Biological Applications of Large Electric Fields: Some History and Fundamentals

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Invited Paper

***Abstract*—The history of electric fields in biology is summarized briefly. Physical concepts important for explaining the action of electric field pulses on biological objects are reviewed: relation of pulse width to frequency spectrum; precise meaning of "conductor" and "dielectric"; electrical properties of living tissues; translatory and rotational motion of electric charges and dipoles; effects of inhomogeneity, diffusion and viscosity; conditions for validity of linear models; electrical mobility of ions in membrane channels and membranes; conditions for radiation; reflection, refraction, and penetration of radiated fields; effect of radiated magnetic fields on chemical reaction rates; radiation pressure; electrostriction; the problem of distinguishing between thermal and nonthermal effects. The rationale for close collaboration among biologists, engineers, physicists, and physicians is discussed.**

***Index Terms*—Bioelectricity, dielectrophoresis, ion channels, large electric fields, magneto-chemistry, radiation pressure, thermal versus nonthermal effects.**

I. Introduction

THIS paper is based on the author's introductory address at "Electromed99." It is concerned with "large" electric fields. "Large" designating here fields roughly as large or larger than those which can cause nerve stimulation in vertebrates at frequencies below 100 Hz. The subject is introduced by indicating when the role of electricity in biology was first recognized. The history of medical applications is then reviewed very briefly, listing easily accessible references for the interested reader. The principal part of the paper encompasses a review of selected concepts from electromagnetic theory that are likely to be of particular importance in the application of large amplitude, but short duration electric field pulses in biology and medicine.

II. History

Probably the earliest written record on biological electricity is found in Egyptian hieroglyphs dated to 4000 B.C. that describe difficulties of fishermen with "sheatfish" or catfish [1]. That same fish, which can give substantial electric shocks, was used by some Roman physicians as therapy for headaches and arthritis and remained the only source of therapeutic electricity until the seventeenth century. Scientific experimentation and analysis of electricity in biology began with the work of Benjamin Franklin (1706–1790) and Luigi Galvani (1737–1798) [1] Galvani used a bimetallic arch (zinc and copper) to produce muscular contractions in a frog leg. A practicing physician, he attributed the effect to "animal electricity existing in the body." This started a controversy with Alessandro Volta, professor of physics in Pavea, who repeated Galvani's experiment and discovered that the electric potential required contact between the two dissimilar metals. Another Italian, Carlo Matteuci (1811–1865) was then the first to measure a true biogenic impulse in frog muscle.

Experimental exploration of bioelectric phenomena proceeded rather rapidly after about 1840 in France, Germany, and England. In 1887 August Waller recorded the first electrocardiogram and even earlier, in 1872, Thomas Green in the U.S. resuscitated five of seven patients with cardiac arrest due to chloroform anesthesia. He used a 300 V battery and thus pioneered the first application of high voltage in human medicine [2]. Closed chest ventricular pacing in patients with atrioventricular block was introduced in the U.S. by Zoll in 1952 using 2 ms, 150 V pulses at rates between 30 and 180 per minute [2], [3]. Later, in the 1950's, implantable pacemakers became commercially available.

Very large electric fields, up to 300 V/m can usually restore the normal heart beat in ventricular fibrillation if applied quickly. Ventricular fibrillation is one of the leading causes of death in the Western world with about 1200 cases each day. The first defibrillator was produced by William Kouwenhoven, an electrical engineer, in 1930 [3]. Many refinements were made since that time and a D.C. defibrillator system developed in 1962 by Bernard Lawn, a cardiologist at the Harvard Medical School, is still used today. However, ventricular fibrillation and methods for stopping it are still a very active research area. An important reason for this is that presently used transchest defibrillation energy, 200–360 Joule with currents of 2–3 A, sometimes produces permanent injury [4]. Reduction of external energy input to the minimum necessary for defibrillation is clearly desirable.

Stimulation of nerve and muscle activity is a nonthermal effect of electric fields in the sense that it can be produced with currents or charge transfer, at dc or low frequencies, well below those necessary to produce appreciable temperature increase in tissue. However, when the frequency of current introduced into the body is increased, the threshold for nerve and muscle stimulation increases rapidly [5] as illustrated by Fig. 1. The relation

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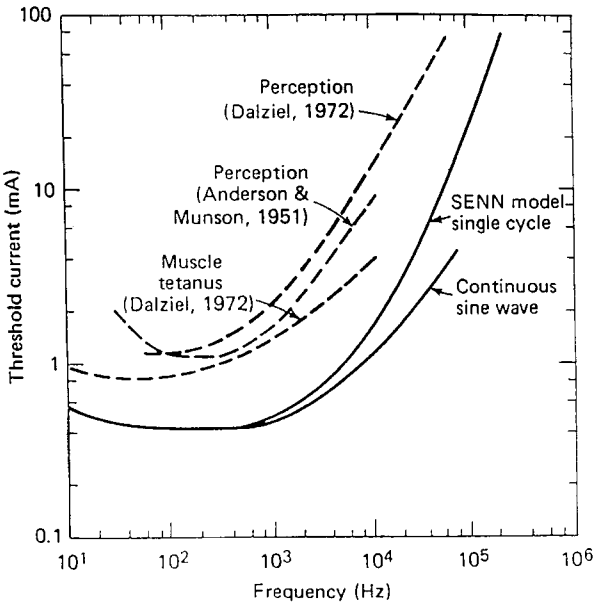

Fig. 1. Frequency dependence of threshold for sinusoidal current stimulation. Solid curves are for myelinated nerves. "Single cycle" means one entire period. "SENN" is the "spatially extended linear model" (see [5]). Source: Fig. 4.20 in [5], with permission of the publisher.

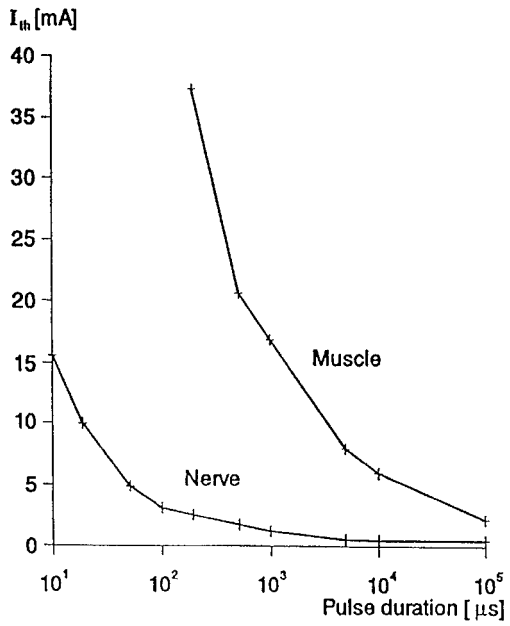

Fig. 2. Experimentally determined strength-duration relationship for motor nerve stimulation and for direct stimulation of muscle (threshold values for square-wave pulses). Source: Fig. 21.9 in [1] and [53], with permission of the publisher.

between pulse duration and nerve/muscle stimulation is illustrated by Fig. 2.

