Model for Some Nonthermal Effects of Radio and Microwave Fields on Biological Membranes

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Abstract—**A model is presented for mechanisms by which nonthermal effects could take place in biological materials as a result of microwave and radio-frequency fields. Both shifts in ion concentrations across a membrane and the orientation of long chain molecules are shown to be possible.**

Introduction

THERE HAS BEEN considerable controversy for some time about the possible existence of nonthermal effects of microwave and radio-frequency (RF) fields on biological materials. It is the purpose of this paper to explore two possible mechanisms by which nonthermal phenomena might take place and to estimate the magnitude of the threshold for these effects.

By way of background, there are at least six experimental results which lead us to look for nonthermal mechanisms, and two of them suggest membranes are a place to look [1]–[6]. Baranski [1] has shown that powers of 5–10 mW/cm^2 change the permeability of blood cell membranes to hemoglobin. We also have previously shown that the mechanism for death for zebra fish embryos exposed to pulsed microsecond fields in the 5–10-kV/cm range leads to a form of death which might be explained by a change in the porosity of membranes leading to an osmotic pressure imbalance [2].[1]

In the first part of this paper we will examine the effect of RF fields on the equilibrium concentration of the charge particles on opposite sides of a membrane, and we will estimate the effect of the nonlinear Boltzmann equation on both the concentration shift and the ion current which flows as a result of the membrane's rectifying properties. In the second portion of the paper we will look briefly at the size of the torque which can be expected to be exerted on long chain molecules containing the dipole moments or induced dipole moments.

The Concentration Balance at a Potential Barrier

If the concentration of charged particles varies in space and if there is no net current, it is necessary that the field-driven drift current balance the diffusion current so that a potential barrier is formed to maintain the concentration difference. This results in the Boltzmann or Nernst equation, showing that the concentration of charged particles across a potential barrier is related by

$$C_1 = C_2 \exp \frac{V_{21}}{\zeta V_T} \qquad V_T = \frac{kT}{q} \tag{1}$$

where

- C_1 concentration on one side of a barrier,
- C_2 concentration on the other side of the barrier,
- V_{21} potential across the barrier,
- V_T thermal energy expressed as a voltage,
- k Boltzmann's constant,
- q charge on an electron,
- T absolute temperature,
- ζ a constant of the order of unity which takes into account recombination or generation in the barrier region and possible geometric variations with voltage.

If an electric field is applied to the medium containing this potential barrier, the voltage V_{21} across the barrier will be varied and with it the relative equilibrium concentrations between two regions. The case of interest is one where an ac field is superimposed upon the dc potential that exists at equilibrium so that

$$V_{21} = V_o + V_m \cos \omega t \tag{2}$$

where

- V_o initial dc potential or equilibrium potential,
- V_m peak value of the ac voltage across the membrane.

In most cases of interest, the ac field will be small so that we can substitute (2) into (1) and expand in a power series, which yields

$$C_1 = C_2 \left[\exp \frac{V_o}{\zeta V_T}\right]\left[1 + V_m^2/4\zeta^2 V_T^2 + \frac{V_m}{\zeta V_T}\cos \omega t + \frac{V_m^2}{4\zeta^2 V_T^2}\cos 2\omega t \cdots\right]. \tag{3}$$

The important thing to note from this equation is that even small values of an applied ac field lead to a shift in the equilibrium concentration, which is proportional to $V_m^2/4\zeta^2 V_T^2$. Additionally, it should be noted that if V_m is a modulated wave, the sum and difference frequency components may be generated. If the difference frequency is close to the natural frequency rate of a nerve system, there is some

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[1] The experiments by Jones have come to our attention and show changes in the frequency rate of nerve cells in the presence of microwave energy.

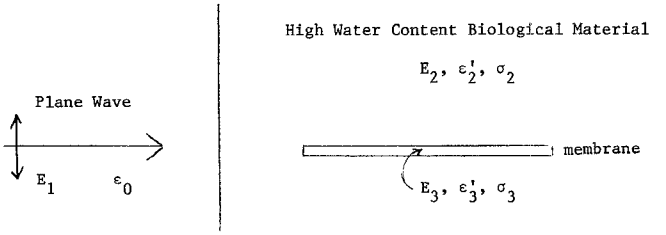

Fig. 1. Schematic for electromagnetic wave incident on a high-water-content dielectric material with a membrane at a right angle to it.

possibility for locking the nerve response to this difference frequency.

