HANDBOOK OF BIOLOGICAL EFFECTS OF ELECTROMAGNETIC FIELDS

THIRD EDITION

Bioengineering and Biophysical Aspects of Electromagnetic Fields

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Preface

We are honored to have been asked to carry on the tradition established by Dr. Postow and the late Dr. Polk in the first two editions of the *Handbook of Biological Effects of Electromagnetic Fields*. Their editions of this handbook were each recognized as the authoritative standards of their time for scientists working in bioelectromagnetics, the science of electromagnetic field effects on biological systems, and for others seeking information about this field of research.

In revising and updating this edition of the *Handbook of Biological Effects of Electromagnetic Fields*, we have expanded the coverage to include more material on diagnostic and therapeutic applications. At the same time, in updating and expanding the previous editions' coverage of the basic science and studies related to the possible biological effects of the electromagnetic fields, we have added new material on the related physics and chemistry as well as reviews of the recent developments in the setting standards for exposure limits. Following the previous edition's lead, we have charged the authors of the individual chapters with providing the reader, whom we imagine is fairly well founded in one or more of the sciences underlying bioelectromagnetics but perhaps not in the others or in the interdisciplinary subject of bioelectromagnetics itself, with both an introduction to their topic and a basis for further reading. We asked the chapter authors to write what they would like to be the first thing they would ask a new graduate student in their laboratory to read. We hope that this edition, like its two predecessors, will be useful to many as a reference book and to others as a text for a graduate course that introduces bioelectromagnetics or some of its aspects.

As a ''handbook'' and not an encyclopedia, this work does not intend to cover all aspects of bioelectromagnetics. Nevertheless, taking into account the breadth of topics and growth of research in this field since the last edition, we have expanded the number of topics and the number of chapters. Unavoidably, some ideas are duplicated in chapters, sometimes from different viewpoints that could be instructive to the reader; and different aspects of others are presented in different chapters. The increased amount of material has led to the publication of the handbook as two separate, but inter-related volumes: *Biological and Medical Aspects of Electromagnetic Fields (BMA)* and *Bioengineering and Biophysical Aspects of Electromagnetic Fields (BBA)*. Because there is no sharp dividing line, some topics are dealt with in parts of both volumes. The reader should be particularly aware that various theoretical models, which are proposed for explaining how fields interact with biological systems at a biophysical level, are distributed among a number of chapters. No one model has become widely accepted, and it is quite possible that more than one will in fact be needed to explain all observed phenomena. Most of these discussions are in the *Biological and Medical* volume, but the *Bioengineering and Biophysics* volume's chapters on electroporation and on mechanisms and therapeutic applications, for example, also have relevant material. Similarly, the chapters on biological effects of static magnetic fields and on endogenous electric fields in animals could equally well have been in the *Biological and Medical* volume. We have tried to use the index and cross-references in the chapters to direct the reader to the most relevant linkages, and we apologize for those we have missed.

Research in bioelectromagnetics stems from three sources, all of which are important; and various chapters treat both basic physical science and engineering aspects and the biological and medical aspects of these three. Bioelectromagnetics first emerged as a

separate scientific subject because of interest in studying possible hazards from exposure to electromagnetic fields and setting exposure limits. A second interest is in the beneficial use of fields to advance health, both in diagnostics and in treatment, an interest that is as old as the discovery of electricity itself. Finally, the interactions between electromagnetic fields and biological systems raise some fundamental, unanswered scientific questions and may also lead to fields being used as tools to probe basic biology and biophysics. Answering basic bioelectromagnetic questions will not only lead to answers about potential electromagnetic hazards and to better beneficial applications, but they should also contribute significantly to our basic understanding of biological processes. Both strong fields and those on the order of the fields generated within biological systems may become tools to perturb the systems, either for experiments seeking to understand how the systems operate or simply to change the systems, such as by injecting a plasmid containing genes whose effects are to be investigated. These three threads are intertwined throughout bioelectromagnetics. Although any specific chapter in this work will emphasize one or another of these threads, the reader should be aware that each aspect of the research is relevant to a greater or lesser extent to all three.

The reader should note that the chapter authors have a wide variety of interests and backgrounds and have concentrated their work in areas ranging from safety standards and possible health effects of low-level fields to therapy through biology and medicine to the fundamental physics and chemistry underlying the biology. It is therefore not surprising that they have different and sometimes conflicting points of view on the significance of various results and their potential applications. Thus authors should only be held responsible for the viewpoints expressed in their chapters and not in others. We have tried to select the authors and topics so as to cover the scientific results to date that are likely to serve as a starting point for future work that will lead to the further development of the field. Each chapter's extensive reference section should be helpful for those needing to obtain a more extensive background than is possible from a book of this type.

Some of the material, as well as various authors' viewpoints, are controversial, and their importance is likely to change as the field develops and our understanding of the underlying science improves. We hope that this volume will serve as a starting point for both students and practitioners to come up-to-date with the state of understanding of the various parts of the field as of late 2004 or mid-2005, when authors contributing to this volume finished their literature reviews.

The editors would like to express their appreciation to all the authors for the extensive time and effort they have put into preparing this edition, and it is our wish that it will prove to be of value to the readers and lead to advancing our understanding of this challenging field.

Frank S. Barnes
Ben Greenebaum

Editors

Frank Barnes received his B.S. in electrical engineering in 1954 from Princeton University and his M.S., engineering, and Ph.D. degrees from Stanford University in 1955, 1956, and 1958, respectively. He was a Fulbright scholar in Baghdad, Iraq, in 1958 and joined the University of Colorado in 1959, where he is currently a distinguished professor. He has served as chairman of the Department of Electrical Engineering, acting dean of the College of Engineering, and in 1971 as cofounder/director with Professor George Codding of the Political Science Department of the Interdisciplinary Telecommunications Program (ITP).

He has served as chair of the IEEE Electron Device Society, president of the Electrical Engineering Department Heads Association, vice president of IEEE for Publications, editor of the *IEEE Student Journal* and the *IEEE Transactions on Education*, as well as president of the Bioelectromagnetics Society and U.S. Chair of Commission K—International Union of Radio Science (URSI). He is a fellow of the AAAS, IEEE, International Engineering Consortium, and a member of the National Academy of Engineering.

Dr. Barnes has been awarded the Curtis McGraw Research Award from ASEE, the Leon Montgomery Award from the International Communications Association, the 2003 IEEE Education Society Achievement Award, Distinguished Lecturer for IEEE Electron Device Society, the 2002 ECE Distinguished Educator Award from ASEE, The Colorado Institute of Technology Catalyst Award 2004, and the Bernard M. Gordon Prize from National Academy of Engineering for Innovations in Engineering Education 2004. He was born in Pasadena, CA, in 1932 and attended numerous elementary schools throughout the country. He and his wife, Gay, have two children and two grandchildren.

Ben Greenebaum retired as professor of physics at the University of Wisconsin–Parkside, Kenosha, WI, in May 2001, but was appointed as emeritus professor and adjunct professor to continue research, journal editing, and university outreach projects. He received his Ph.D. in physics from Harvard University in 1965. He joined the faculty of UW–Parkside as assistant professor in 1970 following postdoctoral positions at Harvard and Princeton Universities. He was promoted to associate professor in 1972 and to professor in 1980. Greenebaum is author or coauthor of more than 50 scientific papers. Since 1992, he has been editor in chief of *Bioelectromagnetics*, an international peer-reviewed scientific journal and the most cited specialized journal in this field. He spent 1997–1998 as consultant in the World Health Organization's International EMF Project in Geneva, Switzerland. Between 1971 and 2000, he was part of an interdisciplinary research team investigating the biological effects of electromagnetic fields on biological cell cultures. From his graduate student days through 1975, his research studied the spins and moments of radioactive nuclei. In 1977 he became a special assistant to the chancellor and in 1978, associate dean of faculty (equivalent to the present associate vice chancellor position). He served 2 years as acting vice chancellor (1984–1985 and 1986–1987). In 1989, he was appointed as dean of the School of Science and Technology, serving until the school was abolished in 1996.

On the personal side, he was born in Chicago and has lived in Racine, WI, since 1970. Married since 1965, he and his wife have three adult sons.

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Introduction

Charles Polk*

Revised for the 3rd Edition by Ben Greenebaum

Much has been learned since this handbook's first edition, but a full understanding of biological effects of electromagnetic fields has is to be achieved. The broad range of what must be studied has to be a factor in the apparent slow progress toward this ultimate end. The broad range of disciplines involved includes basic biology, medical science and clinical practice, biological and electrical engineering, basic chemistry and biochemistry, and fundamental physics and biophysics. The subject matter ranges over characteristic lengths and timescales from, at one extreme, direct current (dc) or $\sim 10^4$ km-wavelengths, multimillisecond ac fields and large, long-lived organisms to, at the other extreme, submillimeter wavelength fields with periods below 10^{-12} s and subcellular structures and molecules with subnanometer dimensions and characteristic times as short as the 10^{-15} s or less of biochemical reactions.

This chapter provides an introduction and overview of the research and the contents of this handbook.