Excellent and very detailed references on the characteristics of nerve and muscle stimulation are available [1], [5]. Depending on current density and duration of current flow, high-frequency electromagnetic energy at levels which do not produce nerve or muscle stimulation can produce thermal effects [6]. The present conference is mainly concerned with biological effects of short duration, large amplitude electric field pulses, *in vitro* and *in vivo*, under conditions that produce neither nerve stimulation nor appreciable heat. An example is electroporation *in vitro* [7]. Heating effects will be discussed later in this paper.

TABLE I
QUALITATIVE RELATIONS BETWEEN PULSE CHARACTERISTICS IN THE TIME DOMAIN AND THEIR FREQUENCY CONTENT

Time domain	Frequency spectrum
(A) Narrow width (T)	Broad spectrum
(B) Undirectional ("DC" pulse)	Spectrum $\pm\Delta f$ centered at f=0
(C) Pulses superimposed on carrier f_0	Fourier spectrum of "DC' pulse is shifted to be centered at f_0 [for rectangular pulse, first zeroes are at $f_0 \pm(1/T)$]
(D) Single pulse replaced by pulse sequence with repetition rate f_r	Continuous spectrum replaced by a "line" spectrum with lines separated by f_r Relative amplitudes of spectral lines, i.e. envelope of spectrum is the same as in (B) or (C).

III. PULSES, FREQUENCY SPECTRA, AND ELECTRICAL PROPERTIES

A. Pulses and Frequency Spectra

Detailed mathematical discussions of the relation between the shape of pulses in the time domain (including superposition on a carrier frequency) and their frequency spectra can be found in numerous text books, e.g., [8]–[10]. Since, on the one hand, pulse duration, pulse shape and pulse repetition frequency have been found to affect virtually all biological effects of electric fields and, on the other hand, electrical properties of living tissues and cells are usually presented as a function of frequency, it is useful to review the most important aspects of the relation between description of signals in the time and frequency domains. However, it is, in general, not possible to reconstruct the response in the time domain of a nonlinear system, where properties depend on the amplitude of the signal, by superposition of responses to individual frequencies. Thus, when the electrical properties of a cell or cell membrane change in some amplitude range with the amplitude of the voltage applied to it, the equivalence of time and frequency domain analyzes can only be applied over the range of voltage amplitudes where no change of electrical properties occurs. With this important caveat we note the qualitative relations between pulse characteristics in the time domain and the corresponding frequency spectra indicated on Table I. The bandwidths $\pm\Delta f$ shown on the table as examples are from the frequency with peak amplitude to the first zero corresponding to a rectangular pulse of duration T.

B. Electrical Properties of Biomaterials

Concerning the electrical properties of biological materials, we note first that most tissues and body fluids (but not mem-

TABLE II
CONDUCTION CURRENT/DISPLACEMENT CURRENT

		Skeletal muscle		
f	λ	σ	ε_r	$\frac{\sigma}{2\pi f\varepsilon}$
GHz		Siemens/ m || ⊥		
10^{-7}	3000 km	0.5 0.075	10^6	90
0.001	300 m	0.70	2200	5.72
0.01	30 m	0.80	176	8.17
0.1	3 m	0.90	68	2.38
1	30 cm	1.4	55	0.46
10	3 cm	8.0	38	0.38
35	8.6 mm	40	19	1.08

branes, proteins and nucleic acids) are neither "good" electrical conductors nor "good" dielectrics. The same material can be a "good" conductor at one frequency and at another a "good" dielectric. It is the ratio of conduction current density J_C to displacement current density J_D which characterizes these properties:

$$\frac{J_C}{J_D} = \frac{\sigma E}{\frac{\partial D}{\partial t}}. \tag{1}$$

In (1), it is assumed that the conduction current is due to an applied electric field and that the relation between J_C and E is linear (Ohm's law—which is not necessarily satisfied in living systems, particularly if E is very large). D is the electric displacement in Coulombs per m^2 and is given by

$$D = \varepsilon_0 E + P = \varepsilon_0 E(1 + P/\varepsilon_0 E) = \varepsilon_0 \varepsilon_r E \tag{2}$$

where ε_0 is the dielectric permittivity of free space, P is the dipole moment per unit volume and ε_r the relative dielectric "constant". Again, if the dielectric is linear, i.e., if the ratio $P/(\varepsilon_0 E)$ is independent of the magnitude of E and if ε_r is not a function of t

$$\left|\frac{\partial D}{\partial t}\right| = \left|\varepsilon_0 \varepsilon_r \frac{\partial E}{\partial t}\right| = \varepsilon_0 \varepsilon_r \omega E \tag{3}$$

where sinusoidal steady state at radian frequency $\omega = 2\pi f$ is assumed for the last equality. Biological materials are "dispersive" and ε_r is, in general, a function of t and therefore of ω. If the value of ε_r measured at frequency ω is used in (3), we obtain from (1) and (3)

$$\frac{J_C}{J_D} = \frac{\sigma}{\omega \varepsilon_0 \varepsilon_r}. \tag{4}$$

Table II shows values of this ratio for skeletal muscle from 100 Hz to 35 GHz, indicating that skeletal muscle is neither a "good" electrical conductor $(J_C/J_D) \gg 1$, nor a "good" dielectric, $(J_C/J_D) \ll 1$, except at frequencies below about 1 MHz (where it is essentially a relatively good electrical conductor). Other tissues, with lower water content, such as brain white and gray matter, have somewhat lower conductivity ($\sigma \approx 0.4$ to 0.7 S/m at 100 MHz). Still others, such as bone, have even much lower conductivity ($\sigma \approx 0.06$ S/m at 100 MHz); however, their ε_r values are also smaller, particularly below 1 MHz. Thus, at most frequencies and for most bulk tissues, the mathematical approximations often made to quantitatively describe the response to electromagnetic fields of "pure" conductors or dielectrics are not possible. Detailed data on the origin and value of electrical properties of biomaterials can be found in [11].

Membranes which surround individual cells, cell nuclei and some organs in eukaryotes, as well as bacterial cells, can be relatively good dielectrics or electrical insulators even at extremely low frequencies [11]–[13]. Membrane conductivities are in the range of 10^{-9} to 10^{-7} S/m [13] and membrane $\varepsilon_r \approx 7$ (based on a membrane capacitance of 10^{-2} F/m^2 [11] and an average membrane thickness of 6 nm), although the lipids, which form the basic membrane structure have $\varepsilon_r \approx 2$ to 2.5 [7], [12]. Cell membranes are highly nonuniform and are traversed by ion channels which open and close in response to transmembrane potential differences in the tens of millivolt range.

