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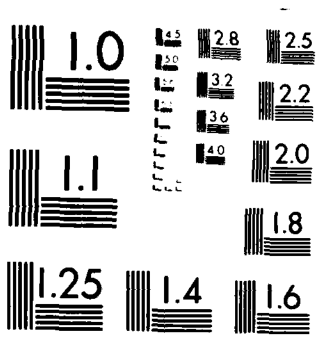

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An evaluation of the applicable literature conducted by scientific and engineering ~~experts~~ assembled by the A I B S was completed for the 1977-1984 period. The expert committee concluded from their evaluation that electromagnetic field exposure associated with the U.S. Navy's Extremely Low Frequency (ELF) Communication System is unlikely to produce adverse public health effects or adverse effects on plants and animals. Information included in this report pertains to:

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BIOLOGICAL AND HUMAN HEALTH EFFECTS OF EXTREMELY LOW FREQUENCY ELECTROMAGNETIC FIELDS

Post-1977 Literature Review

Report of the Committee on
Biological and Human Health Effects
Of Extremely Low Frequency Electromagnetic Fields

American Institute of Biological Sciences

Arlington, Virginia

March 1985

Opinions expressed by the committee members are their own and do not necessarily reflect the opinions of the American Institute of Biological Sciences nor the institutions with which the authors are affiliated.

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PREFACE

The report that follows had its genesis in a request from the Naval Electronics Systems Command to the American Institute of Biological Sciences (AIBS) to provide an evaluation and analysis of the extant professional literature published since January 1977 about the biological and human health effects of extremely low frequency (ELF) non-ionizing electromagnetic radiation germane to the Department of the Navy's ELF Communications Program. This report is the product of a committee of scientists (Committee on Biological and Human Health Effects of Extremely Low Frequency Electromagnetic Fields) organized by the AIBS and the conclusions of the report are those of the members.

The report reflects the Committee members' knowledge, as well as their evaluation of commissioned topical resource papers developed by other scientists, books, research reports, project reports, articles, and papers from peer-reviewed journals that discussed or described biological and human health effects of non-ionizing electromagnetic radiation in the frequency range of 1 - 300 Hz. In some instances articles about frequencies above 300 Hz were evaluated if, in the opinion of the individual reviewer, the information was important to understanding of the issue under consideration. Both domestic and international literature published in English or other languages was included in the evaluation.

In 1977, a National Academy of Sciences' committee completed a study of the literature and the biological research programs associated with ELF electric and magnetic fields. The study was commissioned by the Navy in 1976. The Academy committee concluded:

> A number of concerns raised over the years that Seafarer ELF fields might constitute a source of dangerous, even catastrophic, environmental contamination have been raised and found invalid and unwarranted. The Committees' considerated opinion is that such fields will not cause a significant and adverse biologic disturbance, except in the event of electric shock, which is of serious concern. In fact, apart from the possible result of electric shock, the Committee cannot identify with certainty any specific biologic effects that will definitely result from exposure to the proposed Seafarer fields.

The AIBS Committee members are in agreement with the conclusions of the 1977 Academy report, and based on their finding in this study, the Committee believes that it is still unlikely that exposure of living systems to ELF electric and magnetic fields in the range of those associated with the Navy's ELF Communications System can lead to adverse public health effects or to adverse effects on plants or animals. However, because of certain ambiguities in the scientific literature, the Committee recommends that the Navy continue to monitor the literature and respond appropriately to any significant new information.

The ELF study is another in a long history of AIBS programs bringing together the advisory resources of the bioscience community and Federal agency projects. The Institute is grateful to the members of the ELF Report Committee, resource paper authors, and committee advisors and editors for their contributions and also recognizes the special effort of Molly Frantz, the AIBS Project Coordinator. Appreciation is expressed to H. B. Graves, General Chairman of the report Committee and the study for his diligence in organizing and bring the study to conclusion. Appreciation is also expressed to Cindy DeWeese and Mary Presswood, whose support services were invaluable to the completion of this project.

Donald R. Beem

Donald R. Beem, Ph.D.
AIBS - ELF Project Director

BIOLOGICAL AND HUMAN HEALTH EFFECTS
OF EXTREMELY LOW FREQUENCY ELECTROMAGNETIC FIELDS

Post-1977 Literature Review

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BIOLOGICAL AND HUMAN HEALTH EFFECTS OF
EXTREMELY LOW FREQUENCY ELECTROMAGNETIC FIELDS

Post-1977 Literature Review

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CHAPTER I

OVERVIEW, SUMMARY, AND CONCLUSIONS

OVERVIEW

Background

In 1958, the United States Navy expressed interest in an antenna system that would operate in the extremely low frequency (ELF) (less than 300 Hz) range of the electromagnetic spectrum. The ELF Communications System allows submarines to receive messages at operational depths and speeds, negating the need to deploy an antenna at or near the surface, because ELF transmissions can penetrate hundreds of feet of seawater, making detection by hostile antisubmarine forces unlikely. An ELF communications test facility was constructed in North Carolina in 1962 and was successfully tested in 1963. The original concept was for a much more extensive system than that now proposed and was for an underground system rather than the overhead antennas now envisioned.