0.1 Near Fields and Radiation Fields

In recent years it has become, unfortunately, a fairly common practice—particularly in nontechnical literature—to refer to the entire subject of interaction of electric (E) and magnetic (H) fields with organic matter as biological effects of nonionizing radiation, although fields that do not vary with time and, for most practical purposes, slowly time-varying fields do not involve radiation at all. The terminology had its origin in an effort to differentiate between relatively low-energy microwave radiation and high-energy radiation, such as UV and x-rays, capable of imparting enough energy to a molecule or an atom to disrupt its structure by removing one or more electron\s with a single photon. However, when applied to dc or extremely low-frequency (ELF), the term ''nonionizing radiation'' is inappropriate and misleading.

A structure is capable of efficiently radiating electromagnetic waves only when its dimensions are significant in comparison with the wavelength λ. But in free space $\lambda = c/f$, where c is the velocity of light in vacuum (3×10^8 m/s) and f is the frequency in hertz (cycles/s); therefore the wavelength at the power distribution frequency of 60 Hz, e.g., is 5000 km, guaranteeing that most available human-made structures are much smaller than one wavelength.

The poor radiation efficiency of electrically small structures (i.e., structures whose largest linear dimension $L \ll \lambda$ can be illustrated easily for linear antennas. In free space the radiation resistance, R_r of a current element, i.e., an electrically short wire of length ℓ carrying uniform current along its length [1], is

$$R_r = 80\pi^2 \left(\frac{\ell}{\lambda}\right)^2 \tag{0.1}$$

*Deceased.

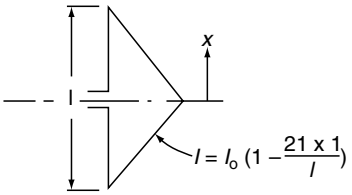

FIGURE 0.1
Current distribution on short, thin, center-fed antenna.

whereas the R_r of an actual center-fed radiator of total length ℓ with current going to zero at its ends, as illustrated in Figure 0.1, is

$$R_r = 20\pi^2 \left(\frac{\ell}{\lambda}\right)^2 \tag{0.2}$$

Thus, the R_r of a 0.01 λ antenna, 50 km long at 60 Hz, would be 0.0197 Ω. As the radiated power $P_r = I^2 R_r$ where I is the antenna terminal current, whereas the power dissipated as heat in the antenna wire is $I^2 R_d$; when I is uniform, the P_r will be very much less than the power used to heat the antenna, given that the ohmic resistance R_d of any practical wire at room temperature will be very much larger and R_r. For example, the resistance of a 50-km long, 1/2-in. diameter solid copper wire could be 6.65 Ω. At dc, of course, no radiation of any sort takes place, as acceleration of charges is a condition for radiation of electromagnetic waves.

The second set of circumstances, which guarantees that any object subjected to low-frequency E and H fields usually does not experience effects of radiation, is that any configuration that carries electric currents sets up E and H field components which store energy without contributing to radiation. A short, linear antenna in free space (short electric dipole) generates, in addition to the radiation field E_r, an electrostatic field E_s and an induction field E_i. Neither E_s nor E_i contribute to the P_r [2,3]. Whereas E_r varies as $1/r$, where r is the distance from the antenna, E_i varies as $1/r^2$, and E_s as $1/r^3$. At a distance from the antenna of approximately one sixth of the wavelength ($r = \lambda/2\pi$), the E_i equals the E_r, and when $r \ll \lambda/6$ the E_r quickly becomes negligible in comparison with E_i and E_s. Similar results are obtained for other antenna configurations [4]. At 60 Hz the distance $\lambda/2\pi$ corresponds to about 800 km and objects at distances of a few kilometers or less from a 60-Hz system are exposed to nonradiating field components, which are orders of magnitude larger than the part of the field that contributes to radiation.

A living organism exposed to a static (dc) field or to a nonradiating near field may extract energy from it, but the quantitative description of the mechanism by which this extraction takes place is very different than at higher frequencies, where energy is transferred by radiation:

1. In the near field the relative magnitudes of E and H are a function of the current or charge configuration and the distance from the electric system. The E field may be much larger than the H field or vice versa (see Figure 0.2).
2. In the radiation field the ratio the E to H is fixed and equal to 377 in free space, if E is given in volt per meter and H in ampere per meter.
3. In the vicinity of most presently available human-made devices or systems carrying static electric charges, dc, or low-frequency (<1000 Hz) currents, the E and H fields will only under very exceptional circumstances be large enough to produce heating effects inside a living object, as illustrated by Figure 0.3. (This statement assumes that the living object does not form part of a conducting path

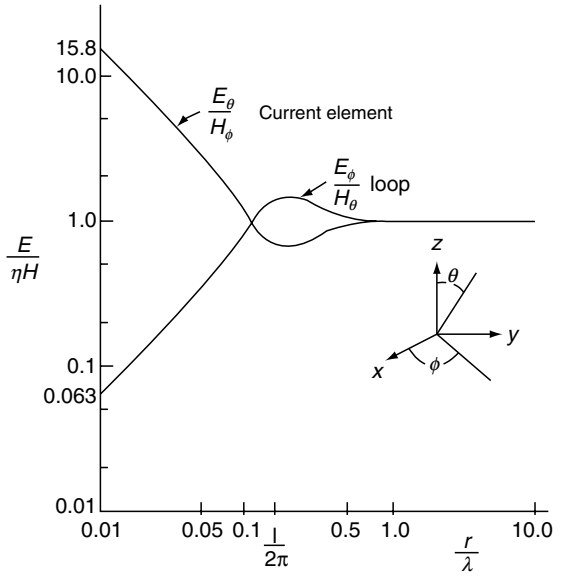

FIGURE 0.2
Ratio of E to H field (divided by wave impedance of free space $\eta = 377\ \Omega$) at $\theta = 90°$; for electric current element at origin along z-axis and for electrically small loop centered at the origin in x–y plane.

that permits direct entrance of current from a wire or conducting ground.) However, nonthermal effects are possible; thus an E field of sufficient magnitude may orient dipoles, or translate ions or polarizable neutral particles (see Chapter 3 and Chapter 4 in *BBA**).

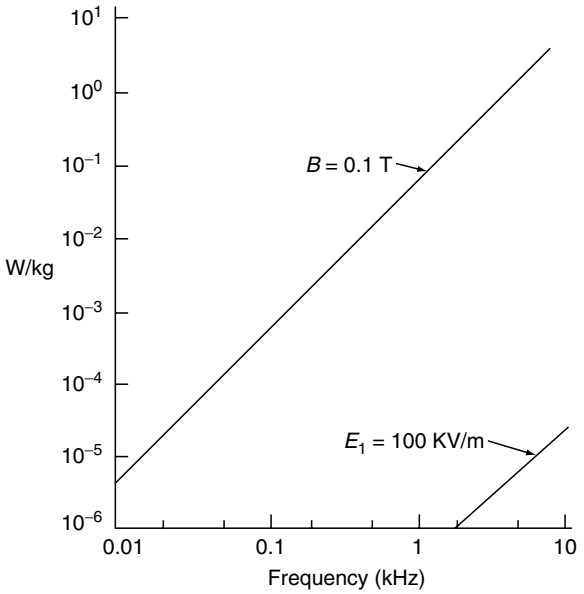

FIGURE 0.3
Top line: Eddy current loss produced in cylinder by sinusoidally time-varying axial H field. Cylinder parameters are conductivity $\sigma = 0.1\,\mathrm{S/m}$, radius 0.1 m, density $D = 1100\,\mathrm{kg/m^3}$, RMS magnetic flux density $0.1\,\mathrm{T} = 1000\,\mathrm{G}$. Watt per kilogram $= \sigma B^2 r^2 w^2 / 8D$; see Equation 0.15 and use power per volume $= J^2/\sigma$, *Lower line:* Loss produced by 60-Hz E field in Watt per kilogram $= \sigma\, E_{\mathrm{int}}{}^2/D$, where external field E_1 is related to E_{int} by Equation 0.9 with $\varepsilon_2 = \varepsilon_0 \times 10^5$ at 1 kHz and $\varepsilon_0 = 8 \times 10^4$ at 10 kHz.

**BBA*: *Bioengineering and Biophysical Aspects of Electromagnetic Fields* (ISBN 0-8493-9539-9); *BMA*: *Biological and Medical Aspects of Electromagnetic Fields* (ISBN 0-8493-9538-0).

4. With radiated power it is relatively easy to produce heating effects in living objects with presently available human-made devices (see Chapter 10 in *BBA* and Chapter 5 in *BMA*). This does not imply, of course, that all biological effects of radiated radio frequency (RF) power necessarily arise from temperature changes.

The results of experiments involving exposure of organic materials and entire living organisms to static E and ELF E fields are described in *BBA*, Chapter 3. Various mechanisms for the interaction of such fields with living tissue are also discussed there and in *BBA*, Chapter 5. In the present introduction, we shall only point out that one salient feature of static (dc) and ELF E field interaction with living organisms is that the external or applied E field is always larger by several orders of magnitude than the resultant average internal E field [5,6]. This is a direct consequence of boundary conditions derived from Maxwell's equations [1–3].