Since many protein molecules embedded in the cell membrane are polyelectrolytes (i.e., contain many ionized or ionizable groups), the cell membrane is in effect negatively charged at physiological pH (≈7.2) of the extra-cellular fluid. The relatively immobile charges of the protein molecules attract more mobile "counter-ions" from the surrounding fluid, creating an electrical double layer on the cell surface [12]. Partial displacement of this double layer by an applied low frequency electric field then makes entire cells into large electric dipoles [11], [12]. This leads to the enormously large ε_r at ELF (see first row in Table II). Counterion formation and behavior on cell surfaces is complex [14], [15] and can affect cell-to-cell communication [16].

Individual protein molecules can also have very large permanent electric dipole moments (≈10^{-27} cm) which lead to orientational polarization when an electric field is applied. In their dry state they can have properties of electronic semi-conductor [12]. In aqueous solution within living systems they cause an increase in relative permittivity above that of water (≈80 for frequencies below 10 GHz). The "dielectric increment" $\delta\varepsilon$ is usually given as the total increase in ε_r per gram of protein per gram of solution. Its value in these units is between 0.1 and 2. The relaxation frequency, i.e., the frequency at which the orientational polarization falls to half its low frequency value, lies in the range of 1–10 MHz. Polar side chains of protein molecules have a somewhat higher relaxation frequency [11].

IV. MECHANISMS OF FIELD-ORGANISM INTERACTION

"Organisms" to be considered are eukaryotes, prokaryotes, and viral particles, including (where applicable) their organs, cells, and membranes.

A. Linear Motion of Electric Charges and Dipoles

In a uniform electric field E, a charge q experiences a force $F = qE$ and in a viscous environment its velocity v is largely determined by Stokes' law

$$F = 6\pi\eta a v \tag{5}$$

TABLE III
MEASURED ION CHANNEL CONDUCTANCS

	G in pS	Tissue	Ref
K^+	145	skeletal muscle	19
Ca^{2+}	20	cardiac	20,21
Ca^{2+}	10	skeletal muscle	20

where a is the radius of the particle, which is approximated as a rigid sphere, and η is the viscosity in Newton-s/m^2. Stokes' law assumes that the moving particle is much larger than the molecules of the medium. This is clearly not true for ions in solution, but more complex theories give only factors other than the 6π in (5) [17]. The electric mobility of the charged particles is defined by

$$\mu = \frac{v}{E} \text{ m}^2/(\text{volt-second}) \tag{6}$$

and values for biologically important ions in free solution are between 10^{-8} and 10^{-7} m^2/(Vs) [12], [17], e.g., $(5)10^{-7}$ for Na^+ or $(8)10^{-8}$ for K^+. Equating qE to F given by (5), and using $\mu = (5)10^{-8}$ m^2/(Vs) and $a = 0.12$ nm gives a viscosity $\eta = (1.13)10^{-3}$ (Ns/m^2) which is slightly above that of water at 37 °C. The viscosity inside aqueous ion channels that traverse membranes can also be estimated. Some ion channels are open all the time, e.g., K^+ "leak channels" in nerve membranes which permit concentration gradient maintained K^+ efflux that causes cell membrane polarization (making the exterior of an axon positive relative to the interior). Other K^+ channels, as well as other ion channels, are inherently nonlinear devices. They are not simple resistors, but resistors in series with, or incorporating, a switch. The opening stimulus for a "voltage gated" channel is a change in membrane potential, while for a "ligand gated" channel it is chemical binding of a "ligand." That ligand can be a neurotransmitter, hormone, cyclic AMP, or a "G-protein." The Na^+ and some K^+ channels are voltage gated, the acetylcholine receptor in nerves and at nerve-muscle junctions is ligand gated, while different types of Ca^{2+} channels are voltage gated, ligand-gated, or activated by stretch [22].

Opening and closing of channels, which are complex protein molecules, involves conformational changes in both their intracellular and extracellular segments [18]. However, once in their open state, they display a linear current-voltage relation if the transmembrane voltage is sufficiently small ($\leq$0.1 V). Values of experimentally obtained conductances G of some ion channels are shown on Table III. Ion concentrations inside and outside cells, as well as ion radii are indicated on Table IV. From these data one can estimate ion mobility by using (5) and (6) and

$$G = \frac{\sigma A}{\ell} \tag{7}$$

$$\sigma = Cq\mu \tag{8}$$

where σ = channel conductivity, A = average channel cross section area = πr^2, r = average channel radius $\approx$ 0.8 nm (the smallest value reported for gap junctions [23]), ℓ = channel length $\approx$ 6 nm, C = ion concentration in ions/m^3, q = ionic charge. Estimating the ion concentration inside channels as the mean between extra- and intra-cellular concentrations, and using the other values from Tables III and IV, one obtains for the K^+ channel $\mu = (5.76)10^{-8}$ m^2/(Vs) and for the Cardiac Ca^{2+} channel $\mu = (5.89)10^{-7}$ m^2/Vs. The corresponding values of effective viscosity are, respectively, $(1.28)10^{-3}$ and $(1.92)10^{-4}$ Ns/m^2. The η value for the K^+ channel is near the viscosity of water, while that for the Ca^{2+} channel is 3.6 times smaller. However, the 6π factor in (5) is questionable, as discussed previously, and the values used for r, ℓ, and C in these calculations are only estimates. One may therefore conclude only that the effective viscosity inside open ion channels, operating in the linear (Ohm's law) region, is probably not very different from that of water.

TABLE IV
ION CONCENTRATION AND ION RADIUS a

	Concentration Inside cells	outside cells	a
	mM/ℓ		nm
K^+	150*	5.5*	0.12
Ca^{2+}	0.0001	1.2	0.15

*Spinal motor neurons
(Based on [22])

The apparent viscosity of the fluid inside the ion channels, if fluid is present, is certainly much lower than the viscosity for transverse motion in the membrane outside the channels. For membranes in their normal, liquid crystal state, indirectly measured values for most membranes are 1–10 Ns/m^2, although those of erythrocytes are reported as 200 Ns/m^2 [24].

