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Comments

Comments on the Use of Electromagnetic Fields in Biological Studies

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Summary. For biological or cellular experiments using electromagnetic fields it is essential that the parameters defining the field be accurately specified if the results are to be meaningful and are to be compared with the same experiment conducted in a different laboratory. The interaction of living systems with electric and magnetic fields can come only through forces exerted on the charges on the system. If the charges are stationary the only origin of the force is the electric field. The electric field may be established by charge distributions, as in "capacitative plate" experiments, or by time-varying magnetic fields. A geometry commonly used to produce time-varying magnetic fields consists of a pair of coaxial coils each of equal radius and separated by a distance about equal to the radius. The electric field induced by a varying current in such a pair of coils varies both in space and in time. The field is always zero on the axis of symmetry, and increases to a maximum near the radius of the coils. The strength is proportional to the time-rate-of-change of the current in the coil, which depends not only on the amplitude and shape of the voltage pulse applied to the coil but also on the resistance and inductance of the coil. The purpose of this note is to describe how the important physical parameters may be determined.

Key words: Pulsed electromagnetic fields — Capacitative plate experiments — Osteogenesis — Wound healing.

There is now an extensive literature on the application of both steady and time varying electric and magnetic fields to cellular systems both *in vivo* and *in vitro*. Work in the field will expand due to the exciting results obtained to date. Two examples will illustrate the point.

It has been determined experimentally that appropriate pulsed magnetic fields [1] as well as electric fields [2] promote osteogenesis and wound healing, and that dc electric fields cause cultured epithelial cells [3, 4] and cultured neural crest cells [5] to elongate perpendicularly to the field and migrate along the field. The fact that the exact mechanism or mechanisms involved in these phenomena is not understood has led to a flurry of activity. Serious quantitative study is now being given, for example, to understanding the enhanced ion transport across cellular membranes induced by the electric field associated with a changing magnetic field.

In many of the research publications describing results of the application of magnetic and electric fields to biological systems the descriptions of the experimental arrangements do not permit determining the critical physical parameters. As a result it is not possible to compare quantitatively the results of an experiment carried out in one laboratory with those from another laboratory. In a recent editorial [1] Bassett emphasizes the problem: ". . . as this field of endeavor reaches a new level of scientific and clinical maturity, it is increasingly important to employ terms which, through their precision have universal comprehensibility . . ." and (it is necessary that) "biologists, biochemists, dentists, and physicians, among others, overcome a natural reluctance to deal with electrical principles on a routine working basis."

The purpose of this note is to describe for "biologists, biochemists, dentists and physicians" how to determine the one important parameter, the electric field, associated with the electric and magnetic field configurations most commonly used and to encourage its use when describing an experiment. To do this properly it is necessary to begin with a description of how electromagnetic fields interact with biological systems. Because my biologically and

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medically oriented colleagues find the mathematical and physical descriptions difficult to digest the details are given in a paper to be published elsewhere (Parkinson WC, accepted for publication).

The interaction of living systems with electric and magnetic fields comes through forces exerted on the electric charges contained in the atoms, molecules, and larger components of the system. The forces arise through the interaction of these charges with the applied or induced electric field E. The magnetic field B exerts a force only if the charge is moving. At the very low velocities existing at the normal biological temperatures the magnetic force may be ignored. In any given experiment there is a simple way to determine that the magnetic force can in fact be ignored. This is described below. The magnetic field itself is not of interest and a *changing* magnetic field is of interest only in that it induces an electric field. The electric field that exerts the force, does *not* necessarily bear a simple relationship to the changing magnetic field. The magnitude of the force on an electron, an ion, or any charged object in an electric field is $F = qE$ where q is the magnitude of the charge and E is the strength of the electric field (which may well be varying in time). The direction of the force is in the direction of the electric field E for a positive charge and opposite for a negative charge. A charge q in a magnetic field B will experience a force $F = qvB\sin\theta$ where v is the magnitude of the velocity of the charge and θ is the angle between the direction of v and the direction of B. Thus if v is zero the force due to B is zero. The interaction of electric dipoles with E and magnetic dipoles with B are included in the above statements.

We look first at the induced electric fields produced by time varying magnetic fields, and then at electric fields produced in "capacitive plate" type arrangements.

Magnetic Fields and Induced Electric Fields

General Remarks

Magnetic fields are produced by the flow of charge, that is by currents. This is true even for permanent magnets. A geometric form frequently used in PEMF (pulsed electromagnetic field) experiments consists of two identical, coaxial coils separated a distance about equal to their radius, similar to the well-known Helmholtz configuration (Fig. 1). We will assume there is no ferromagnetic material such as iron in the vicinity. Other coil shapes have been used but their use in research is to be discouraged because it is not a simple matter to determine the

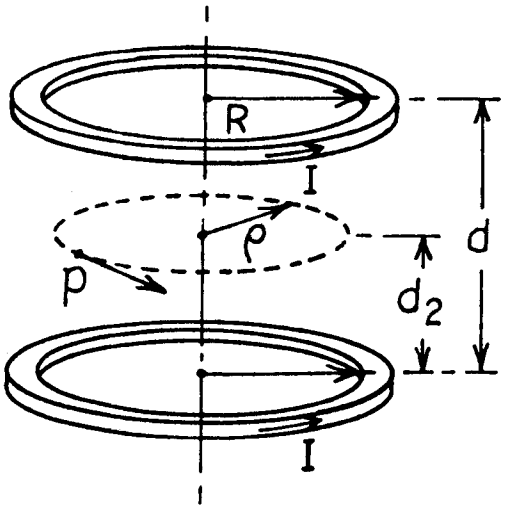


Fig. 1. Geometry of Helmholtz-like coils. The two identical coaxials each of radius R and separated a distance d equal to R carry equal currents. The coils usually are wound with several turns of wire. The radius R is then the mean radius and the separation d is the mean distance.

