

## A Mechanism for Action of Oscillating Electric Fields on Cells

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**The biological effects of electromagnetic fields have seriously concerned the scientific community and the public as well in the past decades as more and more evidence has accumulated about the hazardous consequences of so-called “electromagnetic pollution.” This theoretical model is based on the simple hypothesis that an oscillating external electric field will exert an oscillating force to each of the free ions that exist on both sides of all plasma membranes and that can move across the membranes through transmembrane proteins. This external oscillating force will cause a forced vibration of each free ion. When the amplitude of the ions’ forced vibration transcends some critical value, the oscillating ions can give a false signal for opening or closing channels that are voltage gated (or even mechanically gated), in this way disordering the electrochemical balance of the plasma membrane and consequently the whole cell function.** © 2000 Academic Press

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On both sides of every cell membrane, there are free ions (mainly  $K^+$ ,  $Na^+$ ,  $Cl^-$ ,  $Ca^{2+}$ ) which (a) control the cell volume, by causing osmotic forces that are responsible for the entrance or exit of water, (b) play an important role in different metabolic cell processes—signal transduction processes, and (c) create the strong electric field (about  $10^7$  V/m) that exists between the two sides of all cell membranes.

Of course, this involves not only the plasma membrane (which surrounds the whole cell) but also the inner cell membranes, for example, the membranes of mitochondria, chloroplasts, endoplasmic reticulum, or Golgi apparatus.

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Ion flux through cell membranes is caused by forces due to concentration and voltage gradients between the two sides of the membrane. Under equilibrium conditions, the net ion flux through the membrane is zero and the membrane has a voltage difference,  $\Delta\Psi = \Psi_o - \Psi_i$ , between its external and internal surface, with the internal negative in relation to the external, which is called the “membrane’s electrical potential.” This potential difference across the plasma membrane of animal cells varies between 20 and 200 mV (1–4).

Therefore, the intensity,  $E_m = \Delta\Psi/s$ , of the transmembrane electric field (assuming  $s = 100 \text{ \AA} = 10^{-8}$  m, the width of the membrane, and  $\Delta\Psi = 100 \text{ mV} = 0.1$  V) has a value on the order of  $10^7$  V/m.

The “leak” channels of  $K^+$  ions (and the channels of the other cations), which of course are passive transport proteins, seem to be the main cause for the existence of the membrane’s electrical potential (1), in cooperation with the  $K^+-Na^+$  pump, while the rest of the electrogenic pumps contribute to a smaller degree (2, 4). It is also the majority of negative-charged lipids, on the inner surface of the lipid bilayer, in all membranes, that contribute (5).

The potential difference across the plasma membrane, under equilibrium conditions, caused by a certain type of ion, is given by the Nernst equation

$$\Psi_o - \Psi_i = -\frac{RT}{zF_c} \ln \frac{C_o}{C_i},$$

where  $\Psi_o$  and  $\Psi_i$  are the electrical potential on the external and internal surface of the membrane, respectively;  $R$  is the “global constant of the perfect gases,”  $T$  is the absolute temperature (K),  $z$  is the ion’s electric charge (in electrons) or the ion’s valence,  $F_c$  is Faraday’s constant, and  $C_o$  and  $C_i$  are the concentrations of the ions on the external and internal side of the membrane, respectively, at equilibrium, in other words, when the net flux of the ion is zero.

The total electrical potential difference across the membrane will be the sum of the contributions from all the existing ions, restoring the final balance between osmotic and electrical forces.

An external electric field will exert forces on these ions, with two possible results: (1) polarization of constant magnitude and direction in the cell if the field is static, and (2) forced vibration of the above free ions if the field is an oscillating one. Our work is focused on this second case, which is the most complicated.

As is evident from the above, in the present theoretical model we assume that the primary site of interaction between an external electromagnetic field and the cell is the plasma membrane. As for the inner cell membranes, we consider that the free-ion layer which surrounds the plasma membrane (and the whole cell) shields (at least to some degree) the cytoplasm, the inner cell organelles and inner membranes, from external fields.