In addition to ion channels that traverse membranes, other natural channels with much larger cross sections exist [23]. They transport protein molecules and are also gated by transmembrane voltage. Lumen diameters up to 4 nm have been deduced from measurements [23]. In biological systems,charge motion takes place not only as a consequence of electric fields, but also due to differences in charged particle concentration. Fick's law [1] gives the electrical diffusion current density

$$J_{\text{di}} = qD\nabla C \text{ A/m}^2 \tag{9}$$

where q is the particle charge, C is the particle concentration, and D is the diffusion constant

$$D = \mu_m kT \tag{10}$$

with μ_m = mechanical mobility = (μ/q), k = Boltzman's constant and T = absolute temperature. Noting that conduction current density $J_c = \sigma E = \mu q C E$ while $J_{\text{di}} = \mu kT\nabla C$ and using (6), it is easily shown that the velocity of charges due to a concentration gradient is given by (6) if E is replaced by an equivalent electric field

$$E_{\text{eq}} = \frac{kT\nabla C}{qC}. \tag{11}$$

For a singly charged ion at 37 °C the value of (kT/q) is 0.026 75. Thus, a ratio $(\nabla C/C) = 37.4$ m^{-1} is necessary to produce the same charge velocity as a 1-V/m electric field in a fluid of given electric mobility μ.

Electric dipoles of moment $\mathbf{p}$ will not be moved linearly by a uniform electric field, but will only be turned (to the extent

that the "friction" against the surrounding medium allows) to become aligned with the direction of the applied field. The torque exerted by the electric field $\mathbf{E}$ on $\mathbf{p}$ is given by

$$L = p \times E. \tag{12}$$

The implications of (12) for the theory of dielectric materials are discussed in [25], [11], [12]. Dipoles will, however, undergo linear translation in a nonuniform electric field, giving rise to the phenomenon of "dielectrophoresis" [26]. "Dielectrophoresis requires relatively high field strengths. In media with low ε_r (e.g., 2–7) it is usually $\geq 10^4$ V/m. In media with larger ε_r (e.g., water with $\varepsilon_r \approx 80$) lower fields (~500 V/m) can produce observable effects." [26]. When the difference in ε_r between a particle and the surrounding medium is large, interesting effects, such as particle bunching and formation of "pearl-chains" (cell chains) can occur. Since conditions for dielectrophoretic effects are often satisfied in the highly inhomogeneous biological environment upon application of large electric fields, the information in [26] is very useful for the analysis of bio-electric phenomena.

B. Dielectric "Breakdown"

In air, some molecules are always ionized due to cosmic radiation and emission of small amounts of radon from soil. In the presence of very high electric fields (such as those created by friction between ice crystals in the rapidly moving air of thunderclouds), the ordinarily small number of ionized particles increases rapidly as they are accelerated and ionize other particles by collision. In principle, the same effect occurs in dielectric materials ("insulators") other than air. But when the number of free charges that can be accelerated is small, or if the viscous friction is sufficiently high to keep charged particles from reaching energy levels adequate for ionization of other particles, the required breakdown electric field strength E_b becomes larger. Thus, $E_b \approx (3)10^6$ V/m for air, but $(15)10^6$ V/m for oil, $(30)10^6$ V/m for glass and $(2)10^8$ V/m for mica.

The situation in the principal "good" multimolecular dielectrics of biological systems (where $\sigma < \omega\varepsilon$), i.e., membranes, is somewhat different. Dielectric breakdown of the type just described will occur at sufficiently high values of E. However, substantial changes in biological function will follow if only the shape or orientation of the many receptors and pre-existing ion channels is even slightly changed. Thus, "electroporation" [7] which will be discussed in detail by several papers in the present conference, is often reversible [27] and does not necessarily constitute electrical breakdown. In some cases it may be analogous to stretching of an elastic medium to just below the breaking point. Nevertheless,we noted that ion mobility in pre-existing open membrane channels is on the order of $(6)10^{-8}$ to $(6)10^{-7}$ m^2/(Vs), giving ion velocities of 10 to 100 m/s in a $(1/6)10^9$ V/m intra-membrane electric field. This is not much below the thermal velocity, 250 m/s, of a Ca^{++} ion at 37 °C. On the other hand, charge mobility in an undisturbed membrane with $\eta \geq 1$ Ns/m^2 would be $(1.1)10^{-10}$ m^2/(Vs) giving a charge velocity of ~ 0.02 m/s in a $(1/6)10^9$ V/m field. Application of such a field is therefore much more likely to cause structural changes in pre-existing ion channels than in the relatively solid membrane between channels.

An electric potential difference of about 1 V across a 6-nm-thick cell membrane can initiate electroporation [7]. Such a potential difference would correspond to an electric field of $(1/6)10^9$ V/m inside a 6-nm-thick membrane with uniform electrical properties over its entire thickness. At low frequencies, the capacitive reactance of the cell membrane is much larger than the resistance of the cell interior and therefore almost the entire potential drop across the cell, due to an electric field in the extra-cellular medium, occurs across the cell membrane. For a 1-V pulse with frequency content roughly below 1 MHz, this would correspond to $\{1\text{ V}/(10\ \mu\text{m})\} \approx 10^5$ V/m in the medium which surrounds a 10-μm diameter cell.

C. Radiation Effects

Many applications of electric fields to biological systems do not involve electromagnetic radiation, but can be analyzed using only electrostatic theory or "quasi-electrostatics" [28]. Electromagnetic radiation involves field and associated energy propagation with a finite time delay, such that $E = E(t - x/v)$, where t = time, x = distance and v = propagation velocity. Its principal characteristic is that the field magnitude in an ion-free, unbounded dielectric decreases as $(1/r)$, where r = distance from radiator. In electrostatics fields decrease as $(1/r^n)$ with $n \geq 2$ (n depending on the source configuration). Any device carrying time varying current and/or accelerated electrical charges will radiate electromagnetic fields. However, the amplitude of the radiated field becomes only significant in comparison with locally stored and absorbed energy when the size (linear dimension D) of the radiator is significant in comparison with the wavelength (λ). A short dipole or current element has a radiation resistance $R_R \approx 200(D/\lambda)^2\ \Omega$. Thus, a 10–cm dipole at 60 Hz (wavelength $\lambda = 5000$ km) will have a radiation resistance $R_R \approx 4\ \mu\Omega$. This will usually be much less than the ohmic (dissipation) resistance R of the dipole and of the wires leading to it. Consequently, for any current input I, the power I^2R, dissipated as heat, will be much larger than the radiated power I^2R_R. Nevertheless, there will be an electrical field in the vicinity of even this short dipole, but its magnitude will decrease (depending on field direction) as $1/r^2$ or $1/r^3$.

When D/λ becomes large enough for radiation to become significant, it will still be so only when r is also large enough. For a current element in an ion-free and unbounded dielectric the radiation field $(\propto 1/r)$ will be equal to the "induction field" $(\propto 1/r^2)$ when $r = (\lambda/2\pi)$ and will obviously become more significant as the distance r increases. Thus a 10-cm radiator supplied by a 100-MHz source will already have a reasonably significant radiation resistance $(R_R \approx 0.22\ \Omega)$, but the radiated field will be larger than the induction field only at distances $r > 0.5$ m. In addition, the "beam" or "radiation pattern" (i.e., relative field amplitude as a function of angular position of the observer) generated by a radiator will become constant only at a distance $r \geq (D^2/\lambda)$, where D is the largest linear dimension of the radiator (which may be the diameter of the open end of a waveguide or of a reflecting "dish"). It follows that the radiation effects discussed below need to be considered in biological environments subjected to electric field pulses only if pulse spectra have significant energy content at frequencies where (D/λ) and (r/λ) are above the indicated critical values.