A literature review of the potential biological effects that might result from operating the proposed underground communications system was conducted in 1967 and 1968. Results of the review did not support the conclusion that adverse biological effects were probable, but the research available was deemed insufficient to allow definitive conclusions on this issue. Therefore, a biological research program was initiated in 1968 to establish the levels of electric and magnetic fields at which biological effects might occur and the levels at which deleterious biological effects might be suggested.

In the meantime, construction of a second test facility was completed in Wisconsin in 1969, and an ecological monitoring program in the vicinity of the Wisconsin submarine communications testing system (Project Sanguine) was initiated. A botanical impact study was conducted at the North Carolina test facility, and a health survey of the Wisconsin site personnel plus a series of laboratory studies was also initiated in 1969.

In 1971, the American Institute of Biological Sciences (AIBS) established a panel of scientists to review proposals submitted in response to a Department of the Navy request for research proposals on the biological effects of ELF electric and magnetic fields. Of the 53 proposals submitted for consideration in September 1971, nine were funded. The AIBS panel also conducted a review of the literature and of ongoing studies on the biological effects of ELF electric and magnetic fields. Additional laboratory studies were begun in 1972, partially as a result of the 1971 AIBS review. Following yet another independent review of the ELF research programs in 1972 (this time by the Electromagnetic Radiation Advisory Committee of the Navy's Bureau of Medicine and Surgery (BuMed)), five additional research programs were initiated. By 1973, another review by an ad hoc committee formed by BuMed recommended four additional studies, which were begun in 1974.

In 1974, the National Academy of Sciences' (NAS) National Research Council convened an ad hoc committee to evaluate ELF electric and magnetic fields biological effects research, and its Office of Telecommunications Policy's "Program for Control of Electromagnetic Pollution of the Environment: The Assessment of Biological Hazards of Monitoring Electromagnetic Radiation" has reviewed the Navy-sponsored biological research program each year since 1973.

In 1976, the Navy requested NAS to establish a panel of scientists to once again review the literature and the biological research programs associated with ELF electric and magnetic fields. This review, published in 1977, concluded that

> A number of concerns raised over the years that Seafarer ELF fields might constitute a source of dangerous--even catastrophic--environmental contamination have been raised and found invalid and unwarranted. The Committees' considered opinion is that such fields will not cause a significant and adverse biologic disturbance, except in the event of electric shock, which is of serious concern. In fact, apart from the possible result of electric shock, the Committee cannot identify with certainty any specific biologic effects that will definitely result from exposure to the proposed Seafarer fields. (NAS 1977).

A number of reviews of the biological effects of ELF electric and magnetic fields have been published since the 1977 NAS report. Grissett (1980) reviewed the literature of ELF electric and magnetic fields published after the 1977 NAS report and concluded that data accumulated since the NAS report were consistent with the 1977 conclusions of no adverse biological effects.

Most other reviews to date agree with Sheppard's (1983) statement made after he conducted a review of ELF biological effects literature (with a strong emphasis on 60-Hz research):

> Present scientific knowledge about the effects of 60-Hz electric fields does not permit unequivocal determination of the extent of possible hazard to human health, but to date no health hazards due to 60-Hz HVTL electric fields are established...as a group, the foregoing factors lead to the conclusion that a strongly expressed biological effect in humans is not very likely, and to the further conclusion that a pathological effect is even less likely.

In an environmental health criteria document on extremely low frequency electric and magnetic fields published by the World Health Organization (1984), one of the conlusions was:

> It is now possible from present knowledge to make a definitive statement about the safety or hazards associated with long-term exposure to sinusoidal electric fields in the range of 1-10 kV/m. In the absence of specific evidence of particular risk or disease syndromes associated with such exposure, and in view of the experimental findings on the biological effects of exposure, it is recommended that efforts be made to limit exposure, particularly to members of general population, to levels as low as can be reasonably achieved.