Let us assume, for simplicity, that the oscillating electric field is an alternating (harmonic) one. An alternating, external electric field will exert a periodic force on every ion on both sides of the plasma membrane, as well as on the ions within channel proteins, while they pass through them. This external periodic force will cause on every ion a forced vibration.

When the amplitude of the ions vibrational movement transcends some critical value, the oscillating ions can give false signals for the opening or closing of channel proteins that are voltage-gated (or even mechanically gated). Such an event would disorder the membrane's electrochemical balance and, consequently, the whole cell function.

#### MECHANISM OF ACTION OF AN ALTERNATING ELECTRIC FIELD ON CELLS

*Forces exerted on a free ion.* Let us consider an external, alternating electric field of intensity  $E = E_0 \sin \omega t$  and circular frequency  $\omega = 2\pi\nu$  ( $\nu$ , the frequency). [The electromagnetic fields we deal with are mostly produced artificially and their frequencies range from 0 to  $3 \times 10^{11}$  Hz.]

This external field will exert a periodic force of magnitude  $F_1 = Ezq_e = E_0 zq_e \sin \omega t$  on every free ion that can pass across the plasma membrane, through the transmembrane proteins ( $z$ , the ion's valence and  $q_e = 1.6 \times 10^{-19}$  C, the electron's charge). This force will displace the ion, let us say at a distance  $x$  from its initial position, as this was defined from the electrochemical equilibrium across the membrane.

Additionally, assuming the ion was initially in a state of electrochemical equilibrium, which will be distorted because of the displacement, it will receive from the developed electrochemical gradient a restoration force  $F_2 = -Dx$ , which we can reasonably assume, at least for small displacements, to be proportional to the

displacement distance,  $x$ . Such an assumption is very logical, since every system in a state of equilibrium would exert a restoration force if the equilibrium were slightly distorted and this restoration force would be of opposite direction to and proportional to the magnitude of the distortion. The distortion, in our case, is the displacement  $x$ .  $D$  is the restoration constant, which we know from harmonic oscillations is  $D = m_i \omega_0^2$ , where  $m_i$  is the ion's mass and  $\omega_0 = 2\pi\nu_0$ , with  $\nu_0$  the ion's oscillation self-frequency if it were left free after the displacement  $x$ . ["Self-frequency" of an oscillating system is the frequency of the system's spontaneous oscillation.] In our case, as we shall see, this restoration force is very small compared to the other forces and does not play any important role.

Finally, we consider that the ion, as it moves, receives a damping force,  $F_3 = -\lambda u$ , where  $u$  is the ion's velocity and  $\lambda$  is the attenuation coefficient for the ion's movement, which depends upon the internal friction coefficient (viscosity),  $n$ , of the medium in which the ions move (that is, the cytoplasm, the extracellular medium, and the channel proteins) and the radius  $\alpha$  of the supposed spherical ion. [In more detail,  $\lambda = 6\pi n\alpha$  and  $F_3 = -6\pi n\alpha u$  (Stokes force).]

Let us calculate the attenuation coefficient  $\lambda$ : Assuming that the viscosity of the medium in which the ions move is that of water at 37°C,  $n = 7 \times 10^{-4}$  kg/m · s, and the ion's radius is  $\alpha \cong 10^{-10}$  m, we get  $\lambda = 6\pi n\alpha \Rightarrow \lambda \cong 10^{-12}$  kg/s. [The attenuation coefficient  $\lambda$  can also be calculated from "patch-clamp" conductivity measurements. In the case of  $\text{Na}^+$  ions, moving through open  $\text{Na}^+$  channels, it has the value  $\lambda \cong 6.4 \times 10^{-12}$  kg/s (1).]

*Forced-vibration equation for a free ion.* The ion, because of the above forces, will obtain an acceleration  $a$  and its movement equation (let us say for the  $x$  direction) will be

$$m_i a = -\lambda u - Dx + E_0 zq_e \sin \omega t \Rightarrow m_i \frac{d^2 x}{dt^2} + \lambda \frac{dx}{dt} + m_i \omega_0^2 x = E_0 zq_e \sin \omega t. \quad [1]$$

Equation [1] is the movement equation of a free ion in the vicinity of a cell's plasma membrane under the influence of an external, alternating electric field.