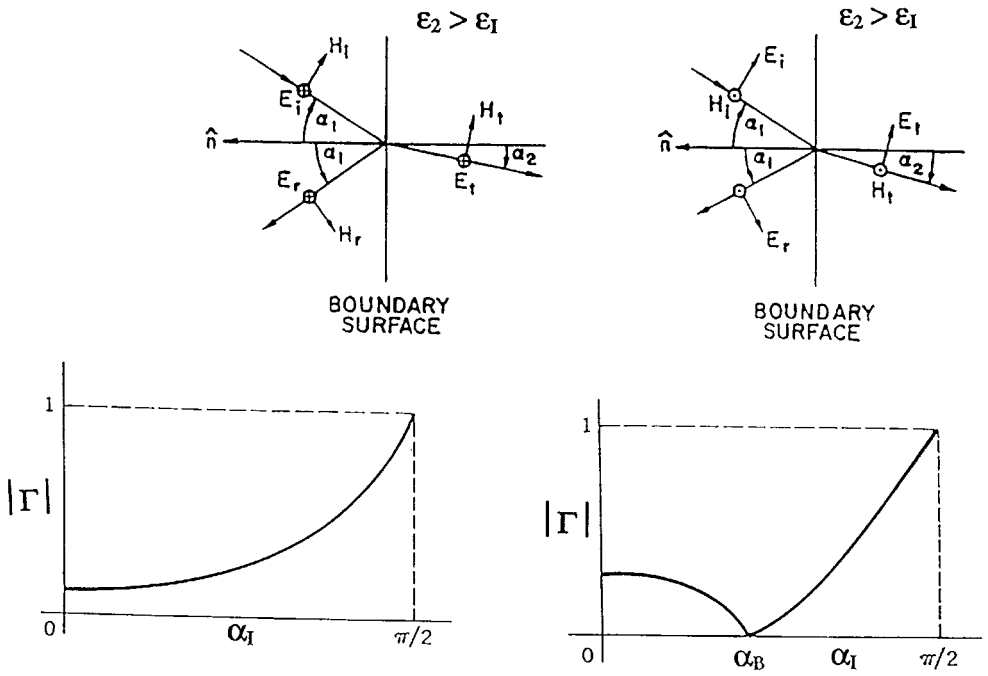

Fig. 3. Dependence of reflection coefficient Γ on angle of incidence α_I at plane boundary between dielectrics. Source: Fig. 13 in [29], with permission of the publisher.

Well known effects of radiation, amply discussed in the bioelectromagnetics literature [29], [30] are finite penetration of a field into an electrically conducting medium, reflection and refraction. An electromagnetic wave, incident from a dielectric medium (such as air) will decrease exponentially in amplitude after entering a good conductor. At a plane boundary the "skin depth" δ, equal to the distance at which the transmitted field $E_T = (E_{\text{incident}} - E_{\text{reflected}})$ has decreased to $(1/e)$ of its value at the boundary surface is given by

$$\delta = \frac{1}{\sqrt{\pi f \mu \sigma}} \tag{13}$$

where f = frequency, μ = magnetic permeability (=$4\pi 10^{-7}$ H/m for most bio-substances) and σ = conductivity. Thus, at 100 GHz, where $\sigma \approx 20$ S/m for muscle, δ is very small (≈0.36 mm). This does not mean, however, that mm waves cannot have biological effects much below skin depth, because nerve endings and other receptor cells in the skin, that are affected by the field, can send chemical signals or their own electrical signals to deeper lying tissue.

Much of the incident field can be reflected at the boundary between two dielectric materials or at a dielectric-conductor boundary. Details of this phenomenon are discussed in many references e.g., [29], [30]. However, for the experimentalist it is worth pointing out that polarization of the incident wave can substantially affect reflection. This is illustrated by Fig. 3 for a plane boundary between two dielectrics. The reflection coefficient Γ = (reflected field amplitude/incident field amplitude) depends strongly on the angle of incidence α_I. Furthermore, the dependence of Γ on α_I is very different for perpendicular polarization (electric field vector perpendicular to the plane of incidence), as on the left side of Fig. 3, and parallel polarization (electric field vector parallel to plane of incidence) as on the right side of the figure. As a result of the requirement for continuity of the electric field component parallel to the boundary, and continuity of electric displacement perpendicular to it, parallel polarization will give zero reflection at the "Brewster angle" α_B.

The other salient characteristic which differentiates radiated from electrostatic and induction ("near") fields, is that in a plane radiated wave the ratio of electric to magnetic field magnitude (H) is fixed. This ratio, called the wave impedance, is

$$Z_D = \frac{E}{H} = \sqrt{\frac{\mu}{\varepsilon}} \tag{14}$$

in an ion-free dielectric, and

$$Z_C = \frac{E}{H} = \sqrt{\frac{j\omega\mu}{\sigma}} \tag{15}$$

in a conducting medium with conductivity σ (we use $j = \sqrt{-1}$). At low frequencies, on the other hand, or in any situation where radiation is negligible, the magnitudes of E and H fields are nearly independent of one another. One may recall that the electric field inside a parallel plate capacitor depends upon the voltage between the plates, ε_r of the medium, and plate separation. It can be very large while, at the same time, the magnetic field would be practically zero if a large impedance in series with the capacitor prevents current flow.

One consequence of the fixed ratio between E and H is that a large radiated electric field will necessarily be accompanied by a large magnetic field. Selecting as illustration muscle tissue with $\sigma = 0.9$ S/m at 100 MHz (compare Table II), we find by (15) that $H = E/(29.6)$ A/m, and the magnetic flux density $B = \mu_0 H = (4\pi)10^{-7} H$. For an electric field in tissue of 10^5 V/m this gives $B = 4.24$ mT (or 42.4 gauss). Such a

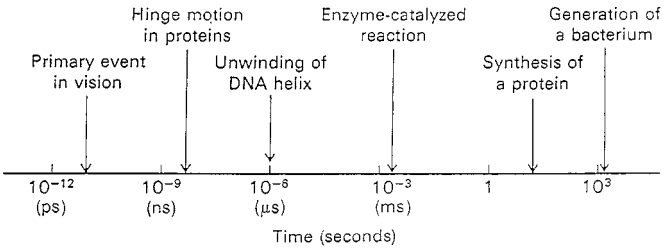

Fig. 4. Typical time rates of some biological processes. Source: Figs. 1–6 in [33], with permission of the publisher.

field can be large enough to affect free-radical dependent chemical reactions [31], including mutogenesis [32]. The pertinent experiments were performed with static and low frequency (60 Hz) magnetic fields, but many bio-chemical reactions, including some that have free-radical intermediate products, take place within periods of less than 1 ms [33]. This is illustrated by Fig. 4. Theoretical discussions of why the rates of radical pair chemical reactions are affected by magnetic fields as a consequence of the Pauli exclusion principle can be found in [34]–[36].