Another recent review of biological effects, including public health concerns, of electric and magnetic fields in the ELF range was conducted by a Florida State Science Advisory Commission, which included expertise in biology, psychology, engineering, medicine, physics, and risk assessment. The Commission (FEMFSAC 1985) concluded that it was not possible to make definitive statements that 60-Hz electric and magnetic fields do or do not pose a public health problem. They further concluded that:

> The Commission unanimously believes that the scientific information now available supports the conclusion that it is unlikely that 60-Hz electric and magnetic fields associated with high voltage transmission lines has led, or can lead, to public health problems. However, some ambiguities in the currently available science precludes our categorically concluding that absolutely no public health problem exists.

As one would expect of such a diverse area, the conclusion of no probable adverse public health effects of ELF electric and magnetic fields is not universal. Becker and Marino (1982) reviewed the literature concerning "electromagnetism and life" and concluded that

> Man-made EMFs are present in the environment at levels shown by experiment to be capable of affecting biological function. It

follows, therefore, that uncontrolled exposure to such EMFs is a potential public health risk. The regulatory response to the environmental EMF problem has been slow, and the nature of the proof demanded has frequently been inappropriate.

Electric and Magnetic Fields Produced by the Navy ELF Communications System

The AIBS Committee requested that the U. S. Navy prepare a document describing the characteristics of the ELF Communications System and the available theoretical and experimental knowledge about the electric and magnetic fields generated by the system. That document is included in the Committee's report as Appendix A. Those parts that are particularly relevant to the subject of the Committee report are discussed here.

The ELF Communications System will consist of two sites, approximately 148 miles apart: one in the Upper Peninsula of Michigan and one in the Chequamegan National Forest near Clam Lake in northwestern Wisconsin. The Wisconsin transmitter has two 14-mile-long antennas, one oriented essentially north-south and the other essentially east-west. Each antenna carries 300 A of current; maximum voltage is 4.8 kV. The Michigan transmitter has one essentially north-south and two essentially east-west antennas. The total antenna length is 56 miles. Each antenna carries 150 A; maximum voltage is 4.8 kV. The antenna construction resembles a rural power distribution line with a conductor mounted on 30- to 55-ft-high utility poles and a 35- to 75-ft-wide cleared right-of-way. Each transmitter site has two power amplifiers, rated at 650 kw, one for the north-south antenna and one for the east-west antenna(s). Each end of the antenna terminates in a distributed ground system. The ground system designs vary according to local geology and use 2 to 4 miles of bare wire buried 6 to 8 ft deep and several well-type grounds, approximately 100 ft deep.

Standard utility and state commerical power-distribution guidelines will be followed in right-of-way management. Appendix A notes that the specifications related to the electrical safety of the grounding system are more stringent than those followed by utilities for electrical generation, transmission, and distribution systems.

The electromagnetic fields are caused by the antenna current and are therefore proportional to the antenna current, i.e., 300 A in Wisconsin and 150 A in Michigan. The information to be transmitted is digital, i.e., it consists of "zeros" and "ones." The modulation used is Minimum Shift Keying (MSK), which is a phase-continuous type of frequency modulation. If a "zero" is to be transmitted, the frequency of the antenna current is 72 Hz; for a "one", the frequency is 80 Hz. The center frequency (or carrier) is therefore 76 Hz. Important properties of MSK modulation are that the current amplitude is free of transients in the antenna current because the shift from one frequency to the other is phase-continuous; little energy is generated outside the signal bandwidth. Transmitting system components generally provide high attenuation for out-of-band frequency components so that the out-of-band energy is further reduced.

Both electric and magnetic fields will be generated by the ELF Communications System, and these fields will, in turn, induce weak electric fields and body currents inside the bodies of organisms exposed to them. Electric-power transmission and distribution systems, household and personal appliances, shop equipment, etc., also produce electric and magnetic fields, and these fields can be stronger (sometimes much stronger) than those produced by the ELF Communications System.

The electric and magnetic fields generated by the ELF antenna voltage and currents can conveniently be divided into three classes:

- Electric fields in air or high impedance fields exist between the overhead antenna and ground and are a function of antenna height. Because the ends of the antenna are grounded, the voltage varies along the antenna line. The nominal calculated field is 120 V/m at ground level. However, because only certain aspects of the antennas are simulated in these calculations, it is not surprising that the fields actually produced by the system exceed the calculated maxima at some points. The measured data given by the Navy in Appendix A include values as high as 157 V/m. It will be assumed that the actual maximum electric field produced under an antenna is about 160 V/m; it should be remembered, however, that this value is based on only a few data points and the engineering judgment of the authors. As one moves away from the antenna, the ground-level electric field decreases approximately $1/(s^2+H^2)$, where s is the horizontal distance measured perpendicular to the antenna and h is the height of the antenna. These field levels are about the same as those generated by rural power distribution lines and more than a factor of 10 lower than those generated by high voltage transmission lines that produce high impedance electric fields.