0.2 Penetration of Direct Current and Low-Frequency Electric Fields into Tissue

Assuming that the two materials illustrated schematically in Figure 0.4 are characterized, respectively, by conductivities σ_1 and σ_2 and dielectric permittivities ε_1 and ε_2, we write E-field components parallel to the boundary as E_{P} and components perpendicular to the boundary as $E_{\perp}$. For both static and time-varying fields

$$E_{\mathrm{P1}} = E_{\mathrm{P2}} \tag{0.3}$$

and for static (dc) fields

$$\sigma_1 E_{\perp 1} = \sigma_2 E_{\perp 2} \tag{0.4}$$

as a consequence of the continuity of current (or conservation of charge). The orientations of the total E fields in media 1 and 2 can be represented by the tangents of the angles between the total fields and the boundary line

$$\tan\theta_1 = \frac{E_{\perp 1}}{E_{\mathrm{P1}}}, \quad \tan\theta_2 = \frac{E_{\perp 2}}{E_{\mathrm{P2}}} \tag{0.5}$$

From these equations it follows that

$$\tan\theta_1 = \frac{\sigma_2}{\sigma_1}\frac{E_{\perp 1}}{E_{\mathrm{P1}}} = \frac{\sigma_2}{\sigma_1}\frac{E_{\perp 2}}{E_{\mathrm{P2}}} = \frac{\sigma_2}{\sigma_1}\tan\theta_2 \tag{0.6}$$

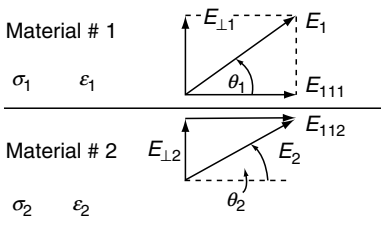

FIGURE 0.4
Symbols used in description of boundary conditions for E-field components.

If material 1 is air with conductivity [7] $\sigma_1 = 10^{-13}$ S/m and material 2 a typical living tissue with $\sigma_2 \approx 10^{-1}$ S/m (compare Chapter 3 in *BBA*), $\tan\theta_1 = 10^{12}\tan\theta_2$, and therefore even if the field in material 2 (the inside field) is almost parallel to the boundary so that $\theta_2 \cong 0.5^\circ$ or $\tan\theta_2 \approx (1/100)$, $\tan\theta_1 = 10^{10}$ or $\theta_1 = (\pi/2 - 10)^{-10}$ radians. Thus an electrostatic field in air, at the boundary between air and living tissue, must be practically perpendicular to the boundary. The situation is virtually the same at ELF although Equation 0.4 must be replaced by

$$\sigma_1 E_{\perp 1} - \sigma_2 E_{\perp 2} = -\mathrm{j}\omega\rho_s \tag{0.7}$$

and

$$\varepsilon_1 E_{\perp 1} - \varepsilon_2 E_{\perp 2} = \rho_s \tag{0.8}$$

where $\mathrm{j} = \sqrt{-1}$, ω is the radian frequency ($= 2\pi \times$ frequency), and ρ_s is the surface charge density. In Chapter 3 in *BBA* it is shown that at ELF the relative dielectric permittivity of living tissue may be as high as 10^6 so that $\varepsilon_2 = 10^6\ \varepsilon_0$, where ε_0 is the dielectric permittivity of free space $(1/36\ \pi)\ 10^{-9}$ F/m; however, it is still valid to assume that $\varepsilon_2 \leq 0^{-5}$. Then from Equation 0.7 and Equation 0.8

$$E_{\perp 1} = \frac{\sigma_2 + \mathrm{j}\omega\varepsilon_2}{\sigma_1 + \mathrm{j}\omega\varepsilon_1} E_{\perp 2} \tag{0.9}$$

which gives at 60 Hz with $\sigma_2 = 10^1$ S/m, $\sigma_1 = 10^{-13}$ S/m, $\varepsilon_2 \approx 10^{-5}$ F/m, and $\varepsilon_1 \approx 10^{-11}$ F/m

$$E_{\perp 1} = \frac{10^{-1} + \mathrm{j}_4 10^{-3}}{10^{-13} + \mathrm{j}_4 10^{-9}} E_{\perp 2} \approx \frac{\sigma_2}{\mathrm{j}\omega\varepsilon_1} = -\mathrm{j}\,(2.5 \times 10^7) E_{\perp 2} \tag{0.10}$$

This result, together with Equation 0.3 and Equation 0.5, shows that for the given material properties, the field in air must still be practically perpendicular to the boundary of a living organism: $\tan\theta_1$: $2.5(10^7)\tan\theta_2$.

Knowing now that the living organism will distort the E field in its vicinity in such a way that the external field will be nearly perpendicular to the boundary surface, we can calculate the internal field by substituting the total field for the perpendicular field in Equation 0.4 (dc) and Equation 0.9 (ELF). For the assumed typical material parameters we find that in the static (dc) case

$$\frac{E_{\text{internal}}}{E_{\text{external}}} \approx 10^{-12} \tag{0.11}$$

$$\rho_f = \frac{3(\sigma_2\varepsilon_1 - \sigma_1\varepsilon_2)E_0}{2\sigma_1 + \sigma_2} \cos\vartheta\ \text{C/m}^2$$

and for 60 Hz

$$\frac{E_{\text{internal}}}{E_{\text{external}}} \approx 4(10^{-8}) \tag{0.12}$$

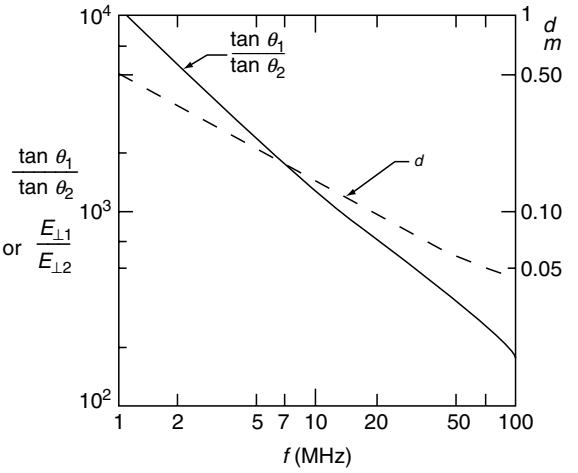

FIGURE 0.5
Orientation of *E*-field components at air–muscle boundary (or ratio of fields perpendicular to boundary); depth (d) at which field component parallel to boundary surface decreases by approximately 50% ($d = 0.6938$).

Thus, a 60-Hz external field of 100 kV/m will produce an average E_{internal} field of the order of 4 mV/m.

If the boundary between air and the organic material consists of curved surfaces instead of infinite planes, the results will be modified only slightly. Thus, for a finite sphere (with ε and σ as assumed here) embedded in air, the ratios of the internal field to the undisturbed external field will vary with the angle θ and distance r as indicated in Figure 0.5, but will not deviate from the results indicated by Equation 0.7 and Equation 0.8 by more than a factor of 3 [3,8]. Long cylinders ($L \ll r$) aligned parallel to the external field will have interior fields essentially equal to the unperturbed external field, except near the ends where the field component perpendicular to the membrane surface will be intensified approximately as above (see Chapter 9 and Chapter 10 in this volume).

0.3 Direct Current and Low-Frequency Magnetic Fields

Direct current H fields are considered in more detail in the Chapter 3, Chapter 5, and Chapter 8 in *BBA*. ELF H fields are considered in various places, including Chapter 5 and Chapter 7 in *BBA* and Chapter 2 and Chapter 11 in *BMA*. As the magnetic permeability μ of most biological materials is practically equal to the magnetic permeability μ_0 of free space, $4\pi(10^{-7})$ H/m, the dc or ELF H field ''inside'' will be practically equal to the H field ''outside.'' The only exceptions are organisms such as the magnetotactic bacteria, which synthesize ferromagnetic material, discussed in Chapter 8 of *BBA*. The known and suggested mechanisms of interaction of dc H fields with living matter are:

1. Orientation of ferromagnetic particles, including biologically synthesized particles of magnetite.
2. Orientation of diamagnetically or paramagnetically anisotropic molecules and cellular elements [9].
3. Generation of potential differences at right angles to a stream of moving ions (Hall effect, also sometimes called a magnetohydrodynamic effect) as a result of the magnetic force $F_{\text{m}} = qvB \sin \theta$, where q is the the electric charge, v is the

velocity of the charge, B is the magnetic flux density, and sin θ is the sine of the angle θ between the directions v and B. One well-documented result of this mechanism is a ''spike'' in the electrocardiograms of vertebrates subjected to large dc H fields.

4. Changes in intermediate products or structural arrangements in the course of light-induced chemical (electron transfer) reactions, brought about by Zeeman splitting of molecular energy levels or effects upon hyperfine structure. (The Zeeman effect is the splitting of spectral lines, characteristic of electronic transitions, under the influence of an external H field; hyperfine splitting of electronic transition lines in the absence of an external H field is due to the magnetic moment of the nucleus; such hyperfine splitting can be modified by an externally applied H field.) The magnetic flux densities involved not only depend upon the particular system and can be as high as 0.2 T (2000 G) but also $<$0.01 mT (100 G). Bacterial photosynthesis and effects upon the visual system are prime candidates for this mechanism [10,11].
5. Induction of E fields with resulting electrical potential differences and currents within an organism by rapid motion through a large static H field. Some magnetic phosphenes are due to such motion [12].

Relatively slow time-varying H fields, which are discussed in the basic mechanisms and therapeutic uses chapters (Chapter 5 of *BBA* and Chapter 11 in *BMA*), among others, may interact with living organisms through the same mechanisms that can be triggered by static H fields, provided the variation with time is slow enough to allow particles of finite size and mass, located in a viscous medium, to change orientation or position where required (mechanism 1 and 2) and provided the field intensity is sufficient to produce the particular effect. However, time-varying H fields, including ELF H fields, can also induce electric currents into stationary conducting objects. Thus, all modes of interaction of time-varying E fields with living matter may be triggered by time-varying, but not by static, H fields.