induced electric field E for such coils. If a steady direct current (dc current) is sent through the coils (connected to be aiding) a steady magnetic field B will exist in the region of the coils, the magnitude and direction of which can be easily measured using commercially available gaussmeters (such as the model 750AR gaussmeter, RFL Industries, Boonton, NY). However, there is *no* induced electric field in the region. There is no electric field associated with a constant (unvarying in time) magnetic field; thus there is no force acting on the charges in the biological system provided they are at rest. The charges of course are not at rest; there is motion due to thermal energy. The velocity, given by $v = \sqrt{3kT/m}$ where m is the mass of the body carrying the charge q, will in general be small and to this extent the magnetic force can be ignored. However, its existence should not be forgotten in any detailed analysis.

If now the current in the coils is varied with time, either sinusoidally or pulsed, there will be an induced electric field E that will vary with time, as well as a magnetic field B that also will vary with time. B is proportional to the current i, while E is proportional to the time rate of change of the current, that is to di/dt. It is well here to state two important facts, facts that have caused difficulty in interpretation of data. First, there is in general no simple quantitative connection between the *voltage* V applied to the coils and the fields B and E. The current and the rate of change of current produced by V depend on the inductance L and resistance R of the coils as well as the time variation in V.

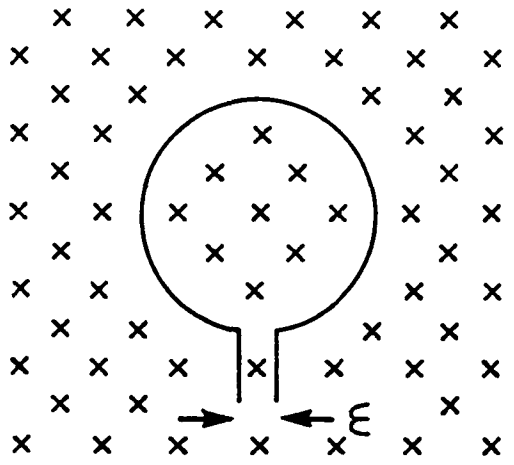


Fig. 2. An open loop conductor in a time varying magnetic field will have an emf $\mathcal{E}$ induced across the open ends. The magnetic field is represented by the ×'s and is taken as perpendicular to the paper.

Second, while a loop of wire anywhere in the field will have induced across the open ends (Fig. 2) a *voltage* $\mathcal{E} = -A(dB/dt)$ where A is the area of the loop perpendicular to the field, this gives no quantitative information about the force on the charges, that is, about the electric field at a given point. (The symbol $\mathcal{E}$ is used for induced voltage to distinguish it from the voltage V that is applied to the coils to cause the current.) However, for coils with circular symmetry, such as the Helmholtz configuration, the field can be determined from a measurement of the induced voltage in a circular loop of wire, but *only* if the loop is concentric with the axis of the field coils. This is detailed below. It is important in the interpretation of experimental results to distinguish between the variation of E in space, which depends on the geometry of the coil, and the variation of E with time, which depends on the shape of the applied voltage pulse V, the resistance R, and the inductance L. While the value of E at any point in space can be calculated for coils of arbitrary shape it is not a simple matter. Even for a pair of coaxial circular coils (Fig. 1) the calculation is not elementary but once carried out the results can be obtained for different size coils with relative ease using simple computer programs. Graphs of E and B in the midplane of the pair of circular coils of Fig. 1 are given in Fig. 3A and B. Note particularly that E is zero on the axis ($\rho = 0$) and increases as the radius ρ increases to approximately the value R and then decreases. This is the first and most important fact. Thus if it is indeed the induced electric field E that is producing an effect on the cell activity then the results will depend critically on the location of the cell in the coil geometry. There should be no