*Solution of Equation [1].* Equation [1] is a second-order linear differential equation with constant coefficients and has a particular solution of the type

$$x_p = A_1 \cos \omega t + A_2 \sin \omega t$$

or

$$x_p = A \cos(\omega t - \varphi), \quad [2]$$

where  $A$  is the amplitude of the forced vibration and  $\varphi$  is the phase difference between the forced vibration and the external, periodical force.

From Eqs. [1] and [2], after operations (method of undetermined coefficients), we get

$$A = \frac{E_0 z q_e}{\sqrt{m_i^2(\omega^2 - \omega_0^2)^2 + \lambda^2 \omega^2}} \quad [3]$$

and

$$\tan \varphi = \frac{m_i(\omega^2 - \omega_0^2)}{\lambda \omega}. \quad [4]$$

The general solution of Eq. [1] will be the sum of the particular solution [2] and the general solution  $x_0$ , of the corresponding homogeneous differential equation,

$$m_i \frac{d^2 x}{dt^2} + \lambda \frac{dx}{dt} + m_i \omega_0^2 x = 0, \quad [5]$$

which is

$$x_0 = C_1 e^{\xi_1 t} + C_2 e^{\xi_2 t}, \quad [6]$$

where  $C_1$  and  $C_2$  are constants that can be calculated from the initial conditions if we apply them to the general solution and  $\xi_1$  and  $\xi_2$  are the roots of the corresponding "characteristic equation" of Eq. [5]:

$$m_i \lambda^2 + \lambda \xi + m_i \omega_0^2 = 0. \quad [7]$$

The discriminant of the "characteristic equation" [7] is

$$\Delta = \lambda^2 - 4m_i^2 \omega_0^2$$

and its roots are

$$\xi_{1,2} = \frac{-\lambda \pm \sqrt{\lambda^2 - 4m_i^2 \omega_0^2}}{2m_i}.$$

Theoretically,  $\Delta$  can be positive, negative, or even zero, and then the homogeneous differential equation [5] represents a free and damping oscillation, with respectively strong, weak, or critical attenuation.

All the experimental evidence of cytosolic free ions' spontaneous oscillations, as well as membrane potential spontaneous oscillations, in many different types of cells shows that the frequencies of such oscillations do not transcend a value of 1 Hz. Most of the oscillations of this kind display frequencies ranging from 0.016 to 0.2 Hz (6–11). We think it is very reasonable to assume

that the frequencies of these spontaneous ionic oscillations represent (or they are very close to) the ions' self-frequencies,  $\nu_0 = \omega_0/2\pi$ .

Hence, for a typical ion, let us say  $\text{Na}^+$ , where  $m_i = 3.8 \times 10^{-26}$  kg and with  $\lambda = 10^{-12}$  kg/s, we get  $\lambda \gg 2m_i\omega_0$ .

Then  $\Delta > 0$  and we will have a "strong" attenuation ("overdamping") for  $x_0$ . The roots  $\xi_1, \xi_2$  of Eq. [7] in this case will be real, unequal, and negative (the quantities  $\lambda, m_i$ , and  $\omega_0$  are positive). Because  $\xi_1, \xi_2 < 0$ , the solution of [5],  $x_0 = C_1 e^{\xi_1 t} + C_2 e^{\xi_2 t}$ , theoretically, will decrease to zero as time  $t$  increases. As we shall see, this does not happen actually because  $\xi_1 \cong 0$ .

According to above values for  $m_i, \lambda, \omega_0$ , and  $\omega$ , the amount  $m_i^2(\omega^2 - \omega_0^2)^2$  in Eq. [3] is negligible compared to the amount  $\lambda^2 \omega^2$ . So practically, the amplitude  $A$  of the particular solution is

$$A = \frac{E_0 z q_e}{\lambda \omega} \quad [8]$$

(just as in a case of resonance, when  $\omega = \omega_0$ ).

As we shall see, this finally found to be the amplitude of the ion's forced vibration.