In view of Faraday's law, a time-varying magnetic flux will induce E fields with resulting electrical potential differences and ''eddy'' currents through available conducting paths. As very large external ELF E fields are required (as indicated by Equation 0.9 through Equation 0.12) to generate even small internal E fields, many human-made devices and systems generating both ELF E and H fields are more likely to produce physiologically significant internal E fields through the mechanism of *magnetic* induction.

The induced voltage V around some closed path is given by

$$V = \oint E \cdot \mathrm{d}\ell = -\int\int \frac{\partial B}{\partial t}\mathrm{d}s \tag{0.13}$$

where E is the induced E field. The integration $\oint E\ \mathrm{d}\ell$ is over the appropriate conducting path, $\partial B/\partial t$ is the time derivative of the magnetic flux density, and the ''dot'' product with the surface element, ds, indicates that only the component of $\partial B/\partial t$ perpendicular to the surface, i.e., parallel to the direction of the vector ds, enclosed by the conducting path, induces an E field. To obtain an order-of-magnitude indication of the induced current that can be expected as a result of an ELF H field, we consider the circular path of radius r, illustrated by Figure 0.6. Equation 0.13 then gives the magnitude of the E field as

$$E = \frac{\omega B r}{2} \tag{0.14}$$

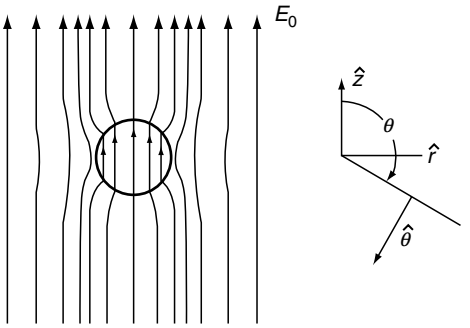

FIGURE 0.6
E field when sphere of radius R, conductivity σ_2, and dielectric permittivity ε_2 is placed into an initially uniform static field ($E = 2E_0$) within a medium with conductivity σ_1 and permittivity ε_1. The surface charge density is $\rho_r = \dfrac{3(\sigma_2\varepsilon_1 - \sigma_1\varepsilon_2)E_0}{2\sigma_1 + \sigma_2}\cos\theta$ C/m^2.

$$r < R \quad \bar{E} = \frac{3\sigma_1 E_0}{2\sigma_1 + \sigma_2}\hat{z} \qquad \varepsilon_2, \sigma_2$$

$$r < R \quad \bar{E} = E_0\cos\theta\left[1 + \frac{2R^3(\sigma_2 \propto \sigma_1)}{r^3(2\sigma_1 + \sigma_2)}\right]\hat{r} \qquad \varepsilon_1, \sigma_1$$

$$- E\sin\theta\left[1 - \frac{R^3(\sigma_2 \propto \sigma_1)}{r^3(2\sigma_1 + \sigma_2)}\right]\hat{\theta}$$

where ω is the $2\pi f$ and f is the frequency. The magnitude of the resulting electric current density J in ampere per square meter is*

$$J = \sigma E = \frac{\sigma\omega B r}{2} \tag{0.15}$$

where σ is the conductivity along the path in Siemens per meter. In the SI (Systeme Internationale) units used throughout this book, B is measured in tesla ($T = 10^4$ G) and r in meters. Choosing for illustration a circular path of 0.1 m radius, a frequency of 60 Hz, and a conductivity of 0.1 S/m, Equation 0.14 and Equation 0.15 give $E = 18.85$ B and $J = 1.885$ B. The magnetic flux density required to obtain a current density of 1 mA/m^2 is 0.53 mT or about 5 G. The E field induced by that flux density along the circular path is 10 mV/m. To produce this same 10 mV/m E_{internal} field by an external 60 Hz E_{external} field would require, by Equation 0.12, a field intensity of 250 kV/m.

As the induced voltage is proportional to the time rate of change of the H field (Equation 0.13), implying a linear increase with frequency (Equation 0.14), one would expect that the ability of a time-varying H field to induce currents deep inside a conductive object would increase indefinitely as the frequency increases; or conversely, that the magnetic flux density required to induce a specified E field would decrease linearly with frequency, as indicated in Figure 0.7. This is not true however, because the displacement current density $\partial D/\partial t$, where $D = \varepsilon E$, must also be considered as the frequency increases. This leads to the wave behavior discussed in Part III, implying that at sufficiently high frequencies the effects of both external E and H fields are limited

*Equation 0.15 neglects the H field generated by the induced eddy currents. If this field is taken into account, it can be shown that the induced current density in a cylindrical shell of radius r and thickness Δ is given by $\Delta r < 0.01$ m$^2/[1 + j\Delta r/\delta^2]$, where $H_0 = B_0/\mu_0$ and δ is the skin depth defined by Equation 0.17 below. However, for conductivities of biological materials ($\sigma < 5$ s/m) one obtains at audio frequencies $\delta > 1$ m and as for most dimensions of interest $\Delta r < 0.01$ m^2 the term $j\Delta r/\delta^2$ becomes negligible. The result $-jrH_0/\delta^2$ is then identical with Equation 0.15.

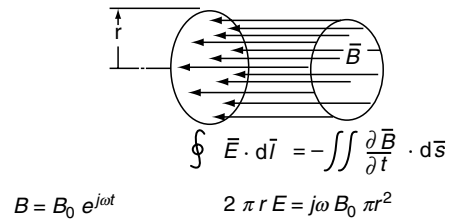

FIGURE 0.7
Circular path (loop) of radius r enclosing uniform magnetic flux density perpendicular to the plane of the loop. For sinusoidal time variation $B = B_0 e^{j\omega t}$.

by reflection losses (Figure 0.8 through Figure 0.10) as well as by skin effect [13], i.e., limited depth of penetration d in Figure 0.5.

0.4 RF Fields

At frequencies well below those where most animals and many field-generating systems have dimensions of the order of one free space wavelength, e.g., at 10 MHz where $\lambda = 30$ m, the skin effect limits penetration of the external field. This phenomenon is fundamentally different from the small ratio of internal to external E fields described in Equation 0.4 (applicable to dc) and Equation 0.9.

Equation 0.9 expresses a ''boundary condition'' applicable at all frequencies, but as the angular frequency ω increases (and in view of the rapid decrease with frequency of the dielectric permittivity ε_2 in biological materials—see Chapter 3 of *BBA*, the ratio of the normal component of the external to the internal E field at the boundary decreases

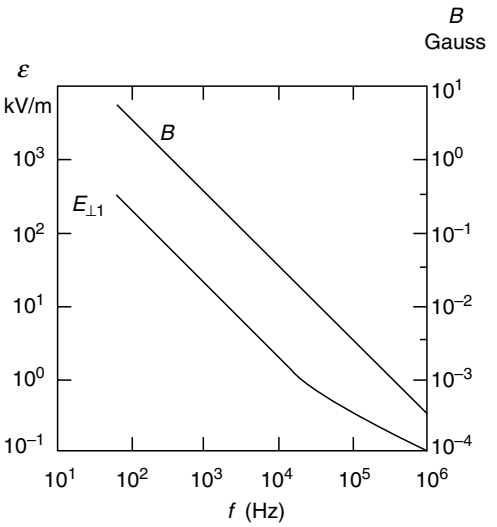

FIGURE 0.8
External E and H field required to obtain an internal E field of 10 mV/m (conductivity and dielectric permittivity for skeletal muscle from Foster, K.R., Schepps, J.L., and Schwan, H.P. 1980. *Biophys. J.*, 29:271–281. H-field calculation assumes a circular path of 0.1-m radius perpendicular to magnetic flux).

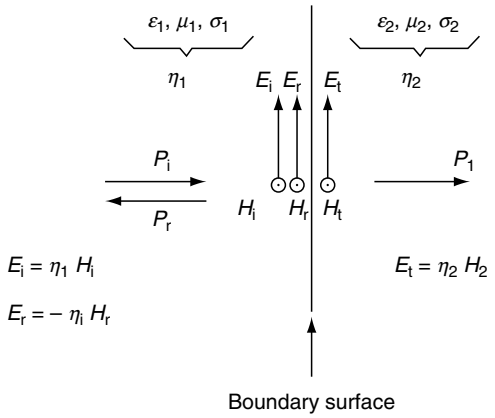

FIGURE 0.9
Reflection and transmission of an electromagnetic wave at the boundary between two different media, perpendicular incidence; P_i = incident power, P_r = reflected power, P_t = transmitted power.

with increasing frequency. This is illustrated by Figure 0.10 where $\tan\theta_1/\tan\theta_2$ is also equal to $E_{\perp 1}/E_{\perp 2}$ in view of Equation 0.3, Equation 0.5, and Equation 0.9. However, at low frequencies the total field inside the boundary can be somewhat larger than the perpendicular field at the boundary; and any field variation with distance from the boundary is not primarily due to energy dissipation, but in a homogeneous body is a consequence of shape. At RF, on the other hand, the E and H fields of the incoming