In order to estimate the effect of microwave or RF fields on the biological subject, we need to have at least an estimate of how an incident field from outside translates into a voltage across a membrane barrier inside a biological subject and of the size of the ion currents which lead to this equilibrium shift in the concentration. The problem of estimating fields inside biological materials has been studied at considerable length by Guy [7], Schwan [8], [9], and others [10].

The problem of calculating the electromagnetic field inside a biological object which results from a plane wave incident upon it is complicated by the geometry and by the stratified inhomogeneous nature of the biological material. However, since we are interested in numbers which are more nearly correct to an order of magnitude than to a few percent, we can start by looking at the plane wave case incident on the homogeneous biological material which is described by the appropriate conductivity σ and the dielectric constant ε' (see Fig. 1). In free space, the power density for a plane polarized field is given by [11]

$$P = E^2/\eta \tag{4}$$

where E is the electric field, and

$$\eta = \sqrt{\frac{\mu}{\varepsilon'[1 - j(\varepsilon''/\varepsilon')]}}.$$

At a plane parallel boundary, the amplitude reflection coefficient R is given by

$$R = \frac{\eta_2 - \eta_1}{\eta_2 + \eta_1} \tag{5}$$

and the transmission coefficient, by

$$\frac{E_2}{E_1} = \frac{2\eta_2}{\eta_2 + \eta_1}. \tag{6}$$

For fields propagating in a lossy dielectric, the attenuation coefficient α is given by

$$\alpha = \omega \sqrt{\frac{\mu\varepsilon'}{2}\left[\left(1 + \left(\frac{\varepsilon''}{\varepsilon'}\right)^2\right)^{1/2} - 1\right]} \tag{7}$$

and the propagation coefficient β, by

$$\beta = \omega \sqrt{\frac{\mu\varepsilon'}{2}\left[\left(1 + \left(\frac{\varepsilon''}{\varepsilon'}\right)^2\right)^{1/2} + 1\right]}. \tag{8}$$

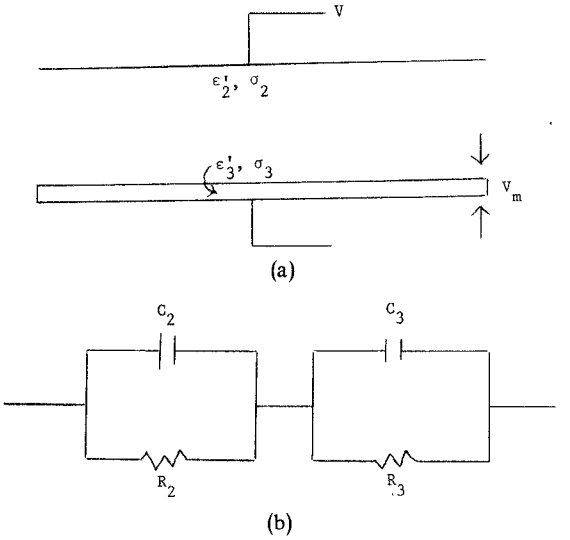

Fig. 2. (a) A two-dielectric model in a capacitor. (b) Equivalent circuit for the two-dielectric model.

The conductivity σ is given by

$$\sigma = \omega\varepsilon''. \tag{9}$$

The values for ε' and σ have been tabulated by Guy [7]. For fields in the gigahertz region, the transmission coefficient for a plane wave into biological material such as muscle with a high water content, from air, is approximately given by

$$E_2 = 0.25E_1$$

near the surface or boundary of the tissue. It is assumed that ε' is approximately equal to 50. In the case of low-loss dielectric biological materials such as fat or bone

$$E_2 \approx 0.46E_1.$$

Typical depths of penetration to the $1/e$ point for microwaves at these frequencies are a few centimeters; so the maximum electric field strength will occur near the surface and at a boundary between fatty tissue and high-water-content tissue, with the exact location depending upon the details of the biological material and its geometry.