- Electric fields in ground or low impedance fields in the ground under the antenna are referred to as the longitudinal fields, which are produced through Faraday induction; the fields at the ground terminal are referred to as step potentials. The longitudinal field is at its maximum directly under the antenna, where calculated values are about 0.15 and 0.07 V/m for the Wisconsin and Michigan sites, respectively. A number of approximations are reflected in these calculations (e.g., the earth is assumed to have a uniform electrical conductivity), so measured values are expected to differ somewhat from calculated values.

Measured data given in Appendix A include values up to 0.23 V/m at the Wisconsin site. However, the quantity of data given in the Appendix is too small to enable any firm conclusions to be drawn. The Committee believes that, until more data are available, it is prudent and conservative to estimate the maximum ground electric fields produced under the ELF Communications System's antennas as about 1 V/m.

The earth is a crucial part of the antenna system of the ELF Communications System. Electric current is conducted through the ground between the two ends of each overhead segment of the System's antennas. This results in electric fields being generated in the ground. These fields, and resulting step potentials, are caused by the current flowing out of the grounding electrodes, which are about a factor of 10 higher than the longitudinal field. The step potential could cause a current to flow in the body of a person in the terminal ground area.

Calculated field strengths near the ground terminals (i.e., the point where the current is injected into the ground) show peak values up to about 5 V/m. (Note that simplifying assumptions are reflected in these calculations.) The 1977 NAS report expressed concern about the large step potentials that were projected using the specifications existing at that time; however, new specifications exist. The system is being redesigned so that the body current will not exceed 1 MA for a 1-m step under worst-case conditions. Generally, one milliampere is considered to be the perception threshold for adult humans and is more stringent than design values for public utilities.

- <u>Magnetic fields</u> are generated both in the air and in the ground by currents in the antennas of the ELF Communications System. These fields are proportional to the antenna current and inversely proportional to the distance from the antenna conductor. Maximum calculated ground-level values for these fields are about 6 μT (0.06 G) and 3 μT for the Wisconsin and Michigan sites, respectively. However, as in electric-field cases, measured values occasionally exceed the calculated maxima. Data given in Appendix A indicate that values up to at least 14 μT are produced at ground level by the Wisconsin facility. The Committee believes that this value is probably a good estimate of the maximum ground level values that will actually be produced by the system.

Table 1 summarizes calculated and measured values for the fields produced near the ELF Communications System.

Table 1. Calculated (Nominal Conditions) and Estimated Maximum Ground-Level Electric and Magnetic Fields Generated by the Field Values Navy ELF Communications System.

Type of Field	Field Values	
	Wisconsin	Michigan
Calculated Nominal Air Electric Field Directly Under an Antenna	120 V/m	120 V/m
Estimated Maximum Air Electric Field Under an Antenna	160 V/m	160 V/m
Calculated Nominal Ground Electric Field in the Ground Directly Under an Antenna	0.15 V/m	0.07 V/m
Calculated Nominal Magnetic Field Directly Under an Antenna	6 μT	3 μT
Estimated Maximum Magnetic Field Under an Antenna	14 μT	7 μT
Calculated Nominal Ground Electric Field in the Ground Near a Ground Terminal	5 V/m	---

The Navy has also made electric- and magnetic-field measurements at larger distances (>1.6 km) from the Wisconsin facility. Some of these measurements are provided in Appendix A. They may be summarized as follows: (1) magnetic fields produced by the facility at a distance of 1.6 km are comparable in magnitude to ambient 60-Hz magnetic fields; (2) electric fields produced in the air at the same distance are much smaller than ambient values; and (3) electric fields produced in the ground at this distance are significantly larger than ambient values (these values are, however, still very small). At distances greater than 10 km from the system, both air electric fields and magnetic fields are much smaller than ambient levels, while ground electric fields are comparable to or smaller than ambient values.

Project Description

The AIBS was to evaluate the professional literature published since

January 1977 for biological and human health effects of extremely low frequency non-ionizing electromagnetic radiation germane to the Department of the Navy's ELF Communications Program. From the evaluation literature, AIBS was to assess the potential biological and human health effects of ELF electric and magnetic fields. The tasks faced by the AIBS Committee on Biological and Human Health Effects of Extremely Low Frequency Electromagnetic Fields were as follows:

- o To assess and summarize the existing professional literature published since January 1977 on the biological effects, including effects on humans, of ELF electric and magnetic fields (1-300 Hz).
- o To identify effects, if any, that are of significant concern.
- o Wherever possible, to relate these effects to the relevant field characteristics of the ELF Communications System (e.g., electric, magnetic, frequency, intensity, and modulation).