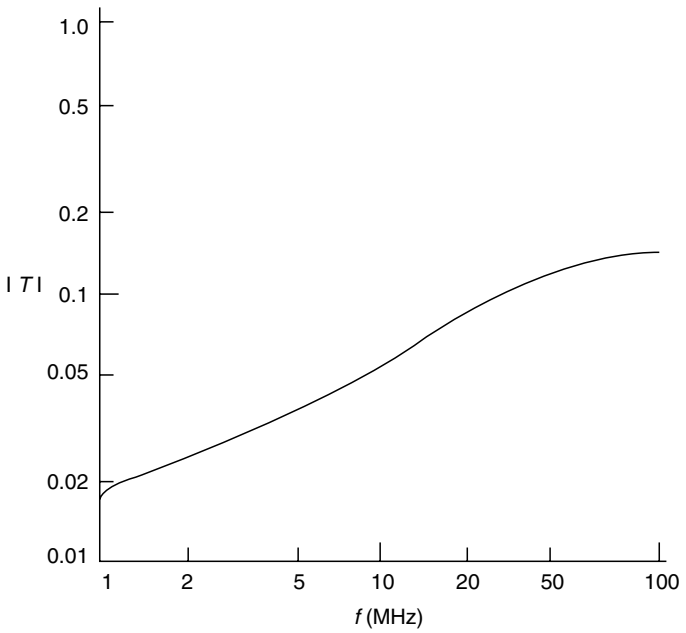

FIGURE 0.10
Magnitude of transmission coefficient T for incident E field parallel to boundary surface. $T = E_t/E_i$: reflection coefficient $r = E_r/E_i = T\text{-}1$. Γ and T are complex numbers; ε_r and σ for skeletal muscle from Chapter 3 in *BBA*.

electromagnetic wave, after reflection at the boundary, are further decreased due to energy dissipation. Both E and H fields decrease exponentially with distance from the boundary

$$g(z) = Ae^{-\frac{z}{\delta}} \tag{0.16}$$

where $g(z)$ is the field at the distance z and A is the magnitude of the field just *inside* the boundary.

As defined by Equation 0.16 the skin depth δ is the distance over which the field decreases to $1/e$ ($= 0.368$) of its value just *inside* the boundary. (Due to reflection, the field A just inside the boundary can already be very much smaller than the incident external field; see Figure 0.8 and Figure 0.9.)

Expressions for δ given below were derived [2,3,13,14] for plane boundaries between infinite media. They are reasonable accurate for cylindrical structures if the ratio of radius of curvature to skin depth (r_0/δ) is larger than about five [13]. For a good conductor

$$\delta = \frac{1}{\sqrt{\pi f \mu \sigma}} \tag{0.17}$$

where a good conductor is one for which the ratio p of conduction current, $J = \sigma E$, to displacement current, $\partial D/\partial t = \varepsilon\,(\partial E/\partial t) = j\omega\varepsilon E$ is large:

$$p = \frac{\sigma}{\omega\varepsilon} \gg 1 \tag{0.18}$$

Since for most biological materials p is of the order of one ($0.1 < p < 10$) over a very wide frequency range (see Chapter 3 of *BBA*), it is frequently necessary to use the more general expression [13]

$$\delta = \frac{1}{\omega\left[\frac{\mu\varepsilon}{2}(\sqrt{1+p^2}-1\right]^{1/2}} \tag{0.19}$$

The decrease of field intensity with distance from the boundary surface indicated by Equation 0.16 becomes significant for many biological objects at frequencies where $r_0/\delta \geq 5$ is not satisfied. However, the error resulting from the use of Equation 0.16 and Equation 0.17 or Equation 0.19 with curved objects is less when $z < \delta$. Thus at $z = 0.693\,\delta$, where $g(z) = 0.5$ A from Equation 0.16 and Equation 0.17, the correct values of $g(z)$, obtained by solving the wave equation in cylindrical coordinates, differs only by 20% (it is 0.6 A) even when r_0/δ is as small as 2.39 [14]. Therefore, Figure 0.10 shows the distance $d = 0.693\,\delta$, at which the field decreases to half of its value just inside the boundary surface, using Equation 0.19 with typical values for σ and ε for muscle from Figure 0.11. It is apparent that the skin effect becomes significant for humans and larger vertebrates at frequencies >10 MHz.

Directly related to skin depth, which is defined for fields varying sinusoidally with time, is the fact that a rapid transient variation of an applied magnetic flux density constitutes an exception to the statement that the dc H field inside the boundary is equal to the H field outside. Thus, from one viewpoint one may consider the rapid application or removal of a dc H field as equivalent to applying a high-frequency field during the switching period, with the highest frequencies present of the order of $1/\tau$, where τ is the rise time of the applied step function. Thus, if $\tau < 10^{-8}$ s, the skin effect will be important during the transient period, as d in Figure 0.5 is <5 cm above 100 MHz. It is also possible to calculate directly the magnetic flux density inside a conducting cylinder as a function of radial position r and time t when a magnetic pulse is applied in the axial

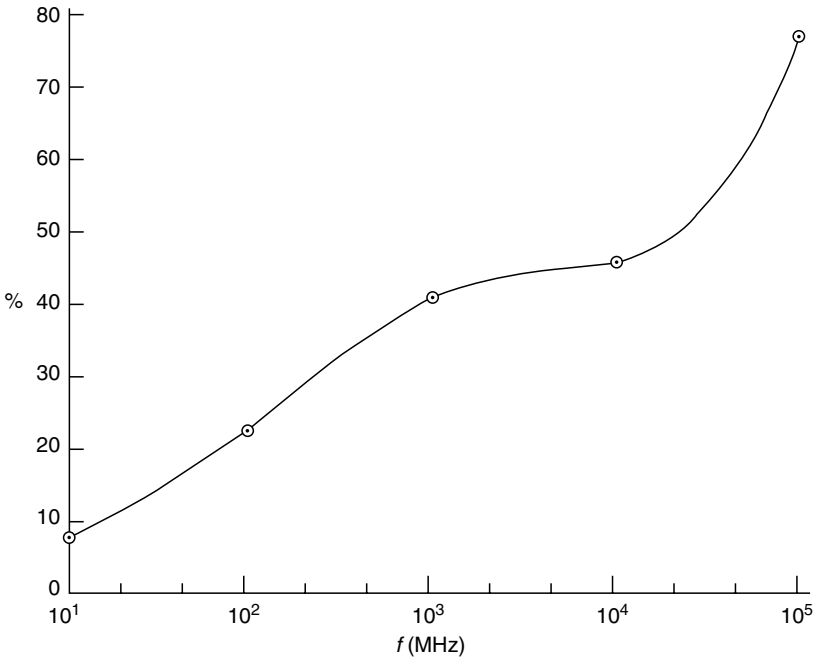

FIGURE 0.11
Ratio of transmitted to incident power expressed as percent of incident power. Air–muscle interface, perpendicular incidence (Equation 0.31, Table 0.1).

direction [15,16]. Assuming zero rise time of the applied field B_0, i.e., a true step function, one finds that the field inside a cylinder of radius a is

$$B = B_0\left[1 - \sum_{k=1}^{\infty} J_0\left(r\frac{v_k}{a}\right)\mathrm{e}^{-t/T_k}\right] \tag{0.20}$$

where $J_0\,(r\,v_k/a)$ is the zero-order Bessel function of argument $r\,v_k/a$ and the summation is over the nulls of J_0 designated v_k (the first four values of v_k are 2.405, 5.520, 8.654, and 11.792).* T_k is the rise time of the kth term in the series and is given by

$$T_k = \frac{\mu_0 \sigma a^2}{v_k} \tag{0.21}$$

As v_k increases, the rise time decreases and therefore the longest delay is due to the first term in the summation with $k = 1$

$$T_1 = \frac{\mu_0 \sigma a^2}{2.405} \tag{0.22}$$

For a cylinder with 0.1 m radius and a conductivity $\sigma \approx 1$ S/m, which is a typical value for muscle between 100 and 1000 MHz, Equation 0.22 gives $T_1 = 2.6 \times 10^{-8}$ s. This finite rise time (or decay time in case of field removal) of the internal H field may be of some importance when pulsed H fields are used therapeutically [17]. It might also be used

*This result is based on solution of $\partial B/\partial t = (1/\mu_0)\nabla^2 B$, which is a consequence of Ampere's and Farraday's laws when displacement is disregarded. Equations 0.20 to 0.22 are therefore only correct when $\mathrm{p} \gg 1$.

to measure noninvasively the conductivity of biological substances *in vivo* through determination of the final decay rate of the voltage induced into a probe coil by the slowly decaying internal field after the applied field is removed [16].

The properties of biological substances in the intermediate frequency range, above ELF (>300 Hz), and below the higher RFs, where wave behavior and skin effect begin to be important (~20 MHz), are discussed in Chapter 3 of *BBA*. However, many subsequent chapters are concerned with biological effects at dc and ELF frequencies below a few kilohertz, while others deal primarily with the higher RFs, >50 MHz. One reason for this limited treatment of the intermediate frequency range is that very little animal data are available for this spectral region in comparison with the large number of experiments performed at ELF and microwave frequencies in recent years.* Another reason is that most electrical processes known to occur naturally in biological systems—action potentials, EKG, EEG, ERG, etc.—occur at dc and ELF frequencies. Therefore, one might expect some physiological effects from external fields of appropriate intensity in the same frequency range, even if the magnitude of such fields is not large enough to produce thermal effects. As illustrated by Figure 0.3 and Figure 0.7, most *E* fields below 100 kHz set up by currently used human-made devices, and most *H* fields below 10 kHz except the very strongest, are incapable of producing thermal effects in living organisms, excluding, of course, fields accompanying currents directly introduced into the organism via electrodes. Thus, the frequencies between about 10 and 100 kHz have been of relatively little interest because they are not very likely to produce thermal or other biological effects. On the other hand, the higher RFs are frequently generated at power levels where enough energy may be introduced into living organisms to produce local or general heating. In addition, despite skin effect and the reflection loss to be discussed in more detail below, microwaves modulated at an ELF rate may serve as a vehicle for introducing ELF fields into a living organism of at least the same order of magnitude as would be introduced by direct exposure to ELF. Any effect of such ELF-modulated microwaves would, of course, require the existence of some amplitude-dependent demodulation mechanism to extract the ELF from the microwave carrier.