Electromagnetic radiation also has momentum and as it impinges on a boundary surface it exerts "radiation pressure" [37], [38]. The instantaneous magnitude is

$$p_r = \varepsilon E^2 \text{ N/m}^2 \tag{16}$$

at a surface where no reflection takes place (ε being $\varepsilon_0\varepsilon_r$ in the region beyond the boundary surface), and

$$p_{rr} = 2\varepsilon_0 E^2 \text{ N/m}^2 \tag{17}$$

at a surface that gives 100% reflection (i.e., where $\Gamma = 1$). When the incident wave is due to a pulse of duration t_o and the medium beyond the boundary surface $(z > 0)$ can be described as fluid in which the sound velocity is v, and where an electromagnetic wave suffers exponential attenuation $\exp(-\alpha z)$ at $z > 0$, it is necessary to multiply (16) by

$$F = 1 - e^{-2\alpha v t_0} \tag{18}$$

to give p_r at $z = 0$ when $t = t_o$. (For details see [39]). When the carrier frequency of the pulse is in the gigahertz region and $t_o \geq 10\,\mu$s, it will often be possible to approximate $F \approx 1$ for biological substances when $\sigma \geq 0.1$ S/m, since $\alpha = \sqrt{\pi f \mu \sigma}$. For $\varepsilon = \varepsilon_0\varepsilon_r$ with $\varepsilon_r = 33$ and $E = 10^5$ V/m, (16) gives $p_r \approx 3$ N/m^2. Atmospheric pressure at sea level is 10^5 N/m^2 = 10^5 Pa. However, the threshold for monaural human hearing (at 1.5 kHz) is about 10^{-3} N/m^2, and for binaural hearing (at 3.5 kHz) about 10^{-5} N/m^2 [40]. Thus pressure changes at a kHz rate, well below that produced by a 10^5 V/m electric field in air, can be physiologically significant.

Internal stress [41], [42] will appear in dielectrics $(\varepsilon_r > 1)$ subjected to an electric field. Approximating biological materials as fluids, it can be shown [39] that the "electrostrictive pressure" p_e at the air–material boundary due to an incident pulsed field E of duration t_o will be at $z = 0$ and $t = t_o$

$$p_e \approx \frac{1}{3}\varepsilon_0 E^2(\varepsilon_r - 1)(\varepsilon_r + 2)F. \tag{19}$$

For $\varepsilon_r \gg 1$ and E being the transmitted component of the electric field at the surface, it follows from (16) and (19) that

$$\frac{p_e}{p_r} \approx \frac{\varepsilon_r}{3}. \tag{20}$$

This relation is useful in the explanation of microwave auditory effects that will be discussed below.

V. Thermal Versus Nonthermal Effects

When electric fields are applied to organisms as very short pulses, and when the repetition rate is sufficiently small, it appears at first that no, or at most very little, temperature increase might be expected. The mathematical formulation for the rate of temperature increase is [43]

$$\frac{\partial T}{\partial t} = \frac{\sigma E^2}{c\rho} - \left(\frac{\partial T}{\partial t}\right)_C \tag{21}$$

where c specific heat capacity (at constant pressure), ρ = density of the material and $(\delta T/\delta t)_C$ is the cooling rate. If cooling is by heat conduction (43)

$$\left(\frac{\partial T}{\partial t}\right)_C \approx \frac{T - T_0}{\tau} \tag{22}$$

where T = temperature at time t, T_o = initial temperature, τ = thermal relaxation time. (21) includes "specific absorption rate" (SAR) [44] defined as

$$\text{SAR} = \frac{d}{dt}\left(\frac{dW}{dm}\right) = \frac{\sigma E^2}{\rho} \text{ W/kg.} \tag{23}$$

"Specific absorption" (SA) is defined [44] by

$$\text{SA} = \int_0^{t_1} (\text{SAR})\, dt \text{ Joule/kg} \tag{24}$$

where t_1 = duration of the applied field.

The application of these expressions to biological systems is difficult, particularly if pulses are very short and if one considers effects on a microscale. There are two principal reasons for this. First, biological tissue and cells are far from electrically (or mechanically and thermally) homogeneous. Therefore, the magnitude of the electric field on a microscale is not known. The most elaborate calculations still have only a resolution to cubes of 3.6 mm side length [45], [46] for 60-Hz fields and 1-mm cubes, only within the human head, for 900 MHz [47]. They give, for humans, field intensities at the organ level, rather than in cells. For small animals calculations have thus far only been published for major body sections [48]. Second, the cooling rate is often not very well known, because it can depend not only on heat conduction, but also on heat radiation and convection. Anatomy, blood and other fluid circulation and external environment (e.g., immersion in water of a marine organism) can play an important role [6].

The difficulty of discriminating between thermal and nonthermal effects of microwave radiation is illustrated by the extensive research, carried out over a period of many years, that

was necessary to explain the microwave acoustic effect [39], [49]. It is known that humans get an audible sensation (hear "clicks") when subjected to pulsed microwave radiation, such as from some radar equipment. Observations indicated that the necessary incident peak electric field (at about 1 GHz) had to be about 1 kV/m (more at higher frequencies) when pulse widths were between 10 and 60 μs and pulse repetition rates (prr) from 200 to 400 Hz. Perceived audio frequencies were not related to prr. Pulsed microwave "hearing" in animals (rats and cats) was confirmed by behavioral experiments, as well as by measurements of evoked electrical potentials in the auditory cortex.

Eventually it was established that the most likely explanation of the effect is "thermo-elastic stress" where a portion of the incident radiation is converted into heat that generates a temperature gradient normal to the surface of the skull. This temperature gradient is accompanied by thermal expansion of the material inside the skull within microseconds. Stress waves then propagate away from the surface. At a plane air-dielectric boundary the resulting pressure [39] is given by

$$p_T = \frac{E_0^2}{Z_D}\frac{3v\beta}{c}F \tag{25}$$

where $\beta =$ coefficient of thermal expansion $= L/(T\Delta L)$ with $L =$ length, $v =$ velocity of sound in the material and, as before, $c =$ specific heat.