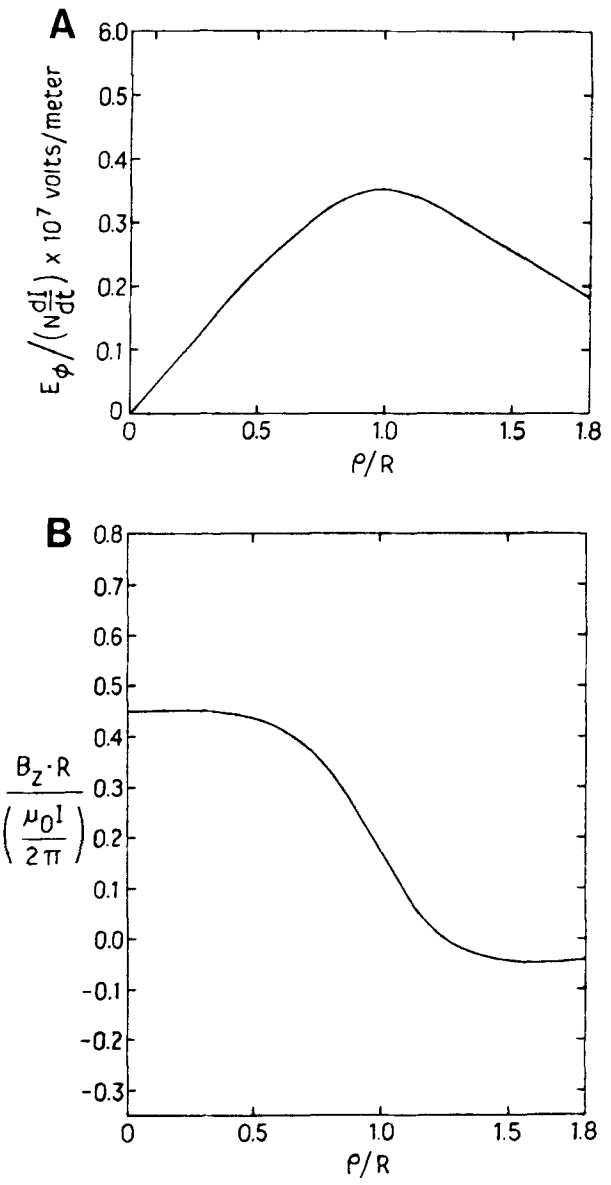


Fig. 3. The fields of the current loops of Fig. 1. (A) The electric field in the plane midway between the coils as a function of radius in units of R. (B) The magnetic field as a function of radius ρ on the midplane.

effect for cells on the axis of the coils. The direction of the E field at any point P in Fig. 1 is in the plane parallel to the coils containing P and tangent to the circle of radius ρ. If each coil contains N turns, then the value of E will be N times that for a single loop. Looking down on the plane containing P the field E is perpendicular to the radius ρ at every point, and constant in magnitude at a fixed radius (Fig. 4A). However, as shown in Fig. 4B the field induced at each point on a circle with its center off axis is not tangent to the circle nor is it constant in

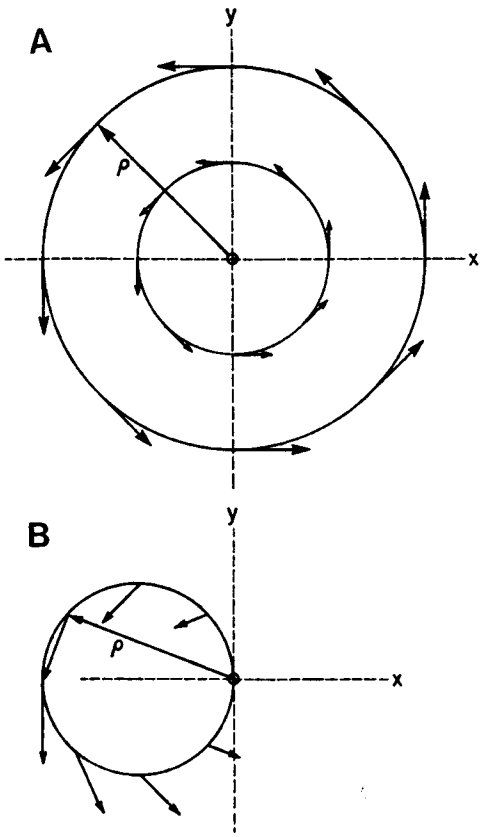


Fig. 4. The electric field in the midplane of the current loops of Fig. 1. (A) The field looking down onto the midplane. The field strength is proportional to the length of the vectors (arrows), symmetrical about the axis of symmetry, and everywhere tangent to the circles whose centers are on the axis. (B) The electric field vectors around a circular loop centered off the axis of symmetry. Each vector has a length approximately proportional to the distance ρ from the origin O for $\rho < R$, and is perpendicular to ρ. Note particularly the electric field is zero on the axis O. The wire loop of Fig. 2 if placed off axis will have a voltage $\mathcal{E} = -A(dB/dt)$ induced in it, but the value of E at any point cannot be determined from a measurement of $\mathcal{E}$.

magnitude. Thus it is crucial to the interpretation of the results of any experiment using EMF that the position of a cell be accurately known with respect to the axis of symmetry of the coils.

We consider next the induced field for sinusoidal and pulsed voltages applied to the coils.

Sinusoidal Voltages

A sinusoidal voltage V applied to the coils of Fig. 1 will result in a current i, which, aside from a constant phase factor, will also be sinusoidal and equal to $i = (V/\sqrt{R^2 + (\omega L)^2})\sin\omega t$ where $\omega = 2\pi f$ is the angular frequency of the voltage source and R and L are the resistance and inductance of the two coils in series. The resistance and inductance are easily measured using an impedance bridge (such as the model 1650A Impedance Bridge, General Radio Company, Concord, MA). The induced electric field, which is proportional to $(di/dt) = (\omega V/\sqrt{R^2 + (\omega L)^2})\cos\omega t$ will be also sinusoidal. At a given point P (Fig. 1) the value of E and therefore the force on a charge at P will vary sinusoidally in time and will reverse in direction each half cycle. The value can be obtained from the graph of Fig. 3A by using the above expression for (di/dt). Alternatively, it can be measured very simply by using a circular pick-up coil of n turns and radius r accurately located with it axis coincident with the axis of the current coils. If the peak or maximum value of the voltage $\mathcal{E}$ induced in the coil is $\mathcal{E}_m$ (measured with an oscilloscope or high empedance voltmeter) then the maximum value of the electric field E_m at the radius r is $E_m = \mathcal{E}_m/2\pi rn$ volts/meter, where r is the radius in meters. We find it convenient to wind several coils of different radii in shallow circular grooves in a lucite plate that can be easily but accurately inserted in the field parallel to the current coils. It is then a simple matter to measure the field at several radial points. A word of caution: the leads from the pick-up coils must be tightly twisted and brought well outside the field coils to avoid unwanted pick-up in the leads.