Among the chapters dealing with RF, Chapter 10 and Chapter 11 of *BBA* give the necessary information for establishing the magnitude of the fields present in biological objects: (1) experimental techniques and (2) analytical methods for predicting field intensities without construction of physical models made with ''phantom'' materials, i.e., dielectric materials with properties similar to those of living objects which are to be exposed. As thermal effects at microwave frequencies are certainly important, although one cannot assume *a priori* that they are the only biological effects of this part of the spectrum, and as some (but not all) thermal effects occur at levels where the thermoregulatory system of animals is activated, thermoregulation in the presence of microwave fields is discussed in Chapter 5 of *BMA*, as well as in Chapter 10 of *BBA*. Not only are the therapeutic applications of microwaves based upon their thermal effects, but also the experimental establishment of possible nonthermal effects at the threshold of large scale tissue heating in particular living systems and also requires thorough understanding of thermoregulatory mechanisms. The vast amount of experimental data obtained on animal systems exposed to microwave is discussed in Chapter 3 and Chapter 4 in *BMA*. Both nonmodulated fields and modulated fields, where the type of modulation had no apparent effect other than modification of the average power level, are considered. These chapters and the Chapter 9 in *BMA* are considered to be very new extension of experiments into exposures to ultra-short and to ultra-high power pulses.

*Though this statement was written in for the second edition in 1995, it continues to be true in 2005—Ben Greenebaum.

At the higher RFs, the external E field is not necessarily perpendicular to the boundary of biological materials (see Figure 0.4 and Figure 0.10), and the ratio of the total external E field to the total internal field is not given by Equation 0.9. However, the skin effect (Equation 0.16 through Equation 0.19) and reflection losses still reduce the E field within any biological object below the value of the external field. As pointed out in Chapter 3, dielectric permittivity and electrical conductivity of organic substances both vary with frequency. At RF, most biological substances are neither very good electrical conductors nor very good insulators, with the exception of cell membranes, which are good dielectrics at RF but at ELF can act as intermittent conductors or as dielectrics and are ion-selective [18–20]). The ratio p (Equation 0.18) is neither much smaller nor very much larger than values shown for typical muscle tissue [21,22] in Table 0.1.

Reflection loss at the surface of an organism is a consequence of the difference between its electrical properties and those of air. Whenever an electromagnetic wave travels, from one material to another with different electrical properties, the boundary conditions (Equation 0.3 and Equation 0.8) and similar relations for the H field require the existence of a reflected wave. The expressions for the reflection coefficient

$$\Gamma = \frac{E_r}{E_i} \tag{0.23}$$

and the transmission coefficient

$$T = \frac{E_t}{E_i} \tag{0.24}$$

become rather simple for loss-free dielectrics ($p \ll 1$) and for good conductors ($p \gg 1$). As biological substances are neither the most general expressions for Γ and T, applicable at plane boundaries, are needed [3,13]. For perpendicular incidence, illustrated by Figure 0.8,

$$\Gamma = \frac{\eta_2 - \eta_1}{\eta_2 + \eta_1} \tag{0.25}$$

$$T = \frac{2\eta_2}{\eta_2 + \eta_1} = 1 + \Gamma \tag{0.26}$$

TABLE 0.1

Ratio p of Conduction Current to Displacement as a Function of Frequency

f (MHz)	σ	ε_r	$p = \frac{\sigma}{\omega\varepsilon_0\varepsilon_r}$
1	0.40	2000	3.6
10	0.63	160	7.1
100	0.89	72	2.2
10^3	1.65	50	0.59
10^4	10.3	40	0.46
10^5	80	6	2.4

where η_1 and η_2 are the wave impedances, respectively, of mediums 1 and 2. The wave impedance of a medium is the ration of the E to the H field in a plane wave traveling through that medium; it is given by [13]

$$\eta = \left(\frac{j\omega\mu}{\sigma + j\omega\varepsilon}\right)^{1/2} \tag{0.27}$$

Clearly Γ and T are in general complex numbers, even when medium 1 is air for which Equation 0.27 reduces to the real quantity $\eta_0 = \sqrt{\mu_0/\varepsilon_0}$, because medium 2, which here is living matter, usually has a complex wave impedance at RFs.

The incident, reflected, and transmitted powers are given by [13]

$$P_i = R_1|E_i|^2\frac{1}{\eta_1^*} = \frac{|E_i|^2}{|\eta_1|^2}R_1 \tag{0.28}$$

$$P_r = R_1|E_r|^2\frac{1}{\eta_1^*} = \frac{|E_r|^2}{|\eta_1|^2}R_1 \tag{0.29}$$

$$P_t = R_1|E_t|^2\frac{1}{\eta_2^*} = \frac{|E_t|^2}{|\eta_2|^2}R_2 \tag{0.30}$$

where the E fields are effective values ($E_{\text{eff}} = E_{\text{peak}}/\sqrt{2}$) of sinusoidal quantities, R_1 signifies ''real part of,'' η^* is the complex conjugate of η, and R_1 and R_2 are the real parts of η_1 and η_2. If medium 1 is air, $\eta_1 = R_1 = 377\ \Omega$, it follows from Equation 0.23, Equation 0.24, and Equation 0.28 through Equation 0.30 and conservation of energy that the ratio of the transmitted to the incident real power is given by

$$\frac{P}{P_1} = |T|^2\frac{\eta_1\eta_2^* + \eta_1^*\eta_2}{2|\eta_2|^2} = 1 - \frac{P_r}{P_i} = 1 - |\Gamma|^2 \tag{0.31}$$

The magnitude of the transmission coefficient T for the air–muscle interface over the 1- to 100-MHz frequency range is plotted in Figure 0.9, which shows that the magnitude of the transmitted E field in muscle tissue is considerably smaller than the E field in air. The fraction of the total incident power that is transmitted (Equation 0.31) is shown in Figure 0.11, indicating clearly that reflection loss at the interface decreases with frequency. However, for deeper lying tissue this effect is offset by the fact that the skin depth δ (Equation 0.19) also decreases with frequency (Figure 0.12) so that the total power penetrating beyond the surface decreases rapidly.

In addition to reflection at the air–tissue boundary, further reflections take place at each boundary between dissimilar materials. For example, the magnitude of the reflection coefficient at the boundary surface between muscle and organic materials with low-water content, such as fat or bone, is shown in Table 0.2.

The situation is actually more complicated than indicated by Figure 0.9 and Figure 0.11, because the wave front of the incident electromagnetic wave may not be parallel to the air–tissue boundary. Two situations are possible: the incident E field may be polarized perpendicular to the plane of incidence defined in Figure 0.13 (perpendicular polarization, Figure 0.13a) or parallel to the plane of incidence (parallel polarization, Figure 0.13b). The transmission and reflection coefficients [8] are different for the two types of polarization and also become functions of the angle of incidence α_1:

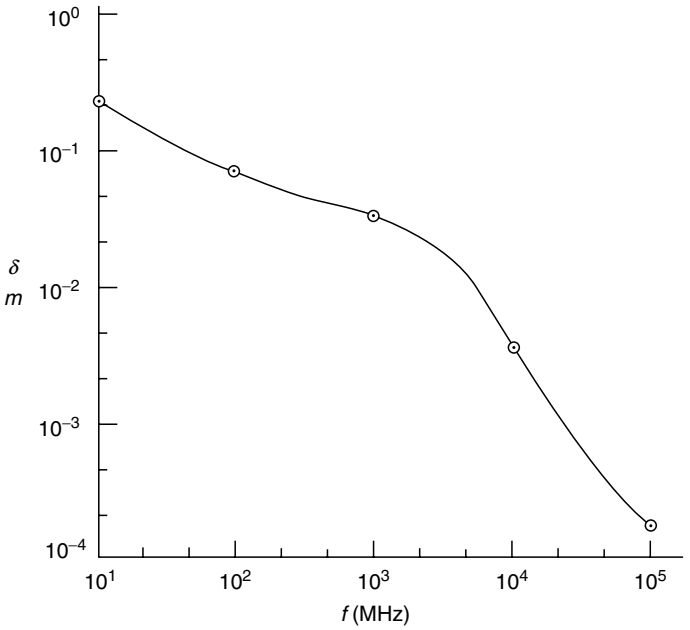

FIGURE 0.12
Electromagnetic skin depth in muscle tissue from plane wave expression (Equation 0.19, Table 0.1).

$$\text{Perpendicular polarization}\begin{cases} T_{\perp} = \dfrac{2\eta_2 \cos\alpha_1}{\eta_2 \cos\alpha_1 + \eta_1 \cos\alpha_2} \\ \Gamma_{\perp} = \dfrac{\eta_2 \cos\alpha_1 - \eta_1 \cos\alpha_2}{\eta_2 \cos\alpha_1 + \eta_1 \cos\alpha_2} \end{cases} \quad (0.32),(0.33)$$

$$\text{Parallel polarization}\begin{cases} T_{\mathrm{p}} = \dfrac{2\eta_2 \cos\alpha_1}{\eta_2 \cos\alpha_2 + \eta_1 \cos\alpha_1} \\ \Gamma_{\mathrm{p}} = \dfrac{\eta_1 \cos\alpha_1 - \eta_2 \cos\alpha_2}{\eta_2 \cos\alpha_2 + \eta_1 \cos\alpha_1} \end{cases} \quad (0.34),(0.35)$$

where α_2 is given by the generalized Snell's law (when both the media have the magnetic permeability of free space) by

TABLE 0.2
Reflection Coefficient ''Capital Gamma'' for Low–Water-Content Materials

	Fat or Bone		
f (MHz)	σ (S/m)	ε_r	Muscle[a]–Fat (Γ)
10^2	0.048	7.5	0.65
10^3	0.101	5.6	0.52
10^4	0.437	4.5	0.52

[a] σ and ε_r for muscle from Table 0.1.