From (16), (18) and (25) we obtain

$$\left|\frac{p_T}{p_r}\right| = \frac{3v\beta}{c\sqrt{\mu_0\varepsilon_0\varepsilon_r}}. \tag{26}$$

Typical values for brain tissue near 1 GHz are [39] $v = 1500$ m/s, $\beta = (4.14)10^{-5}(^\circ\text{C})^{-1}$, $\varepsilon_r \approx 31$ and $c = 3864$ J/(°C) giving $(p_T/p_r) \approx 2600$. Thus, at least for the microwave-acoustic effect, thermo-elastic stress induced by the microwave pulsed power provides a much more likely explanation than either radiation pressure or, recalling (20), electrostrictive pressure. This is so despite the fact that the rate of temperature increase, given by the first part of (21), is only about 0.25 °C/s (leading to $\Delta T \approx (1.5)10^{-5}$ °C at the end of a 10-μs pulse) for a typical perceived sound producing peak absorbed power of 10^6 W/m^3. Earlier experiments [50] have also documented microwave induced transients in water, physiological saline, blood, muscle and brain tissue (incident energy was 0.8 J/m^2 per pulse in 2 to 15 μs pulses modulating a 2.45-GHz carrier). Additional support for the thermoelastic stress explanation is provided by computations extending the model to a spherical "head" [39]. They show that the generated acoustic frequency is inversely proportional to head size, a result in complete agreement with experimental data obtained on both humans and smaller mammals.

The microwave acoustic effect illustrates the need for carefully examining the possibility of thermally mediated effects due to large electric fields. More specifically, it illustrates that very large power levels, applied during a very short period (~10 μs) , can produce one physiologically significant effect (i.e., an audible sensation) that depends upon a very small temperture increase. At the present time it is not known whether the small thermally mediated pressure changes have other physiological consequences, in addition to the observed hearing sensation. The microwave acoustic effect does not prove, of course, that the same (or larger) electromagnetic pulses can produce other, entirely temperature independent biological effects; nor does it provide any information on possible biological consequences [43], [49], [51] of small and large electromagnetic fields that are not applied in pulse form.

VI. Conclusion

Large electric fields, particularly in pulse form, can affect biological systems, either directly or indirectly, through many different mechanisms. Field induced translatory motion and torques on electric charges and dipoles are subject to complex boundary conditions. Chemical reaction rates, molecular binding forces, shape and structure of protein molecules can be modified. Effects may be direct or, in some cases, the result of small temperature changes caused by the absorbed electromagnetic energy. Effects can also result from interaction with pre-existing oscillations [43], [51], [52]. Shape and size of biological objects are crucially important parameters at microwave frequencies, where size in terms of wavelengths can give resonant power absorption. The inhomogeneity and anisotropy (e.g., in muscle) of biological systems makes the explanation of specific effects difficult, even when systems can be modeled by linear differential equations—which is certainly not possible at the highest power levels. Furthermore, living systems while often in a steady state, are not in thermodynamic equilibrium since they depend upon continuous energy input. Research to optimize the application of electric fields in biology—to use the desirable results without undesirable "side-effects"—requires realistic mathematical models. For this very close and continuous collaboration among biologists and physicists, clinicians and engineers is essential.

References

[1] J. Malmivuo and R. Plonsey, *Bioelectromagnetism*. Oxford, U.K.: Oxford Univ. Press, 1995.

[2] L. A. Geddes, "Historical highlights in cardiac pacing," *IEEE Eng. Med. Biol.*, vol. 9, pp. 12–18, June 1990.

[3] F. M. Galioto, "Cardiovascular assist and monitoring devices," in *Biomedical Engineering and Instrumentation*, J. D. Bronzimo, Ed. Boston, MA: PWS, 1986, ch. 3.

[4] W. A. Tacker and L. A. Geddes, *Electrical Defibrillation*. Boca Raton, FL: CRC, 1980.

[5] J. P. Reilly, *Electrical Stimulation and Electropathology*. Cambridge, U.K.: Cambridge Univ. Press, 1992.

[6] E. R. Adair, *Thermoregulation in the presence of microwave fields*, 2 ed, C. Polk and E. Postow, Eds. Boca Raton, FL: CRC, 1995, Handbook of Biological Effects of Electromagnetic Fields, ch. 11, pp. 403–433.

[7] J. C. Weaver and Y. Chizmadzhev, *Electroporation*, 2nd ed, C. Polk and E. Postow, Eds. Boca Raton, FL: CRC, 1995, Handbook of Biolgical Effects of Electromagnetic Fields, ch. 6, pp. 247–274.

[8] A. Papoulis, *The Fourier Integral and Its Applications*. New York: McGraw-Hill, 1962.

[9] L. B. Jackson, *Signals, Systems and Transforms*. Reading, MA: Addison-Wesley, 1991.

[10] H. P. Hsu, *Outline of Fourier Analysis*. New York: Unitech Div. Simon and Schuster, 1967.

[11] K. R. Foster and H. P. Schwan, *Dielectric properties of tissue*, 2nd ed, C. Polk and E. Postow, Eds. Boca Raton, FL: CRC, 1995, Handbook of Biological Effects of Electromagnetic Fields, ch. 1, pp. 25–102.

[12] R. Pethig, *Dielectric and Electronic Properties of Biological Materials*. New York: Wiley, 1979.

[13] O. F. Schanne and E. R. P. Ceretti, *Impedance Measurements in Biological Cells*. New York: Wiley, 1978.