Pulsed Voltages

Consider now a pulsed voltage applied to the coils. The induced electric field E will depend not only on the time distribution of the voltage pulse, but also on R and L. It will not generally have the same waveform as V. For example, if a step voltage pulse of amplitude V is applied at $t = 0$ and remains at V thereafter, the current i will rise exponentially from zero to the final value V/R with a time constant $\tau = L/R$, or $i = (V/R)(1 - e^{-t/\tau})$ as shown in Fig. 5A. Suppose however a rectangular pulse of amplitude V and of duration t_p is applied to the same pair of coils. The resulting current is again given by $i = (V/R)(1 - e^{-t/\tau})$ for $t < t_p$ but by $i = i_0 e^{-(t-t_p)/\tau}$ for $t > t_p$, where $i_0 = (V/R)(1 - e^{-t_p/\tau})$. A graph of i is given in Fig. 5B for three different values of the time constant τ. Because B is proportional to i, these graphs also give the time dependence of B.

The value of E is proportional to di/dt, which for a step pulse is:

$$\frac{di}{dt} = \frac{V}{L} e^{-t/\tau}$$

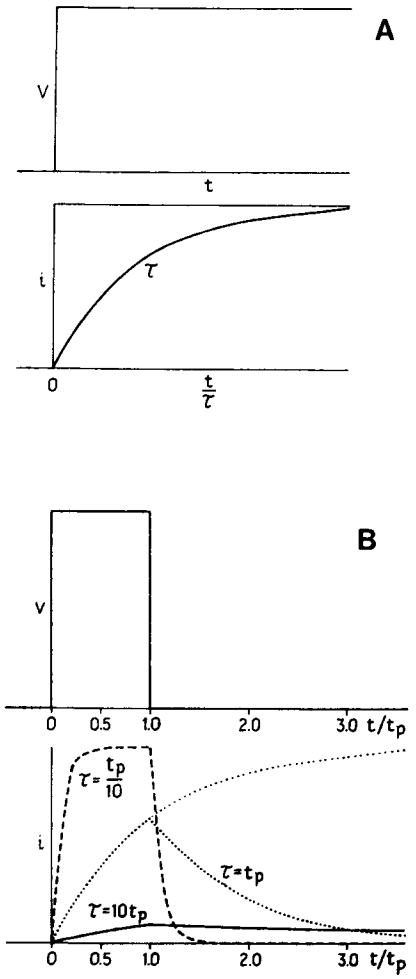


Fig. 5. The current in the coils of Fig. 1 due to an applied voltage V. (A) The current due to a step voltage V of infinite duration applied to a coil having resistance R and inductance L (τ = L/R) increases exponentially from zero to a final value i = V/R with the time constant τ. (B) The current waveforms resulting from a rectangular voltage pulse of amplitude V and duration t_p applied to coils having three different time constants. The curve for $\tau = t_p$ will have reached at $t = t_p$ 63% of the final value for the step voltage of (A). It then decreases (decays) to zero with the time constant τ. Note that for $\tau = t_p/10$ the current essentially reaches its maximum value i = V/R, while for $\tau = 10t_p$ it reaches only 9.5% of i = V/R. The waveform can be measured on an oscilloscope by observing the voltage across a small resistance $R_s \ll R$ inserted in series with the coils.

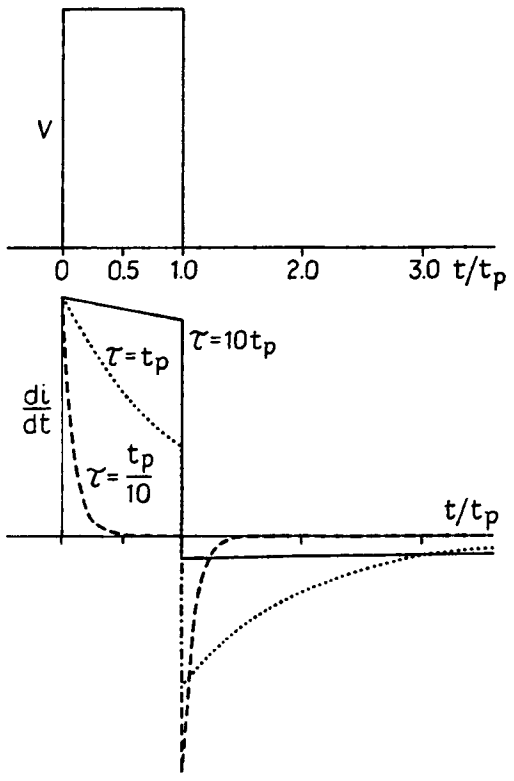


Fig. 6. The time-rate of change (di/dt) of the current i of Fig. 5B. Note particularly that (di/dt) reverses direction at $t = t_p$. The net area under each curve is zero. Because the induced electric field is proportional to di/dt, it to must average to zero. The waveform can be observed on an oscilloscope using the pick-up coil of Fig. 2. Because $\mathcal{E} = -N(d\phi/dt)$, a larger voltage will be observed if the coil contains several closely wound turns N. Since $d\phi/dt$ is proportional to di/dt, the waveform of the induced voltage is the same as di/dt.