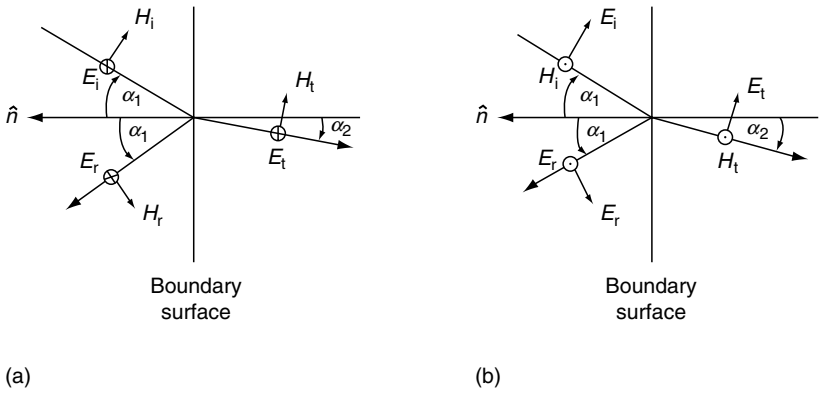

FIGURE 0.13
Oblique incidence of an electromagnetic wave at the boundary between two different media. (a) Perpendicular polarization (E vector perpendicular to plane of incidence); (b) parallel polarization (E vector parallel to plane of incidence). The plane of incidence is the plane formed by the surface normal (unit vector **n** and the direction of the incident wave); $\otimes$ indicates a vector into the plane of the paper; $\odot$ indicates a vector out of the plane of the paper. The orientation of the field vectors in the transmitted field is shown for loss-free dielectrics. For illustration of the transmitted wave into a medium with finite conductivity, where the wave impedance η_2 becomes a complex number, see Stratton, J.A., *Electromagnetic Theory*, McGraw-Hill, New York, 1941, p. 435.

$$\sin\alpha_2 = \frac{\sqrt{\varepsilon}_1}{\sqrt{\varepsilon_2 - \mathrm{j}\frac{\sigma_2}{\omega}}} \tag{0.36}$$

so that $\cos\alpha_2 = \sqrt{1-\sin^2\alpha_2}$ is a complex number unless $\rho_2 = (\sigma_2/\omega\varepsilon_2) = 1$.

As illustration, the variation with angle of incidence of the transmission coefficient for parallel polarization at the air–muscle interface at 10 MHz, is shown in Figure 0.14. It is apparent that the transmitted field is not necessarily maximized by perpendicular incidence in the case of parallel polarization. Furthermore, whenever $p \approx 1$ or $p > 1$ (see Table 0.1, above), α_2 is complex, which causes the waves entering the tissue to be inhomogeneous—they are not simple plane waves, but waves where surfaces of constant phase and constant amplitude do not coincide [3,23]; only the planes of constant amplitude are parallel to the boundary surface.

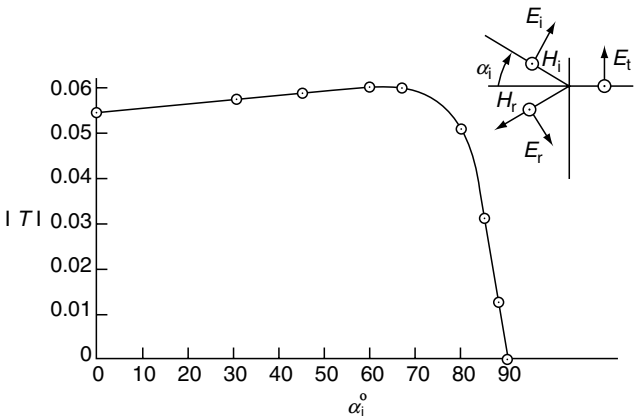

FIGURE 0.14
Magnitude of complex transmission coefficient for parallel polarization versus angle of incidence α_1 at 10 MHz (E field in plane of incidence, H field parallel to boundary plane; $\sigma_2 = 0.7\,\mathrm{S/m}$, $\varepsilon_{r2} = 150$, $T = E_t/E_r$).

Analytical solutions for nonplanar structures taking into account size and shape of entire animals have been given [24] and are also described in the RF modeling Chapter 10 of *BBA*.

0.5 Biophysical Interactions of Fields: Ionization, Ionizing Radiation, Chemical Bonds, and Excitation

RF fields can be characterized as nonionizing radiation. By this we mean that there is not enough energy in a single quantum of energy, hf, to ionize an atom or a molecule at RFs, where h is Planck's constant and f is the frequency. By comparison radiation in the UV or x-rays often lead to ionization. It is desirable to begin by reviewing the differences between ionizing and nonionizing radiations, to explain ionization phenomena and also to discuss related excitation phenomena, which require less energy than ionization. Then a number of the proposed models concerning atomic or molecular-level interactions of fields will be introduced. A number of these theories will be discussed and their predictions compared with experimental results in later chapters, including Chapter 5 through Chapter 7 and Chapter 9 in *BBA*; Chapter 9 and Chapter 11 in *BMA*. Heating, cell excitation, electroporation, and other results of high-intensity fields have been accepted as explanations for many bioelectromagnetic phenomena. For low-intensity exposure, however, no theory is widely accepted as a general explanation for bioelectromagnetic phenomena, and few specific phenomena have accepted explanations. It is quite possible that no general explanation exists and that more than one mechanism of interaction between fields will be found to be operating, depending on the situation. Binhi's book [25] contains a good summary of most recent theoretical proposals, including comparisons with data and critiques of their strong and weak points, as well as his own theory.

We note first that the energy of electromagnetic waves is quantized with the quantum of energy (in joules) being equal to Planck's constant ($h = 6.63 \times 10^{-34}$ J s) times the frequency. This energy can also be expressed in electron volts, i.e., in multiples of the kinetic energy acquired by an electron accelerated through a potential difference of 1 eV (1 eV $\approx 1.6 \times 10^{-19}$ J). Energy quanta for a few frequencies are listed in Table 0.3.

Quantized energy can ''excite'' molecules; appropriate frequencies can couple to vibrational and rotational oscillation; and if the incident energy quantum has sufficient magnitude it can excite other changes in the electron configuration, such as changing an electron to another (unoccupied) energy level or tearing an electron away from one of the constituent atoms, the latter process called as ionization. The energy required to remove one electron from the highest energy orbit of a particular chemical element is called its ''ionization potential.'' Typical ionization potentials are of the order 10 eV; for example, for the hydrogen atom it is 13.6 eV and for gaseous sodium it is 5.1 eV. As chemical binding forces are essentially electrostatic, ionization implies profound chemical changes. Therefore ionization by any outside agent of the complex compounds that make up a living system leads to profound and often irreversible changes in the operation of that system.

Table 0.3 shows that even the highest RF (millimeter waves) has quantum energies well below the ionization potential of any known substance; thus one speaks of nonionizing radiation when referring to electromagnetic waves below UV light frequencies. Ionizing radiation includes UV and higher frequency electromagnetic waves (x-rays, γ-rays).

TABLE 0.3

Wave and Quantum Characteristics of Various Types of Radiation

Name of Radiation or Application	Frequency (Hz)	Wavelength (m)	Energy of 1 Quantum of Radiation (eV)
UHF TV	7×10^8	0.43	2.88×10^{-6}
Microwave radar	10^{10}	3×10^{-2}	4.12×10^{-5}
Millimeter wave	3×10^{11}	1×10^{-3}	1.24×10^{-3}
Visible light	6×10^{14}	5×10^{-7}	2.47
Ionizing UV	10^{16}	3×10^{-4}	41.2
Soft x-ray	10^{18}	3×10^{-10}	4120
Penetrating x-ray	10^{20}	3×10^{-12}	4.12×10^5

This explanation of the difference between ionizing and nonionizing radiation should not imply that nonionizing electromagnetic radiation cannot have profound effects upon inorganic and organic substances. As excitation of coherent vibrational and rotational modes requires considerably less energy than ionization, it could occur at RF; this will be discussed in later chapters. In addition, many other possible biological effects require energies well below the level of ionizing potentials. Examples are tissue heating, dielectrophoresis, depolarization of cell membranes, mechanical stress due to piezoelectric transduction, or dielectric saturation, resulting in the orientation of the polar side chains of macromolecules and leading to the breaking of hydrogen bonds. These and other mechanisms will be discussed by the authors of several chapters (see especially Chapter 5 through Chapter 7 of *BBA* and Chapter 9 of *BMA*), who will also give estimates of rates at which energy must be delivered to produce particular effects.

