can transfer energy to biological elements as small as organelles and molecules that is in excess of thermal noise energy fluctuations; i.e., $S/N \ll 1$. Hence, the fields could not be expected to affect biology through those mechanisms.

However, I found that I could not exclude the possibility that energy transfers from the generation of electrostrictive forces on large elements, such as whole cells, might exceed thermal noise. However, those forces are minute compared to natural forces and, on that basis, it seems unlikely that they can affect biology.

Hence, I conclude that it is most unlikely that RF or microwave fields of an intensity less than 10 mW/cm² incident on humans, can effect physiology significantly.

I also considered a magnetic field interaction that would modify radical pair recombination and demonstrated that no significant effects could be expected from weak fields through that mechanism.

Theoretical implausibility should and does enter into the acceptance of any scientific result; remarkable conclusions, which seem to violate well considered principles, require remarkably strong evidence. Some two centuries ago, Thomas Bayes put the effect of prior

knowledge on probability on a quantitative basis by the recipe (Bayes' Theorem [Bulmer, 1979]),

Posterior probability \propto prior probability \times likelihood

I hold that our prior knowledge establishes that it is unlikely that weak fields generate any biological effect. Hence, any experimental results that seem to indicate such effects, effects that are a priori most improbable, must be especially definitive. Arguably, the present set of positive results, however many [Michaelson and Elson, 1996; Postow and Swicord, 1996], are not that strong.

REFERENCES

- Adair RK. 1994. Biological responses to weak 60 Hz electric and magnetic fields must vary as the square of the field strength. Proc Natl Acad Sci USA 91:9422–9425.
- Adair RK. 1995. Effects of weak high frequency electromagnetic fields on biological systems. In: Klauenberg BJ, Grandolfo M, Erwin DN, editors. Radiofrequency radiation standards. New York: Plenum Press. p 207–222.
- Adair RK. 1999. Effects of very weak magnetic fields on radical pair reformation. Bioelectromagnetics 20:255–263.
- Adair RK. 2002. Microwave resonances in biological systems. Biophys J 82:1147–1152.
- Adair RK, Astumian RD, Weaver JC. 1998. Detection of weak electric fields by sharks, rays, and skates. Chaos 8:576–587.
- Blatt JM, Weiskopf VF. 1952. Theoretical nuclear physics. New York: Wiley.
- Brocklehorst B. 1976. Spin correlation in the geminate recombination of radical ions in hydrocarbons. J Chem Soc Faraday Trans II 72:1869–1884.
- Bulmer MG. 1979. Principles of statistics. New York: Dover.
- Crawford M, Wilson R. 1996. Low dose linearity: The rule of the exception. Hum Ecol Risk Assess 2:305–330.
- Foster KR. 2000. Thermal and non thermal mechanisms of interaction of radio frequency energy with biological systems. IEEE Trans Plasma Sci 28:15–23.

- Foster KR, Schwan HP. 1996. Dielectric properties of tissues. In: Polk C, Postow E, editors. CRC handbook of biological effects of electromagnetic fields. Boca Raton: Chemical Rubber Co. p 25–102.
- Frölich H. 1968. Long range coherence and energy storage in biological systems. Int J Quant Chem 2:641–649.
- Hille B. 1992. Ionic channels of excitable membranes. Sunderland, Massachusetts: Sinauer. 57 p.
- Hodgkins AL, Huxley AF. 1952. A quantitative description of membrane current and its application to conduction and excitation in nerve. J Physiol (London) 117:500-544.
- Kalmijn AJ. 1986. Electroreception in sharks and rays. Nature 212: 1232–1233.
- Kirschvink JL, Kobayashi-Kirschvink A. 1991. Is geomagnetic sensitivity real, replication of the Walker Bitterman magnetic conditioning experiment in honeybees. Am Zoo 31:169– 185.
- Lin JC, Gandhi OP. 1996. Computational methods for predicting field intensity. In: Polk C, Postow E, editors. CRC handbook of biological effects of electromagnetic fields. Boca Raton: Chemical Rubber Co. p 337–402.
- Marion JB, Heald MA. 1980. Classical electromagnetic radiation, 2nd edition. Orlando, Harcourt, Brace, Jovanavich, chapter 10.
- Michaelson SM, Elson EC. 1996. Interaction of nonmodulated and pulse modulated radio frequency fields with living matter: Experimental results. In: Polk C, Postow E, editors. CRC handbook of biological effects of electromagnetic fields. Boca Raton: Chemical Rubber Co. p 435–534.
- Postow E, Swicord M. 1996. Modulated fields and "window" effects. In: Polk C, Postow E, editors. CRC handbook of biological effects of electromagnetic fields. Boca Raton: Chemical Rubber Co. p 535–580.
- Schwan HP. 1985. EM field induced force effects. In: Chiabrera A, Nicolini C, Schwan HP, editors. Interactions between electromagnetic fields and cells. New York: Plenum Publishing Co. 137 p.
- Tenforde TS. 1996. Interaction of ELF magnetic fields with living systems. In: Polk C, Postow E, editors. CRC handbook of biological effects of electromagnetic fields. Boca Raton: Chemical Rubber Co. p 185–230.
- Walker MM, Bitterman ME. 1985. Conditioned responding to magnetic fields by honeybees. J Comp Physiol A157: 67–73.