For a rectangular pulse of duration t_p it is:

$$\frac{di}{dt} = \frac{V}{L} e^{-t/\tau} \qquad \text{for } t < t_p$$

and

$$\frac{di}{dt} = \frac{V}{L}(1 - e^{-t_p/\tau})e^{-(t-t_p)/\tau} \qquad \text{for } t > t_p$$

Plots of di/dt are given in Fig. 6, which therefore give the time variation of E at any point in space. It is obvious that L and R are important parameters. Note particularly that E reverses direction at $t = t_p$ no matter what the value of τ.

The value of the induced field E at any radius r is again easily measured using the same pick-up coils described above and a good oscilloscope. The time variation of E is the same as the induced voltage $\mathcal{E}$ observed on the scope, and the magnitude is again given by $E_m = \mathcal{E}_m/2\pi rn$.

Forces and Impulses Due to E

The force on an ion due to the induced electric field is F = qE where q is the net charge on the ion. For sinusoidal voltages and currents the force reverses direction each half cycle. For pulsed voltages the force that is proportional to (di/dt) reverses direction at $t = t_p$ (Fig. 6). Further the forces averaged

over time in each direction are equal and the *net* force on the ion is zero. Saying it another way, the area under the (di/dt) curve above the axis is just equal to the area under the (di/dt) curve below the axis when taken over a complete cycle of the waveform. Note also that the area under the (di/dt) curve at any instant is $\int(di/dt)dt = \int_0^i di = i$ which is just the value of i plotted in Fig. 5B. Thus the *net* force at any instant after the application of the pulse is proportional to i at that instant, and when i returns to zero the net force will have averaged to zero. Thus the current waveform gives a good view of the net force as a function of time.

The induced electric field will of course cause currents in any conducting material such as culture medium or tissue placed in the field. The induced currents are the result of the electric field exerting a force on the charge carriers. The two principal effects of the current are ohmic heating of the material, and, in the case of free ions as in the culture medium, linear transport of the ions. For time varying fields, either pulsed or sinusoidal, in a uniform medium the transport must be oscillatory with no net displacement when averaged over a long time. However, for a nonuniform medium, such as cells in culture, there may well be a net displacement.

In any given experiment it is relatively simple to determine that the effect of a changing magnetic field comes through the induced electric field and not from the magnetic field itself by comparing the measured effect for cells at a radius ρ to those on the axis at $\rho = 0$. At $\rho = 0$ the electric field is zero and any measured effect can be attributed to the magnetic field itself.

If in fact pulsed or sinusoidal electromagnetic fields have an effect on cellular function, then in view of the above, the effect must come about due to a nonlinear response of the cell. The nonlinear response could exhibit itself in a variety of ways. One obvious mechanism is that the ion transport through the membrane is unilateral, so that an electrical force in one direction urges the transport through the membrane, but the reverse force has no effect. In this case a sinusoidal-induced electric field should produce the effect as well as a pulsed field. A second mechanism might result from the relative magnitudes of the forces; that is, the force in one direction is large but acts for a short time compared to the much smaller reverse force acting for a much longer time ($\tau \gg t_p$), as shown in Fig. 6 for $\tau = 10\ t_p$. Thus the membrane may react to an impulsive force (an impulsive force is one which is applied for a short time compared to the response time of the object on which it acts. The classic example is the baseball bat meeting the baseball. The contact time is extremely short compared to the resulting flight time of the ball). This could result in the redistribution of membrane proteins which is known to have an effect on growth and motility of certain cell types [6]. In Fig. 6 for $\tau = (L/R) \gg t_p$, if L is small (thus R must be small) the value of $di/dt = (V/L)e^{-t/\tau}$ will be large giving a large E on the rise of the pulse. This is the case for the "clinical" coils and waveforms of the EBI system of PEMF (System 204, Electro-Biology Inc., Fairfield, NJ).

Electric Fields from Charge Distributions

Static Electric Fields

Static electric fields are established by static or stationary charge distributions. Consider the "capacitative plate" arrangement shown in Fig. 7A consisting of two parallel metal (conducting) plates of area A spaced a distance d apart and containing a parallel slab of dielectric material (say glass or polystyrene) of thickness d_2 and dielectric constant κ (for glass $\kappa \simeq 4.5$, for polystyrene $\kappa \simeq 2.6$, and for water $\kappa \simeq 80$). A constant potential V applied to the plates will result in an electric field E_1 in the space d_1 of $E_1 = \kappa V/[\kappa d - d_2(\kappa - 1)]$ and a field in the dielectric of $E_2 = V/[\kappa d - d_2(\kappa - 1)]$; the field in the dielectric is less than in d_1 (vacuum or air) by the factor κ as shown in Fig. 7B.