Returning to the discussion of ionization, it is important to note that ionization of a chemical element can be brought about not only by absorption of electromagnetic energy, but also by collision either with foreign (injected) atoms, molecules, or subatomic particles of the requisite energy, or by sufficiently violent collision among its own atoms. The latter process constitutes ionization by heating, or thermal breakdown of a substance, which will occur when the kinetic energy of the colliding particles exceeds the ionization potential. As the average thermal kinetic energy of particles is related to temperature [26] by $W = kT$ where k is Boltzmann's constant ($= 1.38 \times 10^{-23}$ J/K), we find that the required temperature is

$$1.38(10^{-23})T \approx 5 \text{ eV} \approx (5)1.6(10^{-19}) \text{ J}$$

$$T \approx 5(10^4) \text{ K}$$

which is about twice the temperature inside a lightning stroke [27] and orders of magnitude higher than any temperature obtainable from electromagnetic waves traveling through air.

Actually, initiation of lightning strokes is an example of ionization by collision with injected energetic particles. The few free electrons and ions always present in the air due to ionization by cosmic rays are accelerated by the E fields generated within clouds to velocities corresponding to the required ionization energy. Only when the field is large enough to impart this energy over distances shorter than the mean free path of the free electrons or ions at atmospheric pressure can an avalanche process take place: an accelerated electron separates a low-energy electron from the molecule with which it collides and in the process loses most of its own energy; thus, one high-energy free electron is exchanged for two free low-energy electrons and one positive ion. Both the

electrons are in turn accelerated again by the field, giving them high kinetic energy before they collide with neutral molecules; their collision produces four free electrons and the multiplication process continues. The breakdown field strength for air at atmospheric pressure is approximately 3×10^6 V/m, implying a mean free path of electrons

$$\Delta\ell \approx [5\,\text{eV}/3 \times 10^6\,\text{V/m}] \approx 10^{-6}\,\text{m}$$

However, this model is not entirely accurate because the actual mean free path corresponds to energies of the order of 0.1 eV, which is only sufficient to excite vibrational modes in the target molecule. Apparently such excitation is sufficient to cause ionization if the collision process lasts long enough [28].

Except for some laboratory conditions where a sufficiently high potential difference can be applied directly across a biological membrane to bring about its destruction, collisional ionization is generally not a factor in the interaction of electromagnetic waves with tissue: The potential difference required for membrane destruction [29] is between 100 nV and 300 mV, corresponding to a field strength of the order of 2×10^7 V/m, assuming a membrane thickness ($d = 100$ Å; $E = V/d$). However, there is a third mechanism of ionization that is particularly important in biological systems. When a chemical compound of the type wherein positive and negative ions are held together by their electrostatic attraction, such as the ionic crystal NaCl, is placed in a suitable solvent, such as H_2O, it is separated into its ionic components. The resulting solution becomes an electrolyte, i.e., an electrically conducting medium in which the only charge carriers are ions.

In this process of chemical ionization, the Na^+ cations and Cl^- anions are separated from the original NaCl crystal lattice and individually surrounded by a sheet of solvent molecules, the ''hydration sheath.'' If the solvent is H_2O, this process is called ''hydration,'' or more generally, for any solvent, ''solvation.''

A dilute solution of NaCl crystals in H_2O is slightly cooler than the original constituents before the solvation process, indicating that some internal energy of the system was consumed. Actually energy is consumed in breaking up the original NaCl bonds and some, but less, is liberated in the interaction between the dipole moment of the solvent molecule (H_2O in our example) and the electric charges on the ions. Thus, solvents with higher relative dielectric constant ε_r, indicating higher inherent electric dipole moment per unit volume (P), solvate ions more strongly ($\varepsilon_r = 1 + P/[\varepsilon_o E]$, where E is the electric field applied during the measurement of ε_r). For example, H_2O with $\varepsilon_r \approx 80$ solvates more strongly than methanol with $\varepsilon_r \approx 33$. For biological applications it is worth noting that solvation may affect not only ionic substances, but also polar groups, i.e., molecular components which have an inherent dipole moment, such as—C=O, —NH, or —NO_2. Details of the process are discussed in texts on electrochemistry [30,31].

In biological processes not only chemical ionization and solvation of ionic compounds, but also all kinds of chemical reaction take place. One of the central questions in the study of biological effects of E and H fields is therefore not only whether they can cause or influence ionization, but also whether they can affect—speed up, slow down, or modify—any naturally occurring biologically important chemical reaction.

In Table 0.4 typical energies for various types of chemical bonds are listed. For comparison the thermal energy per elementary particle at 310 K is also shown. Complementing the numbers in Table 0.4 one should also point out that:

1. The large spread in the statistical distribution of energies of thermal motion guarantees that at physiological temperatures some molecules always have sufficient energy to break the strongest weak bonds [32].

TABLE 0.4

Bond and Thermal Energies

Type of Bond	Change in Free Energy (Binding Energy) kcal/mol	eV/Molecule
Covalent	50–100	2.2–4.8
Van der Waals	1–2	0.04–0.08
Hydrogen	3–7	0.13–0.30
Ionic[a]	5	0.2
Avg. thermal energy at 310 K	0.62	0.027

[a]For ionic groups of organic molecules such as COO^-, $NH3_3^-$ in aqueous solution.

2. The average lifetime of a weak bond is only a fraction of a second.
3. The weak binding forces are effective only between the surfaces in close proximity and usually require complementary structures such as a (microscopic) plug and hole, such as are thought to exist, for instance, between antigen and antibody [33].
4. Most molecules in aqueous solution form secondary bonds.
5. The metabolism of biological systems continuously transforms molecules and therefore also changes the secondary bonds that are formed.

Comparison of the last columns in Table 0.3 and Table 0.4 shows that millimeter waves have quantum energies, which are only about one order of magnitude below typical Van der Waals energies (waves at a frequency of 10^{12} Hz with a quantum energy of 0.004 eV have a wavelength of 0.3 mm and can still be classified as millimeter waves). One might expect therefore that such waves could initiate chemically important events, such as configurational changes, by e.g., multiple transitions between closely spaced vibrational states at successively high-energy levels [46].

Energies associated with transition from one to another mode of rotation of a diatomic molecule are given by $W = \ell\,(\ell + 1)\,A$ [26,33], where $\ell = 0, 1, 2, 3 \ldots$ and $A = 6 \times 10^{-5}$ eV; thus an electromagnetic wave with a frequency as low as 29 GHz—still in the microwave region—can excite a rotational mode. Vibrational modes of diatomic molecules [26,33] correspond to energies of the order of 0.04 eV, requiring excitation in the IR region. Vibrational frequencies in a typical H-bonded system [34] are of the order of 3000 GHz; however, attenuation at this frequency by omnipresent free H_2O may prevent any substantial effect [34].

Kohli et al. [34] predict that longitudinal and torsional modes of double helical DNA should not be critically damped at frequencies >1 GHz, although relaxation times are of the order of picoseconds, and Kondepudi [36] suggests the possibility of an influence of millimeter waves at approximately 5×10^{11} Hz upon oxygen affinity of hemoglobin due to resonant excitation of heme plane oscillations. Although Furia et al. [37] did not find resonance absorption at millimeter waves in yeast, such was reported by Grundler et al. [38,47]. The latter experiment has been interpreted [39,40] as supporting Fröhlich's theory of cooperative phenomena in biological systems. That theory postulates ''electric polarization waves'' in biological membranes which are polarized by strong biologically generated [18] fields (10^7 V/m). Fröhlich [41,42] suggests that metabolically supplied energy initiates mechanical vibrations of cell membranes. The frequency of such vibrations is determined by the dimensions and the elastic constants of the membranes;

based on an estimate of the sound velocity in the membrane of 10^3 m/s and a membrane thickness of 100 Å (equal to one half wavelength) one obtains a frequency of $5(10^{10})$ Hz. Individual molecules within and outside the membrane may also oscillate, and frequency estimates vary between 10^9 Hz for helical RNA [43] and 5×10^{13} Hz for hydrogen-bonded amide structures [44]. As the membranes and molecules involved are strongly polarized, the mechanically oscillating dipole electromagnetic fields that are able to transmit energy, at least in some situations, over distances much larger than the distance to the next adjacent molecule.

Electromagnetic coupling of this type may produce long-range cooperative phenomena. In particular, Fröhlich [45] has shown that two molecular systems may exert strong forces upon each other when their respective oscillation frequencies are nearly equal, provided the dielectric permittivity of the medium between them is strongly dispersive or excitation is supplied by pumping, i.e., by excitation at the correct frequency from an external source. The mechanism is nonlinear in the sense that it displays a steplike dependence on excitation intensity. Possible long-range effects may be, for example, attraction between enzyme and substrate [42]. These and related topics have been discussed in detail by Illinger [34] and are reviewed in the present volume in Chapter 11 and Chapter 5 of *BBA*.

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