[14] W. C. Chew and P. N. Sen, "Dielectric enhancement due to electrochemical double layer: Thin double layer approximation," *J. Chem. Phys.*, vol. 77, pp. 4683–4693, 1982.
[15] W. C. Chew, "Dielectric enhancement and electrophoresis due to an electrochemicla double layer: A uniform approximation," *J. Chem. Phys.*, vol. 81, pp. 4541–4552, 1984.
[16] C. Polk, "Counter-ion polarization and low frequency, low electric field intensity biological effects," *Bioelectrochem. Bioenergetics*, vol. 28, pp. 279–289, 1992.
[17] J. Koryta, *Ions, Electrodes and Membranes*. New York: Wiley, 1982.
[18] P. M. Vassilev, T. Scheuer, and W. A. Catterall, "Identification of intracellular peptide segment involved in sodium channel inactivation," *Science*, vol. 241, pp. 1658–1661, Sept. 1988.
[19] B. U. Keller, R. Hedrich, W. I. L. C. Vaz, and M. Criado, "Single channel recordings of reconstituted ion channel proteins: And improved technique," *Pflugers Arch, Eur. J. Physiol.*, vol. 411, pp. 94–100, 1988.
[20] R. L. Rosenberg, P. Hess, J. P. Reeves, H. Smilowitz, and R. T. Tsien, "Calcium channels in planar lipid bilayers: Insights into mechanisms of ion permeation and gating," *Science*, vol. 231, pp. 1564–1566, Mar. 1986.
[21] D. Pelzer, A. O. Grant, A. Cavalie, S. Pelzer, M. Sieber, F. Hoffmann, and W. Trautwein, "Calcium channels reconstituted from the skeletal muscle dihydropyridine receptor protein complex," in *Annals New York Academy Sciences, Calcium Channels Structure and Function*, D. W. Wray, R. I. Norman, and P. Hess, Eds. New York: N.Y. Academy Sciences, 1989, vol. 560, pp. 138–154.
[22] W. F. Ganong, *Review of Medical Physiology*. Norwalk, CT: Appleton and Lange, 1993.
[23] A. Finkelstein, "The ubiquitous presence of channels with wide lumen and their gating by voltope," in *Annals of the New York Academy of Sciences, Membrane Transport Driven by Ion Gradients*, G. Semeza and R. Kinne, Eds. New York: New York Academy Sciences, 1985, vol. 456, pp. 26–32.
[24] R. C. Warren, *Physics and the Architecture of Cell Membranes*. Philadelphia, MA: Adam Hilger, 1987.
[25] R. Coelho, *Physics of Dielectrics for the Engineer*. Amsterdam, The Netherlands: Elsevier, 1979.
[26] H. A. Pohl, *Dielectrophoresis—The Behavior of Neutral Matter in Nonuniform Electric Fields*. Cambridge, U.K.: Cambridge Univ. Press, 1978.
[27] R. C. Lee, D. J. Canaday, and S. M. Hammer, "Transient and stable ionic permeabilization of isolated skeletal muscle cells after electric shock," *J. Burn Care Rehab.*, vol. 14, no. 5, pp. 528–540, 1993.
[28] J. R. Wait, *Electromagnetic Wave Theory*. New York: Harper & Row, 1985.
[29] C. Polk, *Introduction*, 2nd ed, C. Polk and E. Postow, Eds. Boca Raton, FL: CRC, 1995, Handbook of Biological Effects of Electromagnetic Fields, pp. 1–23.
[30] M. A. Stuchly and S. W. Stuchly, *Experimental Radiowave and Microwave Dosimetry*, 2 ed, C. Polk and E. Postow, Eds. Boca Raton, FL: CRC, 1995, Handbook of Biological Effects of Electromagnetic Fields, ch. 8, pp. 295–336.
[31] M. B. Taraban, T. V. Leshima, M. A. Anderson, and C. B. Grissom, "Magnetic field dependence of electron transfer and the role of electron spin in heme enzymes: Horseradish peroxidase," *J. Amer. Chem. Soc.*, vol. 119, pp. 5768–5769, 1997.
[32] J. Walleczek, E. C. Shiu, and G. M. Hahn, "Increase in radiation-induced HPRT gene mutation frequency after nonthermal exposure to nonionizing 60 Hz electromagnetic fields," *Radiat. Res.*, vol. 152, 1999.
[33] L. Stryer, *Molecular Design of Life*. San Francisco, CA: Freeman, 1989.
[34] K. A. McLauchlan and V. E. Steiner, "The spin-correlated radical pair as a reaction intermediate," *Mol. Phys.*, vol. 73, pp. 241–263, 1991.
[35] R. B. Frankel and R. P. Liburdy, *Biological effects of static magnetic fields*, 2nd ed, C. Polk and E. Postow, Eds. Boca Raton, FL: CRC, 1995, Handbook of Biological Effects of Electromagnetic Fields, ch. 3, pp. 149–183.
[36] C. Eichwald and J. Walleczek, "Magnetic field perturbations as a tool for controlling enzyme-regulated and oscillatory biochemical reactions," *Biophys. Chem.*, vol. 74, pp. 209–224, 1998.
[37] J. R. Meyer-Arendt, *Introduction to Classical and Modern Optics*. Englewood Cliffs, NJ: Prentice-Hall, 1972.
[38] L. C. Shen and J. Aukong, *Applied Electromagnetism*. Boston, MA: PWS, 1987.
[39] J. C. Lin, *Microwave Auditory Effects and Applications*. Springfield, IL: Charles C Thomas, 1978.
[40] L. I. Beranek, *Acoustics*. New York: McGraw-Hill, 1954.
[41] J. A. Stratton, *Electromagnetic Theory*. New York and London: McGraw-Hill, 1941.
[42] W. R. Smythe, *Static and Dynamic Electricity*, 3rd ed. New York: Hemisphere, 1989.
[43] F. S. Barnes, *Interaction of DC and ELF electric fields with biological materials and systems*, 2 ed, C. Polk and E. Postow, Eds. Boca Raton, FL: CRC, 1995, Handbook of Biological Effects of Electromagnetic Fields, ch. 2, pp. 103–147.
[44] "Biological Effects and Exposure Criteria for Radiofrequency Electromagnetic Fields," National Council on Radiation Protection, Bethesda, MD, NCRP Rep. no. 86, Apr. 2, 1986.
[45] T. W. Dawson, K. Caputa, and M. A. Stuchly, "High-resolution organ dosimetry to low-frequency electric fields," *IEEE Trans. Power Delivery*, vol. 13, pp. 1–8, 1997.
[46] O. P. Gandhi and J. H. Chen, "Numerical dosimetry at power-line frequencies using anatomically based models," *Bioelectromagnetics*, pp. 43–60, 1962.
[47] O. P. Gandhi, G. Lazzi, A. Tinniswood, and Q. S. Yu, "Comparison of numerical and experimental methods for determination of SAR and radiation patterns of handheld wireless telephones," *Bioelectromagnetics*, pp. 93–101, 1999.
[48] W. T. Kaune and R. D. Phillips, "Comparison of the coupling of grounded humans, swine and rats to vertical, 60 Hz electric fields," *Bioelectromagnetics*, vol. 1, pp. 117–129, 1980.
[49] E. Postow and M. L. Swicord, *Modulated Fields and 'Window' Effects*, 2 ed, C. Polk and E. Postow, Eds. Boca Raton, FL: CRC, 1995, Handbook of Biological Effects of Electromagnetic Fields, ch. 12, pp. 535–580.
[50] K. R. Foster and E. E. Finch, "Microwave hearing: Evidence for thermoacoustical auditory stimulation by pulsed microwaves," *Science*, vol. 185, pp. 256–258, 1974.
[51] A. G. Pakhomov, Y. Akyel, O. N. Pakhomova, B. E. Stuck, and M. R. Murphy, "Current state and implications of research on biological effects of millimeter waves: A review of the literature," *Bioelectromagnetics*, vol. 19, pp. 393–413, 1998.
[52] M. J. Berridge and A. Galione, "Cytosolic calcium oscillations," *FASEB J.*, vol. 2, pp. 3074–3082, Dec. 1988.
[53] J. T. Mortimer, *Motor Prostheses*. Bethesda, MD: American Physiological Society, 1981, vol. II, Handbook of Physiology, Section 1: The Nervous System. Motor Control Part I, pp. 155–187.

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