If now the dielectric is replaced by a conductor, say a piece of aluminum, or a volume of culture medium, the field inside the conductor will be zero. The reason is that (by definition) a conductor contains free charges, charges (electrons or ions) that are free to move. They will move to the surface leaving zero field inside as shown in Fig. 7C. (The field inside must be zero or a free charge there would experience a force.) Thus it is not possible in a static arrangement of "capacitative plates" to have an electric field in a conductor. This includes culture medium which is a good conductor ($\sigma = 1$ mho/meter for typical culture medium, 12 mho/meter for 2N NaCℓ, 3.5×10^7 mho/meter for Aℓ and of the order of 10^{-12} for an insulator such as polystyrene). If capacitative plates are used with a flask of culture medium fit snugly between them the electric field is confined to the material of the flask, and the field in the medium is zero.

Stationary Electric Field in a Conducting Medium

How then can one produce a steady or stationary

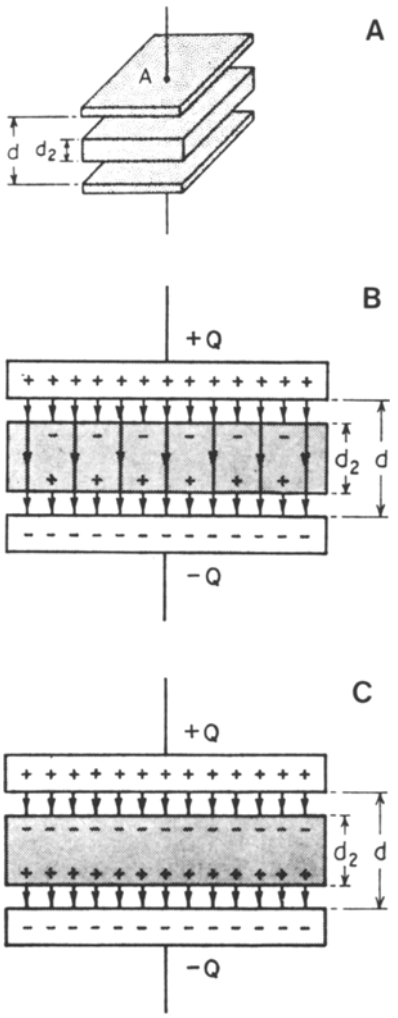


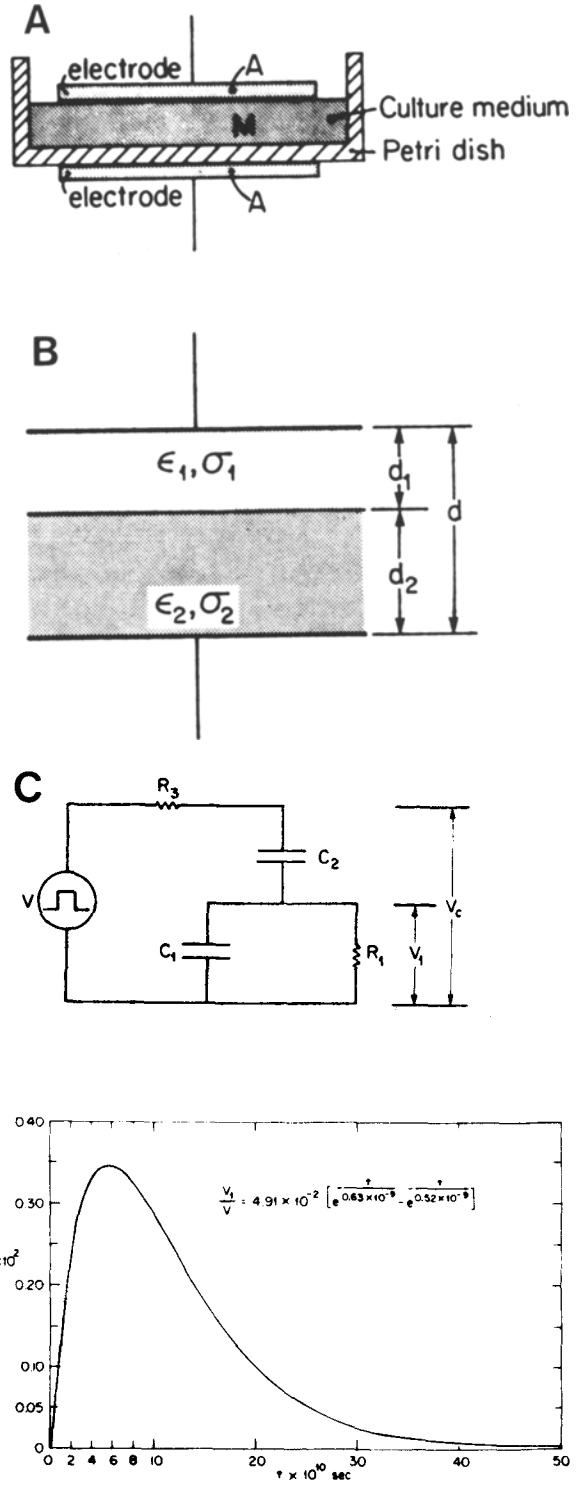
Fig. 7. A parallel "capacitance" plate arrangement. (A) Two metal plates of area A, spaced a distance d apart and containing a dielectric of thickness d_2. The space $d_1 = d - d_2$ is air or vacuum. (B) The electric field in the dielectric d_2 is less than in the air space d_1. (C) The field in a conductor placed between the plates is zero.

electric field in a conducting medium? The answer is by passing a steady (dc) current through the medium. A conductor of conductivity σ, cross-sectional area A, and length ℓ will have a resistance $R = \ell/\sigma A$ ohms, and a potential difference V maintained between the ends of the conductor will cause charges to flow through it, that is, a current I will exist in the conductor. The electric field will be $E = V/\ell = IR/\ell = I/\sigma A$. A charge q in the medium will then experience a force $F = qE$. In such experiments [4, 5] it is important to restrict the current to low values to avoid ohmic (I^2R) heating of the medium. Small channels are usually provided: if $A \sim 10^{-2}$ cm^2, $\ell \sim 1$ cm, and $\sigma \simeq 10^{-2}$ mho/cm, a field of 1000 volts/m is obtained for I = 1 mA, with a power input to the channel of only 10 milliwatts (see Fig. 9A).