Chapters 2 and 3 characterize the biological interactions of the electric and magnetic fields associated with the proposed Department of the Navy ELF Communications System. Chapters 4 through 10 systematically evaluate the relevant literature by particular area(s) of expertise and determine the extent to which concerns about the health and well-being of living organisms, including humans, exposed to the electric and magnetic fields associated with the ELF Communications System are justified. The conclusions presented in each chapter are summarized in Chapter 1.

Committee Limitations

The 1977 review by the NAS expressed concern about step potentials in the area of the Communications System's ground termi.als. Our calculations (Chapter 2) suggest that this remains a potential problem; however, the Navy has developed new specifications that will limit body current equal to or less than 1 mA (Appendix A). The new specifications are sufficiently low that the AIBS Committee decided to limit their consideration of electric fields in the ground near the ELF Communications System.

The AIBS task was limited to scientific and technical questions about the ELF Communications System and its potential effects on living systems. The Committee emphasizes that it was not charged with the task of determining whether or not the proposed ELF Communication System be built and operated, nor did the Committee deal with the value judgments and political questions associated with the System. The evaluation of the strict scientific and technical questions about the adverse biological effects, if any, associated with the ELF Communications System must eventually be reconciled with political and value judgments by the appropriate groups and individuals, which ultimately includes each citizen of the United States.

Criteria for Literature Review

Literature reviews involve scrutiny of reports and manuscripts that inevitably exhibit considerable variation in quality. Biological experiments are subject to inherent background "noise," or variation; studies on the effects of electric and magnetic fields are particularly prone to exposure-system artifacts such as noise, vibration, shock, etc., which amplify this background variability. The AIBS Committee elected to use the following criteria in weighing the merit of studies involving the biological effects of ELF fields. These criteria (including those used by the 1977 NAS Committee) guided the individual Committee members as they surveyed the literature of their particular disciplines:

- The experimental techniques should be chosen to avoid effects of such intervening factors as microshocks, noise, vibration, and chemicals.

- Extreme care should be taken to determine the effective ELF field, voltage, or current in the organism.

- The sensitivity of the experiments should be adequate to ensure a reasonable probability that an effect would be detected if it existed.

- The experimental and observational techniques, methods, and conditions should be objective. Blind scoring should be used whenever there is a possibility of investigator bias; likewise, data analyses should be objective.

- If an effect is claimed, the results should demonstrate it at an acceptable statistical significance by application of appropriate tests.

- A given experiment should be internally consistent with respect to the effects of interest.

- The results should be quantifiable and susceptible to confirmation by other investigators. In the absence of independent confirmation, a result is classified for the studies'purpose as preliminary.

- The protocol for the experiment(s) or study should be scientifically sound.
- The biological and engineering methodologies should be sound and appropriate for the experiment(s) or study.
- The information content should be adequate to judge the worth of the research reported and the conclusions reached.
- The statistical analyses should be appropriate.
- How the data are interpreted should be understood.
- The findings or stated facts should be appropriately documented to distinguish between facts and speculation.

REPORT SUMMARY
CHAPTER 2. Coupling of Living Organisms to ELF Electric and Magnetic Fields

An extrapolation procedure must be carried out in order to use biological data obtained with nonhuman preparations assessing risks to humans exposed to ELF electric and magnetic fields. Chapter 2 introduces dosimetric techniques that can be used in extrapolating biological data across species. The emphasis is on estimating the electric fields and current densities induced at the surface and inside the bodies of humans and animals exposed to ELF electric fields.

The coupling of humans and animals to electric fields in air is discussed. A theoretical method is developed in which the exposed organism is simulated by a homogeneous spheroid. In this approximation, electric fields acting on the surface and inside the body can be calculated. Published experimental data for human and animal exposure to ELF electric fields are summarized.

Humans and animals living in the ground or standing on the ground near a system antenna or a ground terminal will couple to the electric fields in the ground produced by the system. Means of estimating the currents produced in the bodies of these organisms are described.

The ELF Communications System also produces magnetic fields in the air and in the ground in the vicinity of its antennas. This magnetic field penetrates into the bodies of humans and animals essentially without perturbation. Because it is a time-varying field, electric fields are induced inside the bodies of exposed organisms. Methods for estimating these fields are presented. In addition, charged particles that are in motion inside the bodies of these organisms experience Lorentz forces. These forces can do no work themselves, but they can facilitate the transformation of one form of energy into another.