Also, the amount  $m_i(\omega^2 - \omega_0^2)$  is very small compared to the amount  $\lambda \omega$  and from Eq. [4], we get  $\tan \varphi \cong 0$ . In addition,  $\tan \varphi \geq 0$ , for  $\omega \geq \omega_0$ . Hence,  $\varphi \cong 0$ .

Thus, the particular solution [2] becomes

$$x_p = \frac{E_0 z q_e}{\lambda \omega} \cos \omega t. \quad [9]$$

As we said, the general solution of Eq. [1] is  $x = x_p + x_0$ . Substituting  $x_0$  from [6] and  $x_p$  from [9], the general solution of [1] becomes

$$x = \frac{E_0 z q_e}{\lambda \omega} \cos \omega t + C_1 e^{\xi_1 t} + C_2 e^{\xi_2 t}. \quad [10]$$

For a reasonable value of  $\nu_0 = 0.1$  Hz, we can calculate that  $\xi_1 \cong 0$  and  $\xi_2 \cong -2.63 \times 10^{13} \text{s}^{-1}$  (in reality,  $\xi_1 \cong -1.5 \times 10^{-14} \text{s}^{-1}$ ).

If we accept as initial conditions (for  $t = 0$ )  $x_{t=0} = 0$  and  $(dx/dt)_{t=0} = u_0$ , then from [10] we get the equations

$$C_1 + C_2 = -\frac{E_0 z q_e}{\lambda \omega} \quad \text{and} \quad C_1 \xi_1 + C_2 \xi_2 = u_0,$$

from which we get

$$C_1 \cong -\frac{E_0 z q_e}{\lambda \omega} \quad \text{and} \quad C_2 \cong -u_0 4 \times 10^{-14}.$$

For any reasonable value of  $u_0$  (the maximum ion velocity),  $C_2 e^{\xi z t} \cong 0$ . (We think that a reasonable value for  $u_0$  would be about 0.25 m/s, a value that we calculated for  $\text{Na}^+$  ions moving through the  $\text{Na}^+$  channel.<sup>2</sup>)

Thus

$$x_0 \cong -\frac{E_0 z q_e}{\lambda \omega} \quad [11]$$

( $x_0$  in m,  $E_0$  in  $\text{V} \cdot \text{m}^{-1}$ ,  $\omega$  in Hz). In reality  $x_0$  is multiplied by a negligible factor which makes it tend very slowly to zero.

Substituting in [10], we get finally the general solution of Eq. [1]:

$$x = \frac{E_0 z q_e}{\lambda \omega} \cos \omega t - \frac{E_0 z q_e}{\lambda \omega} \quad [12]$$

As we can see,  $x_0$  displaces the ion's forced vibration, at a constant distance

$$-\frac{E_0 z q_e}{\lambda \omega}$$

from its initial equilibrium position, but actually has no effect on the vibrational term, which is

$$\frac{E_0 z q_e}{\lambda \omega} \cos \omega t.$$

So, actually,  $x_0$  plays no role in the ion's vibrational movement.

Thereby, the actual situation is not dependent on  $x_0$  and consequently is not dependent on any initial conditions. The actual vibrational movement of the free ions is described by the equation

$$x = \frac{E_0 z q_e}{\lambda \omega} \cos \omega t. \quad [13]$$

<sup>2</sup> Calculation of the attenuation coefficient,  $\lambda$ , of sodium ions moving inside sodium ion channels: From conductivity measurements on  $\text{Na}^+$  channels with the patch clamp technique, it is known that the intensity of electric current through an open channel of sodium ions is on the order of  $4 \times 10^{-12}$  A, when the transmembrane voltage is 100 mV. This means that  $2.5 \times 10^7$   $\text{Na}^+$  ions per second flow through an open channel (32). Assuming that the channel's length is equal to the membrane's width, let us say  $s = 100 \text{ \AA} = 10^{-8}$  m, and that the ions move through the channel in single file (21), then the transit time of every  $\text{Na}^+$  ion through the  $\text{Na}^+$  channel is on the order of  $10^{-7}$  s and the ions' velocity through the channel is  $u = 2.5 \times 10^7 \times 10^{-8}$  m/s  $\Rightarrow u = 0.25$  m/s. In such a case, on every  $\text{Na}^+$  ion is exerted only the force of the transmembrane electric field,  $E_m z q_e$  ( $E_m \approx 10^7$  V/m,  $z = 1$ ) and the damping force  $-\lambda u$ . So under equilibrium conditions,  $\lambda u = E_m q_e \Rightarrow \lambda = E_m q_e / u \Rightarrow \lambda \cong 6.4 \times 10^{-12}$  kg/s.