Pulsed Electric Fields

If pulses of voltage are applied to the capacitative plates of Fig. 7A, the charges in the culture medium (conductor) must redistribute as the capacitance is alternately charged and discharged and this produces a transient electric field in the medium. The redistribution of charge takes time. This "relaxation" time is determined by the mobility of the charge carriers, which is related to the conductivity of the material. It can be shown [7] that the charge density (charge per unit volume, coulombs/m^3) is given by $\rho = \rho_0 e^{-\sigma t/\epsilon}$ where ρ_0 is the free charge density in the medium at time $t = 0$, the time at which the voltage is changed. The "relaxation" time is the time required for ρ to fall to 1/e of its final value and is $\tau = \epsilon/\sigma$. If $\epsilon = \kappa\epsilon_0 = 80 \times 8.85 \times 10^{-12}$, $\sigma = 10^{-2}$ mho/cm = 1 mho/meter then $\tau \simeq 7 \times 10^{-10}$ sec. These numbers correspond to culture medium. For pure water $\tau \simeq 4 \times 10^{-8}$ sec. These are short times; an ion with thermal velocity would move a distance of the order of 1 μm in 10^{-9} sec.

Consider a typical experiment such as that of Korenstein et al. [8] in which "capacitative plates" are used with tissue culture dishes and culture medium. (The electric fields in the cyclindrical geometry used by Rodan et al. [9] cannot be easily evaluated. The use of the curved copper electrodes as they describe produces an electric field in the culture medium which is a complicated function of the geometry.) Two circular metal electrodes A, each 54 mm in diameter (one in close contact with the bottom of a petri dish P, the other coated with a very thin insulating layer of clear krylon) is in contact with the upper surface of the culture medium M as depicted in Fig. 8A. This arrangement forms a two layer capacitor represented in Fig. 8B. The equivalent circuit is shown in Fig. 8C where C_1 is the capacitance associated with the culture medium of depth $d_1 = 2.25$ mm and C_2 with the polystyrene bottom of the petri dish of thickness $d_2 = 1.25$ mm. Because the conductivity σ_1 of the medium is relatively large ($\sigma_1 \sim 2 \times 10^{-2}$ mho/cm) its resistance R_1 will have a small value ($R_1 \sim 0.49\ \Omega$) and is in parallel with C_1. Since polystyrene is a very good insulator ($\sigma_2 < 10^{-12}$) its resistance can be taken as infinite. In the equivalent circuit R_3 is the internal impedance of the generator producing the voltage V. Since we are interested in what happens at the immediate times the generator switches polarity the



impedance R_3 of the generator can not be ignored. The solution for the voltage V_1 across the culture medium when a rectangular pulse V is applied to the circuit is:

$$V_1 = V \frac{1}{R_3 C_1} \frac{\alpha_1 \alpha_2}{(\alpha_1 - \alpha_2)} [e^{-t/\alpha_1} - e^{-t/\alpha_2}]$$

where α_1 and α_2 are given by:

$$2(\alpha_1, \alpha_2) = [R_1(C_1 + C_2) + R_3 C_2] \pm \sqrt{[R_1(C_1 + C_2) + R_3 C_2]^2 - 4R_1 R_3 C_1 C_2}$$

where for $2\alpha_1$ take the plus sign and for $2\alpha_2$ take the negative sign. For the geometry of Fig. 8A, $\alpha_1 \simeq 0.63 \times 10^{-9}$ sec and $\alpha_2 \simeq 0.52 \times 10^{-9}$ sec for $C_1 = 1140$ pf, $C_2 = 11$ pf, $R_3 = 52.3\ \Omega$, and $R_1 = 0.5\ \Omega$. The potential across the culture medium is plotted in Fig. 2e. Note that it persists for a very short time ($\sim 3 \times 10^{-9}$ sec) compared to the width of the applied pulse [6] (25 μsec) and is very small, ($V_1 \ll V$). It will reverse and be of the same form when the voltage pulse returns to zero. The electric field is $E_1 = V_1/d_1$. Clearly this is not an effective scheme for producing pulsed electric fields in culture.