Chapter 2 concludes with three examples that apply the methods discussed. The first example is the comparison of exposure of a human to the estimated maximum electric and magnetic fields produced by the system. The calculation shows that these two fields induce roughly the same magnitude electric fields inside the subject. The second example is a consideration, on dosimetric grounds, of whether the so-called calcium-efflux experiments, which were performed at frequencies in the range 0 to 32 Hz, have relevance to questions of possible risks resulting from exposure of the human brain to frequencies in the 0 to 30-Hz range and with magnitudes similar to those produced inside the brain tissue used in the calcium-efflux experiments. The final example is a step-potential calculation for a human standing under one of the ELF Communications System antennas.

CHAPTER 3. Possible Biophysical Mechanisms of Electromagnetic Interactions with Biological Systems

Recent literature on the biological effects of extremely low frequency electric and magnetic fields contains several reports of frequency and amplitude "windows." Chapter 3 discusses several theoretical models that may be applicable to the existence of such windows and to the general mechanisms of interaction of ELF electric and magnetic fields with living systems. Much of the available biological effects literature seem not to implicate windows. Increasingly persuasive evidence exists for more than one mechanism of interaction underlying biological effects of extremely low frequency electric and magnetic fields. The proposed theoretical models include the following:

- Cooperative models - models in which small perturbations caused by ELF fields may "resonate" in such a way that some initial event reduces the energy required for other events in neighboring systems to occur (e.g., calcium-binding sites at the level of the cell membrane).

- The Frolich model - Frolich suggested that systems exhibit many different forms of order or organization. Minor energetic contributions are required to excite the various modes of organization of large molecular systems (e.g., proteins and DNA or structures such as the cell membrane), and coherent electric oscillations with the frequency selective responsiveness (windows) may result from sources, including ELF fields, that make small energetic contributions.

- Molecular Interactions-Vibrational Modes - ELF fields may interact directly with cell membranes or interact directly with intracellular structures (e.g., chromosomes or molecules). Calculations and experimental work suggest that the degree of resonant absorption at a particular frequency is structure-dependent (e.g., DNA molecules may exhibit strong resonant absorption at microwave frequencies but resonant modes may be chain-length dependent and also vary as a function of dampening due to the solution in which the structure resides).

- Solitons - Solitons are localized disturbances that propagate through a nonlinear medium unattenuated. Excitation of a molecule (e.g., on the surface of a protein molecule at a cell membrane receptor site) may result in vibrational modes that could lead to large amplitude excitations. A soliton could be created in proteins associated with membrane channels and propagated along the protein, through the cell membrane, and then provide energy for chemical changes inside the cell.

- Dipoles and Dielectrophoresis - Molecules may normally exist in a polar state, or polarization may be induced; in any case, a nonuniform field can cause migration or rotation of polarized or charged molecules. Because cell surfaces and membranes have polar molecules, external fields may induce dipole moment or polarize the cell. Movement of such polarized particles is called dielectrophoresis and may be affected by the frequency of the imposed field or by inherent, internal oscillating low frequency electric fields within the cells.

- Magnetic Field Interactions - Magnetic fields may affect the electrical properties of cells, perhaps through nuclear spin coupling. It is also possible that the earth's magnetic field affects biological phenomena such as changes in calcium efflux of in vitro preparations of brain tissue, for example, by cyclotron-type resonance of specific types of molecules.

Chapter 3 concludes that mechanisms have not yet been established for the vast majority of observed biological effects of extremely low frequency electric and magnetic fields (with possible exceptions such as magnetophosphenes as discussed in Chapter 4 and effects related to induced current flow). This chapter also concludes that no predictive theories yet exist to guide in assessing the hazards, if any, of electric and magnetic fields in the extremely low frequency range.

CHAPTER 4. Biological Effects of ELF Magnetic Fields.

The biological effects of time-varying magnetic fields in the frequency range less than 300 Hz are reviewed in Chapter 4. Magnetic field interaction mechanisms; effects on the visual system (magnetophosphenes); the nervous system and behavior; effects on cell, tissue, and animal systems; and studies on cancer and magnetic fields in humans are presented. For ELF magnetic fields, the primary interaction mechanism is the induction of electric fields and currents in the body. Magnetophosphenes (a flickering illumination within the visual field) occurs in humans exposed to magnetic fields in excess of about 10 mT (at 20 Hz), which is the frequency of maximum visual sensitivity. Magnetophosphenes are reversible, produce no known harmful effects, and are produced only at field strengths far in excess of those encountered under normal conditions, including those produced by the ELF Communications System (Table 1).