Equation [13] represents an harmonic oscillation of constant amplitude, independent of any initial conditions.

As we can see, the amplitude of the forced vibration is given by Eq. [8] and the forced vibration is in phase with the external periodical force.

## RESULTS AND DISCUSSION

Thus, an external alternating electric field will cause on every free ion in the vicinity of the plasma membrane a forced vibration of the same frequency as that of the external field and with vibrational amplitude inversely proportional to the frequency. The ions will oscillate in phase with the field.

The oscillating ions will then represent a periodical displacement of electric charge, able to exert forces on every fixed charge of the membrane, like the charges on the voltage sensors of voltage-gated channels. Hence, the oscillating ions may be able to upset the membrane's electrochemical balance by gating such channels.

Also, ions already inside voltage-gated channels, while they pass through them, are able, because of the forced vibration, to move into position other than the one if there were no external field, giving with their charge a false signal for gating such channels.

Voltage-gated channels are the  $\text{K}^+$  leak channels and the  $\text{Na}^+$  leak channels as well as leak channels of other cations. The state of these channels (open or closed) is determined from electrostatic interaction between the channels' voltage sensors and the transmembrane voltage. They interconvert between the open and the closed state when the electrostatic force acting on the electric charges of their voltage sensors transcends some critical value. The voltage sensors of these channels are four symmetrically arranged, transmembrane, positively charged helical domains, each designated S4 (12–17).

It is known that changes of about 30 mV in membrane potential are able to gate this kind of channel (18–20).

We can prove that a single ion's displacement  $\partial r$ , of  $10^{-12}$  m, in the vicinity of S4 can cause a change of 30 mV, in the membrane's potential:

The intensity of the transmembrane electric field is

$$E_m = \frac{\Delta \Psi}{s}. \quad [14]$$

Also

$$E_m = \frac{F}{q}, \quad [15]$$

where F in this case is the force acting on an S4 domain and q is the effective charge on S4, which we assume to have a value (18)

$$q = 1.7 q_e. \quad [16] \quad \text{kg/s and at a human body temperature } 37^\circ\text{C or } T = 310 \text{ K), according to the relation}$$

From Eqs. [14] and [15], we get:

$$F = \frac{\Delta\Psi}{s} q \Rightarrow \partial F = \partial\Delta\Psi \frac{q}{s} \quad [17]$$

For  $\partial\Delta\Psi = 30 \text{ mV}$ ,  $s = 10^{-8} \text{ m}$ , and substituting  $q$  from [16], Eq. [17] gives  $\partial F = 8.16 \times 10^{-13} \text{ N}$ .

This is the force on the voltage sensor of a voltage-gated channel required normally to interconvert the channel between a closed and an open state.

The force acting on the effective charge of an S4 domain, via an oscillating, single-valence free cation, is

$$F = \frac{1}{4\pi\epsilon\epsilon_0} \cdot \frac{q \cdot q_e}{r^2} \Rightarrow \partial F = -2 \cdot \frac{1}{4\pi\epsilon\epsilon_0} \cdot \frac{q \cdot q_e}{r^3} \partial r \Rightarrow \partial r = \frac{2\pi\epsilon\epsilon_0 \partial F \cdot r^3}{q \cdot q_e} \text{ (ignoring the minus sign).} \quad [18]$$

This is the displacement of a single cation in the vicinity of S4 able to generate the force  $\partial F$ , where  $r$  is the distance between a free ion and the effective charge on S4 domain, which can be conservatively taken as 1 nm (12, 16, 20).  $\epsilon_0 = 8.854 \times 10^{-12} \text{ N}^{-1} \cdot \text{m}^{-2} \cdot \text{C}^2$  is the dielectric constant of vacuum. The relative dielectric constant  $\epsilon$  can have a value of 80 for a water-like medium (cytoplasm or extracellular space) or a value as low as 4 for ions moving inside channel proteins, (5).