Once the average value of the electric field in a biological material is given, we need to estimate the relative field strength across a membrane that is contained within this material. This may be done by looking at the plane parallel case of two lossy dielectric materials in series as shown in Fig. 2. The high-water-content tissue is described by ε'_2 and σ_2, and the membrane material is described by ε'_3 and σ_3. We can find the relative concentration in the field in the membrane material ε'_3 as follows. The voltage across the membrane V_m is related to the applied voltage V by

$$V_m = \frac{VZ_3}{Z_2 + Z_3}$$

$$|V_m| = \frac{|V|}{\left|1 + \frac{Z_2}{Z_3}\right|} \tag{10}$$

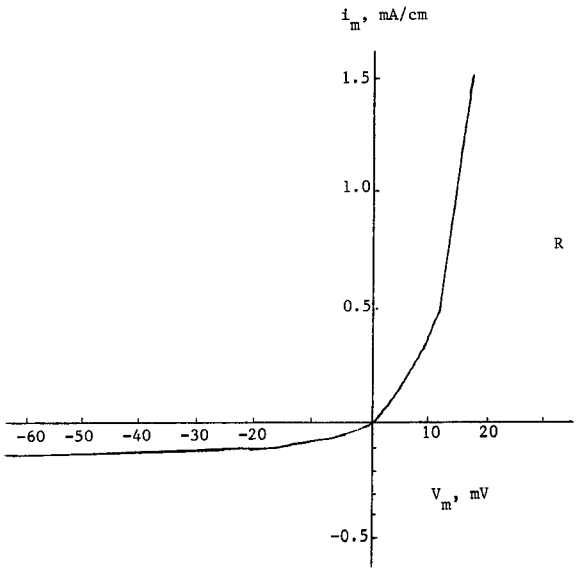

Fig. 3. The steady-state current-potential characteristic for a squid axon membrane as calculated from longitudinal data for the axon. (Reference: Cole, *Membranes Ions and Impulses, A Chapter of Classical Biophysics.* Univ. California Press, 1972, p. 155.)

where

$$Z_2 = \frac{R_2}{1 + j\omega C_2 R_2} \tag{11}$$

$$Z_3 = \frac{R_3}{1 + j\omega C_3 R_3} \tag{12}$$

$$\left|1 + \frac{Z_2}{Z_3}\right| = \left[\frac{(R_3 + R_2)^2 + \omega^2 R_2^2 R_3^2 (C_2 + C_3)^2}{R_3^2(1 + \omega^2 C_2^2 R_2^2)}\right]^{1/2}. \tag{13}$$

Assuming the parallel plate distribution, where ε'_2 and ε'_3 are real dielectric constants, ρ_2 and ρ_3 are the resistivities, and

$$R_3 = \frac{\rho_3 d_3}{A} \qquad C_3 = \frac{\varepsilon'_3 A}{d_3}$$

$$R_2 = \frac{\rho_2 d_2}{A} \qquad C_2 = \frac{\varepsilon'_2 A}{d_2} \tag{14}$$

equation (10) reduces to

$$V_m = \frac{V}{\left|1 + \frac{Z_2}{Z_3}\right|} = \frac{V}{\left[\frac{\rho_2 d_2}{\rho_3 d_3}\right]\left[\frac{[1 + (\rho_3 d_3/\rho_2 d_2)]^2 + \omega^2 \rho_3^2 \varepsilon_3'^2 [1 + (\varepsilon'_2 d_3/d_2 \varepsilon'_3)]^2}{(1 + \omega^2 \varepsilon_2'^2 \rho_2^2)}\right]^{1/2}}. \tag{15}$$

Because the thickness of the medium is very large compared to the thickness of the membrane, the applied voltage is approximately equal to the voltage across the medium.

When $|\omega\rho\varepsilon'|$ is much greater than one, this expression reduces to

$$V_3 \approx V \frac{\varepsilon'_2}{\varepsilon'_3} \frac{d_3}{d_2} \tag{16}$$

or the ratio of the electric fields

$$E_3 \approx \frac{\varepsilon'_2}{\varepsilon'_3} E_2. \tag{17}$$

At low frequencies, where $|\omega\rho\varepsilon'|$ is much less than one, we have

$$E_3 \approx \frac{\rho_3}{\rho_2} E_2. \tag{18}$$

A typical value for $|\omega\rho\varepsilon'| = 1$ is $f = 0.36$ GHz. Thus the key expression at 3 GHz is (17).