Several behavioral and nervous system responses to time-varying magnetic fields have been reported in the literature. Current densities greater than 10 mA/m^2 are necessary to affect appreciably nerve bioelectric activity. Sinusoidal ELF magnetic fields high enough to generate such effects are unlikely to be encountered in homes or in the work place. However, pulsed magnetic fields with large time-rates of change in the magnetic flux density may stimulate nervous tissues. Behavioral responses of birds and bees may be altered under certain circumstances, although the evidence is not conclusive, and evidence for such interaction mechanisms in mammals is even less convincing. Although there are reported correlations between magnetic field intensity and human suicide, the incidences are considered unlikely to reflect a causal relationship.

Firm conclusions concerning effects at the cellular and tissue levels are difficult to draw from the literature review of studies of ELF magnetic field effects on cellular, tissue, and animal systems. However, there is a growing body of evidence that several aspects of the biochemistry and physiology of cells and organized tissues may be perturbed by exposure to ELF magnetic fields that induce electric currents in tissues and extracellular fluids that exceed normal physiological levels. This observation is particularly notable for pulsed magnetic fields with fast rise times. Studies using sinusoidal fields of low intensities (below approximately 1 mT) have generated results that have little consistency across laboratories. Reported effects of very low intensity ELF magnetic fields on cells, tissue, or animals systems must be viewed with caution because of a lack of independent verification or because of potential confounding variables. Chapter 4 concludes that

- o There is currently no persuasive scientific evidence that exposure to magnetic fields in the general range of those associated with the Navy's proposed ELF Communications System (0 to 14 μT) will result in adverse public health effects or adverse effects on nonhuman biological systems.
- o Studies of the correlations between cancer incidence and residential or occupational exposure to ELF magnetic fields also have numerous deficiencies, and currently available data on such relationships are inconclusive.

CHAPTER 5. Cellular Studies of Effects of ELF Electric and Magnetic Fields.

Chapter 5 discusses the effects of ELF electric and magnetic fields at the cellular level of biological organization. Most of the studies reviewed used in vitro preparations. Such studies offer advantages of excellent exposure control and isolation from the influence of extraneous stimuli. However, in vivo studies are necessary to determine whether or not effects observed in vitro will be manifested in the intact animal.

At this time no adequate physical or chemical theory for the biologically significant interactions between exposure to ELF electric and magnetic fields external to the organism and internal body tissues exists. However, insight into the effects on biological processes and events may be obtained even in the absence of mechanisms coupling external electric or magnetic fields into internal tissues. Intensity-response and frequency-response data may also be more readily available from in vitro than from in vivo studies.

The review of the in vitro studies is organized into the following areas:

- o Biochemical processes at the cellular level
- o Intracellular biochemical alterations
- o Pineal melatonin rhythm, pineal cell activity
- o Neurophysiologic studies
- o Studies with cultured cells
- o Effects on bone growth and fracture repair
- o Developmental changes related to pulsed magnetic fields.

Chapter 5 concluded that electric and magnetic fields of various strengths, frequencies, and waveforms can alter biochemical and physiological states and processes in in vitro systems. However, extrapolation of effects in the intact animals is difficult. In addition, in many cases, the in vitro exposure conditions could not occur for any environmental exposure, while in others, the tissue-level field strengths are at the level of some exceptional environmental exposures that could not be achieved by the ELF Communications System. Generally, the electric and magnetic fields associated with the system are very weak. Very few studies have examined effects at that level.

The quality of research conducted with ELF fields varies considerably. Few findings have been replicated or studied intensively enough to be accepted without obvious artifacts or experimental error. However, much of the research is at a preliminary level and requires further intensive study before results can be accepted without serious question.

It is further concluded that:

- With the exception of studies on magnetophosphenes and bone growth, the functional or biochemical changes seen in vitro have not been closely linked to in vivo conditions, nor has the expression of the laboratory observations in a whole organism been established.

- At the very low field strengths typical of the ELF Communications System antenna environment, only the calcium efflux studies appear to involve similar strength electric fields. Only the studies of slime mold mitotic cycle, fibroblast growth, and chick embryogenesis involve magnetic fields like those of the ELF Communications System, and these occur only close to the antenna wire.

- None of the in vitro studies or other studies of cellular systems indicates that significant functional changes might occur in organisms subjected to the electric and magnetic fields in air near the ELF Communications System's antenna.

- On the basis of an analysis of the literature on biological effects of ELF electric and magnetic fields on cellular systems, and despite the considerable uncertainties on issues of biological interest and importance, there is essentially no probability of deleterious biological effects on organisms exposed to the ELF Communications System's fields in air.

CHAPTER 6. Interaction of ELF Electric and Magnetic Fields with Neural and Neuroendocrine Systems.