The concentration of free ions on both sides of mammalian cell membranes is lower than 1 ion per  $\text{nm}^3$  (4). That is why we conservatively calculate  $\partial r$  for one single-valence cation interacting with an S4 domain. If two or more single-valence cations interact (in phase) with S4 domain, from 1 nm distance,  $\partial r$  decreases proportionally. As for ions moving inside channel proteins, it is very logical to assume that they move in single file (21).

From Eq. [18] and for  $\partial F = 8.16 \times 10^{-13} \text{ N}$ , we get

$$\partial r \cong 0.8 \times 10^{-10} \text{ m (for } \epsilon = 80)$$

and

$$\partial r \cong 4 \times 10^{-12} \text{ m (for } \epsilon = 4).$$

As we can see, a single cation's displacement of only few picometers from its normal position is able to interconvert voltage-gated channels between open and closed states (for cations moving already through channels).

Naturally, free ions move because of thermal activity in  $\delta t = 10^{-8} \text{ s}$  at distance  $X_{kT} \cong 5 \times 10^{-9} \text{ m}$  (in a medium with the viscosity of water,  $\lambda = 6\pi\eta\alpha \cong 10^{-12}$

$$X_{kT} = \sqrt{\frac{2kT\delta t}{6\pi\eta\alpha}} \Rightarrow X_{kT} \cong 10^{-4} \cdot \sqrt{\delta t}$$

( $X_{kT}$  in m,  $\delta t$  in seconds, and  $k = 1.381 \times 10^{-23} \text{ J} \cdot \text{K}^{-1}$  is the Boltzmann constant). It has been claimed that thermal motion masks the motion of the free ions caused by an external electric pulse if the displacement caused by the field is smaller than the displacement caused by thermal motion (22). But thermal motion is a random motion in every possible direction, different for every single ion, causing no displacement of the ionic "cloud," whereas forced vibration is a coherent motion of all the ions together in phase. That is why thermal motion does not play an important role in the gating of channels or in the passing of ions through them.

Therefore, any external field which can cause a forced vibration of the ions with amplitude  $A \geq 4 \times 10^{-12} \text{ m}$  is able to influence the function of a cell. Substituting  $A$  from Eq. [8] in the last relation, it comes that a bioactive, external, oscillating electric field of intensity amplitude  $E_0$  and circular frequency  $\omega$  which causes a forced vibration on every single-valence ion ( $z = 1$ ) must satisfy the relation

$$\frac{E_0 q_e}{\lambda \omega} \geq 4 \times 10^{-12} \text{ m.}$$

Since we adopted the smaller value for  $\partial r$  ( $\cong 4 \times 10^{-12} \text{ m}$ ), which counts for cations moving already inside channels ( $\epsilon = 4$ ), we will use the value for  $\lambda$  that we calculated also for cations moving inside channels ( $\lambda \cong 6, 4 \times 10^{-12} \text{ kg/s}$ ) (see footnote 1). Thereby, the last relation becomes

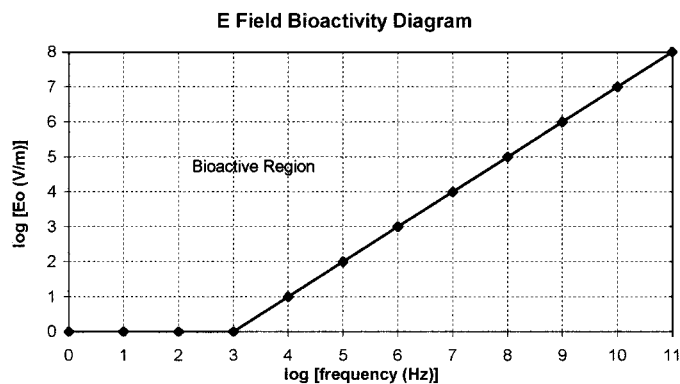
$$E_0 \geq \omega \cdot 1.6 \times 10^{-4} \quad [19]$$

or

$$E_0 \geq \nu \times 10^{-3} \text{ (}\nu \text{ in Hz, } E_0 \text{ in V/m).}^3 \quad [20]$$