In order to obtain the appropriate values for ρ and ε' for the membrane, we start with the values of ρ which can be calculated from Fig. 3. A second estimate can be made from the tables for high- and low-water-content tissue by Guy and at the appropriate frequency. For ε' we start with the widely quoted values for the capacitance of bilipid membranes and cell membranes that range between 0.3 μF/cm^2 and 1 μF/cm^2 [12], [13]. In order to obtain numerical values for the coefficients for calculations in currents at low levels from Fig. 3, we approximate the dc curve in this figure by the equation

$$I = I_o\left(\exp \frac{V}{\zeta V_T} - 1\right).$$

Resulting values are $I_o \approx 0.09$ mA/cm^2 and $\zeta V_T \approx 5.2$ mV.

In order to estimate the value of the resistivity of the membrane within an order of magnitude, we calculated the values at 0.5 mA/cm^2 or 9 mV and assumed a thickness for the membrane of 200 Å. This yields $\rho \approx 9 \times 10^5\ \Omega \cdot$ m. Similarly, an estimate of the dielectric constant for the membrane was obtained by assuming a thickness d_3 of 200 Å and a value of $c = 0.5$ μF/cm^2. This yields $\varepsilon' \approx 11\varepsilon_o$. Correspondingly,

$$Y = \frac{A}{d}(\sigma + j\omega\varepsilon') = \frac{A}{d_3}(1.1 \times 10^{-6} + j\omega 10^{-10}).$$

The frequency at which σ is approximately equal to $\omega\varepsilon'$ is 1.8 kHz, which indicates that at the RF's of interest the dominant term for current transmitted through a membrane is controlled by the dielectric constant. This is significantly lower than ω for $|\varepsilon'\zeta\omega| = 1$ from Guy's tables.

In order to get an estimate of the orders of magnitude involved, there are two cases which are worth examining numerically. The first is a case associated with high pulsed fields such as might be obtained in the vicinity of a radar. In this case, let us assume we have a field of 1 kV/cm in free space incident on the biological material, which is a high-water-content dielectric material with a membrane at a right angle to the field. The corresponding value of the field in the membrane is 2.26×10^3 V/cm, and, if a 200-Å thick membrane is assumed along with a dc value for the nonlinearity, $V_m = 4.52$ mV. The corresponding shift in dc concentration is approximately 19 percent. This also leads to a rectified ion current of approximately 17 μA/cm^2 or 1.06×10^{14} ions/cm^2. To translate into units that are

approximate for a typical cell, we assume a surface area of 10 μm on the side or $A = 10^{-6}$ cm^2. This leads us to ion currents of approximately 10^8 ions per second. We know from experiments on chemotaxis [14] that as few as a few thousand molecules may be important in affecting the response of a white blood cell. Thus it is not inconveivable that exposures at this level of the order of 10 μs could mean significant biological changes in the performance of a cell.

The 1-kV/cm field for a 10-μs exposure would lead to a temperature rise in the high-water-vapor tissue of less than one degree so that the chemical effect could be more important than the thermal one.

The second case of numerical interest is at 10 mW/cm^2. At this power level, the field strength in free space is 1.94 V/cm and the field strength in a high-water dielectric medium enclosed membrane is 4.4 V/cm. The corresponding voltage drop across the membrane is approximately 9 μV. This leads to a concentration shift of approximately one part in 10^6 and a rectified current component $I_{ac} \approx 6 \times 10^{-11}$ amp/cm^2. This in turn corresponds to an ion flow of approximately 4×10^8 ions/cm$^2 \cdot$ s or 400 ions/s for our cell with a 10^{-6}-cm^2 surface area. Thus to obtain 500–1000 molecules per cell would require an exposure of a few seconds. The numbers involved in the equilibrium shift across the barrier and the small size of these ion currents makes it hard to estimate whether or not they are important, particularly in the presence of thermal phenomena and other regulatory feedback processes. However, these nonlinearities provide a mechanism for possible biological change.