A pulsed field for *in vitro* experiments can be produced by using the conducting channel. If a voltage source is capacitatively coupled to the channel as in Fig. 9A the dc current is guaranteed to be zero. The duration of the electric field pulse and the amplitudes in the forward and reverse directions are controlled by the time constant $\tau = RC$ where R is the resistance of the channel and C the coupling capacitor. Waveforms for the electric field are given in Fig. 9B for two values of t_p/τ. (It is assumed the resistance R of the channel of length ℓ is much larger than that of the electrodes.) The an-

Fig. 8. Geometry for a typical "capacitance plate" experiment. While the arrangement shows one plate essentially in contact with the medium, the results apply equally well for plates outside an insulated container provided all the insulating material is lumped in the dimension d_2. (A) The geometry using a Petri dish with culture medium M and circular electrodes of area A. (B) The capacitor equivalent. (C) The equivalent circuit of (A) when the insulating material (polystyrene) has zero conductivity ($\sigma_2 = 0$) so that $R_2 = \infty$. The voltage generator V has an internal resistance R_3. (D) The ratio of the voltage V_1 across the culture medium of conductivity σ_1 to the applied voltage V as a function of time. The electric field (for parallel plates) is V_1/d_1. Note particularly that the peak amplitude of V_1 is very small (V/300 for the example shown) and is of very short duration, approximately 30×10^{-10} seconds.

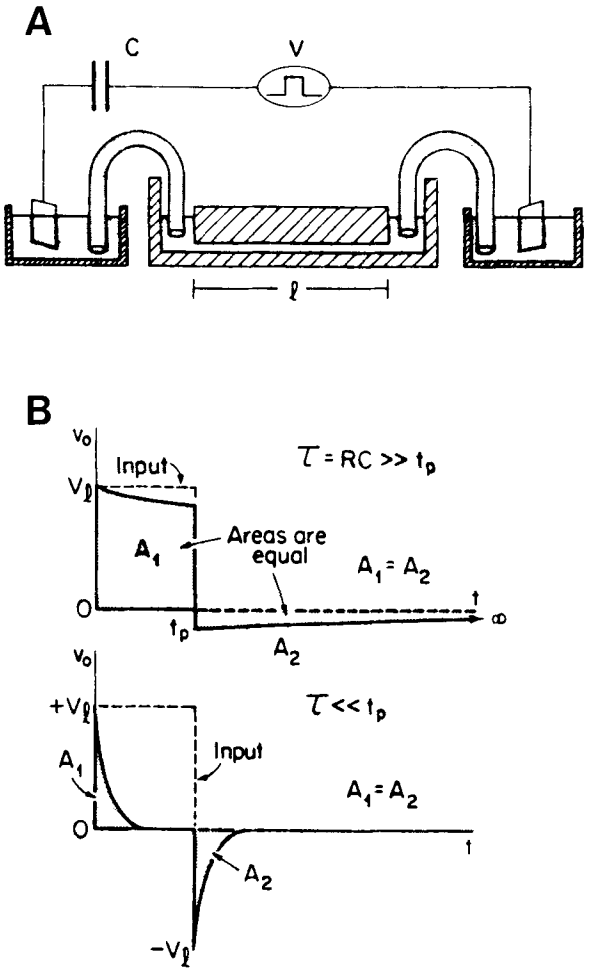


Fig. 9. Geometry for producing pulsed electric fields in a conducting medium. (A) A narrow channel of length ℓ having resistance R is coupled through agar bridges to the electrodes through the capacitance (C). (B) The voltage waveforms across the channel for two different time constants τ, where $\tau = RC$, and t_p is the time duration (width) of the voltage pulse V. There can be no dc current through the channel. The electric field is V_ℓ/ℓ and reverses in direction at $t = t_p$. The net field averaged over time is zero.

alytic expression for the electric field is

$$E = \frac{V}{\ell} e^{-t/\tau} \qquad \text{for } t < t_p$$

$$E = \frac{V}{\ell} (e^{-t_p/\tau} - 1)e^{-(t-t_p)/\tau} \qquad \text{for } t > t_p$$

Note particularly that for any waveform capacitatively coupled to the channel the average value of the output signal (the electric field in this case) is always zero.

Sinusoidal Electric Fields

If a sinusoidal voltage $V = V_0 \sin\omega t$ is applied to the circuit of Fig. 8C the ratio of the voltage V_1 across the culture medium to the applied voltage will be

$$\left|\frac{V_1}{V}\right| = \frac{1}{\sqrt{\left(1 + \frac{R_3}{R_1} + \frac{C_1}{C_2}\right)^2 + \left(\omega R_3 C_1 - \frac{1}{\omega R_1 C_2}\right)^2}}$$

For the values of R_1, R_3, C_1, and C_2 appropriate to the Korenstein arrangement the ratio of V_1 to the applied voltage V at f = 60 Hz is $|V_1/V| = 2 \times 10^{-9}$, and for f = 10^4 Hz $|V_1/V| = 3.5 \times 10^{-5}$. Thus there is essentially no electric field in the culture medium. Again this is due mainly to the low value of the resistance R_1.

Conclusions

In experiments on cellular systems using electromagnetic fields the electric field is the important parameter. If experiments are to be quantified, and most important to be duplicated in other laboratories, it is essential not only that the geometry be specified but also the parameters that determine the electric field at the position of the cells be specified. Due to the relatively high conductivity of the culture medium it is difficult to produce a significant electric field in "capacitative plate" experiments. The amplitude of the field is extremely small compared to the field in the insulating material, and it is of very short duration. When time-varying magnetic fields are used to induce time-varying electric fields it is essential that the position of the cells with respect to the geometry of the coils be carefully specified because the electric field E is a function of position and is zero in the axis of symmetry. The resistance and inductance as well as the voltage signal must be specified.

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