Relation [20] gives the bioactive intensity amplitudes  $E_0$  of an oscillating electric field in response to the frequency  $\nu$  of the field. Figure 1 represents rela-

<sup>3</sup> If the external field is measured by ordinary field meters, which count mean power (their indication depends on the root-mean-squared intensity of the current induced to the instrument), then the indication corresponds in the root mean square (*rms*) value of the field intensity,  $E_{\text{rms}}$ , which is  $E_{\text{rms}} = E_0/\sqrt{2}$  (since the intensity  $E$  of the field is proportional to the induced voltage  $\Psi = \Psi_0 \sin \omega t$ , for which the counted rms value is  $\Psi_{\text{rms}} = \Psi_0/\sqrt{2}$ ). In this case, Eq. [8] becomes  $A = (E_{\text{rms}} \sqrt{2} z q_e)/(\lambda \omega)$  and relation [20] becomes  $E_{\text{rms}} \geq \nu/\sqrt{2} \times 10^3$  ( $\nu$ ,  $\omega$  in Hz,  $E_0$ ,  $E_{\text{rms}}$  in V/m).



**FIG. 1.** The line represents the relation  $E_0 = \nu \times 10^{-3}$  in arbitrary logarithmic scale. The region above the line (with the line included) represents the bioactive combinations ( $\nu$ ,  $E_0$ ) between the frequency and the intensity of an oscillating electric field that satisfy the relation  $E_0 \geq \nu \times 10^{-3}$ .

tion [20] in arbitrary logarithmic scale (in other words, the equivalent relation  $\log E_0 \geq \log \nu - 3 \geq 0$  [21]).

As is evident from the E field bioactivity diagram (Fig. 1), many combinations of ( $\nu$ ,  $E_0$ ) values are able to cause biological effects on cells. According to the diagram, oscillating electric fields with frequencies lower than  $10^3$  Hz (ELF fields) can be bioactive, even at very low intensities of several V/m. As the frequency of the field increases more than  $10^3$  Hz, the minimum intensity of the field able to cause biological effects on cells with the described mechanism increases linearly with frequency. An RF field of  $10^8$  Hz must have an intensity amplitude of at least  $10^5$  V/m, or 1 kV/cm, while a microwave field of  $10^{10}$  Hz must have an intensity amplitude of at least  $10^7$  V/m, or 100 kV/cm, in order to have biological effects.

The E field bioactivity diagram above gives the ( $\nu$ ,  $E_0$ ) combinations which can be bioactive on cells. As for whole organisms, it has been claimed that the conductivity of their bodies shields the interior of the body from external electromagnetic fields, especially at low frequencies (23, 24). We would not be very sure that what is valid for a piece of dielectric material with the same conductivity would be as valid for living organisms and humans, especially, even more when there is quite strong evidence (25–30) that electromagnetic fields of all frequencies (especially at ELF and microwave frequencies) and even at very low intensities can be bioactive on cells and whole organisms.

Therefore, we believe that the present theoretical model provides a possible mechanism for action of oscillating electromagnetic fields on cells in actual biological situations.

It seems possible to us that oscillating ions during forced vibration will also exert mechanical forces—pressure on the plasma membrane able to upset the membrane's electrochemical balance, under certain conditions, by opening or closing mechanically gated

channel proteins, like some  $\text{Ca}^{+2}$  influx channels (31). But of course this can be the subject of separate research, based on the present theoretical model of the ions' forced vibration which we developed in this paper.

In any case, the irregular gating of ion channels caused by the forced vibration of the free ions, caused by external oscillating electromagnetic fields, is a fact that could upset the electrochemical balance of the plasma membrane and, consequently, the whole cell function.

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