The second kind of nonthermal interaction involves the alignment of long chain molecules along electric field lines. An electric field applied to a molecule with a dipole moment or an induced dipole moment produces a torque which tends to align the molecule along the field line. The torque M is applied to the molecule by the field and is given by

$$M = -|m|E \sin \theta$$

where $|m|$ is the magnitude of the dipole moment and θ is the angle between the axis of the dipole and the electric field E. For a fixed dipole

$$|m| = qds$$

where q is the charge and ds is the separation. In the case of an induced dipole moment,

$$|m| = |\alpha E|$$

where α is a property of the molecule.

The energy required to rotate a molecule is proportional to the $|mE|$, and the proportionality constant depends upon the average angular distribution of the dipole moments with respect to the field and whether or not it is an induced or fixed dipole moment. The threshold field for observing an orientation phenomenon is dependent upon the restraining forces in the material. In a membrane, the large fields that naturally exist across cell walls are such that we would expect the dipole moments to be aligned already. Thus we would expect to see changes in the orientation of these molecules only when the membrane is close to the breakdown potential or when the ac fields are of the order of magnitude of the dc fields (approximately 10 kV/cm). However, in a liquid, the threshold voltages are much lower as all that is required in this case is to overcome the forces associated with Brownian motion or to have an energy of an orientation somewhat greater than KT. We have observed shifts in the birefringence of blood plasma with threshold fields of approximately 100 V/cm [15]. A complete description of this work will be reported in another paper.

An alternate way of looking at the effects of the dipole moments is to describe them in terms of the effective dielectric constant. In the case of the induced dipole moment, the effective dielectric constant $\varepsilon = \alpha$/volume. In the case of the fixed dipole constant $|m|/E \cdot$ volume.

The importance of the alignment of long chain molecules in biological fluids is not known at this time. However, it is reasonable to expect that an ordered system would have somewhat different physical and chemical properties than a random distribution. For example, long chain molecules might diffuse through a series of pores more rapidly if they were ordered end on than if they are ordered randomly. Variations in chemical reaction rates with orientation have been observed in molecular beam experiments [16].

Conclusion

Two mechanisms for nonthermal effects have been presented, and it has been shown that the size of the currents which can result from ac electric fields are large enough so that the number of charged ions or charged molecules which can be moved across a membrane are large enough to potentially cause biological changes in the periods of time which are of the order of exposures which are currently being studied.

Additionally, we have observed that long chain molecules can be oriented in moderate electric fields and a model for the torques applied to these molecules was presented.

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Internal EM Field and Absorbed Power Density in Human Torsos Induced by 1–500-MHz EM Waves

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Abstract—**Numerical results on the internal electromagnetic (EM) field and absorbed power density inside a human torso induced by EM waves of frequencies ranging from 1 to 500 MHz and of both vertical and horizontal polarizations are presented. The induced fields inside the torso are shown to be dependent on the frequency and the torso geometry. Theoretical results are obtained based on the tensor integral equation method and some theoretical predictions are compared to existing experimental results.**

I. Introduction

In the study of biological effects induced by electromagnetic (EM) waves and in medical applications utilizing EM radiation, it is important and desirable to know the internal EM field and absorbed power density induced by an EM field inside a human torso.

The existing methods commonly used to predict the induced EM field inside a biological body are based on simplified models of a plane slab [1], [2], a sphere [3]–[5], a cylinder [6], and spheroids [7], [8]. Although these simple models provide estimates of the internal EM fields, the results have limited applicability to biological bodies with irregular shapes illuminated by an EM wave with a frequency higher than the VHF range.

This paper presents numerical results on the internal EM field and absorbed power density inside a human torso induced by EM waves of frequencies ranging from 1 to 500 MHz and of both vertical and horizontal polarizations. Numerical results are obtained based on a recently developed "tensor integral equation method" [9]. This method was found to be quite powerful in quantifying the induced EM field inside an arbitrarily shaped biological body such as a human torso.

The accuracy of this method has been verified theoretically by convergence tests [9] and experimentally by tests conducted in scaled models containing saline solution [10].

For the reader's benefit, the tensor integral equation method and its experimental verification are briefly outlined in Section II. Numerical results on the internal EM field and the absorbed power density in human torsos of various shapes induced by EM waves of various frequencies with different polarizations are presented in Section III.

II. The Theoretical Method and Its Accuracy

Since the tensor integral equation method [9] has been published, only two key equations are quoted here.

If a finite biological body of arbitrary shape, with permit-

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