The neural and neuroendocrine systems are often directly or indirectly implicated in interactions between electric and magnetic fields in the ELF spectrum and justifiably so, for these systems underlie essentially all interactions of animals with their external environment. The review of neural and neuroendocrine system field effects in the ELF spectrum addresses the potential public health implications of such studies.

A review of animal studies that pertain to the chemical or physiological impacts of exposure to ELF electric and magnetic fields on neuroendocrine function is presented.

- Neurochemical data provide evidence that such exposure may, under certain conditions, result in increased arousal responses in animals.

- Neuroanatomical results are controversial, but no persuasive evidence of effects at this level of biological organization are available.

- Neurophysiological studies of ELF fields indicate a general lack of information concerning the effects on the peripheral nervous system.

However, evidence exists suggesting enhanced excitability in nerves of the autonomic nervous system of animals exposed to ELF fields under certain circumstances.

- Neuroendocrinology studies are separated into two classes: pineal gland studies and adrenal gland studies. Evidence of changes in the pineal gland after long-term exposure to 60-Hz electric fields or to rotated magnetic fields is convincing. Changes in the adrenal glands, as indicated by circulating corticosterone concentration, are largely negative except that very transient increases may occur under certain conditions. Such transient spikes of corticosterone are suggestive of arousal responses typical of novel stimulus presentations.

- Behavioral studies of animals exposed to ELF fields indicate that animals can perceive such fields above certain levels. Furthermore, at high strength electric fields (greater than about 90 kV/m, 60 Hz in the rat), it appears that 60-Hz fields are an aversive stimulus. Effects of these fields on motor activity is ambiguous.

It is concluded that results to date show various neurological effects in specific species exposed under carefully controlled conditions to a wide range of ELF field conditions. Extrapolation of these results to humans is currently tenuous, but results to date (as in the 1977 review) indicate that exposure to ELF electric and magnetic fields in the range of those produced by the ELF Communications System do not pose public health problems.

CHAPTER 7. Hematologic and Immunologic Effects of Extremely Low Frequency Electromagnetic Fields

Hematologic and immunologic measurements are commonly used as indicators of general health and well-being of laboratory animals and of humans. Chapter 7 reviews the hematologic and in vitro, as well as in vivo, immunologic studies of animals exposed to ELF electric and magnetic fields. A variety of "significant" changes in hematologic parameters has been reported in animals exposed to such fields, but it is emphasized that the inherent biological variability of these indicators sometimes leads to statistically significant, but not biologically reliable and repeatable, results.

A review of the literature concerning each element of the immune system, the T and B lymphocytes, and macrophages in intact animals leads to the conclusion that

- o the currently available data do not convincingly demonstrate biologically significant reproducible effects of ELF electric and magnetic fields on the immune system of experimental animals. At least some of the positive results reported, particularly in the earlier studies, were probably due to secondary phenomena or artifacts, such as shocks, noise, vibration, and corona, associated with electric field exposure systems.

A review of in vitro immune system effects of exposure to ELF electric and magnetic fields disclosed a variety of interesting and sometimes conflicting results. Chapter 7 concluded that

- o exposure of animals to ELF electric and magnetic fields may lead to a variety of changes in the hematologic and immune systems;
- o these changes are generally temporary and reversible with time, irrespective of field condition;
- o some of the earlier (pre-1978) reported effects of ELF fields on the hematologic and immune systems were probably due to secondary

electric field effects (e.g., shocks, noise, vibration, and ozone), which resulted in stress;

- in vitro studies of the reversible alteration of lymphocyte function during amplitude-modulated exposure to radio frequency radiation are very interesting but require corroborative evidence from both in vitro and in vivo studies; and

- there is currently no convincing evidence from in vitro and in vivo experimental studies for adverse alterations in the hematopoietic or immune systems following ELF field exposures.

CHAPTER 8. Reproductive and Developmental Effects in Mammalian and Avian Species from Exposure to ELF Fields

Effects of ELF electric and magnetic fields on the development, growth, and maturation of avian and mammalian species are reviewed in Chapter 8. These biological events and processes have long been recognized as sensitive indices of a variety of specific external influences and agents. Studies on avian embryos exposed to 60-Hz electric fields ranging from 0.1 to 100 kV/m produced no consistent effect on growth, development, or overall health and well-being. Studies on a variety of mammalian species, primarily rats, mice, guinea pigs, and swine, exposed to 50- to 60-Hz electric fields before and/or during pregnancy and/or during early postnatal development were reviewed. Effects of magnetic fields exposure in birds and in mammals were also reviewed.

Chapter 8 noted that in developmental toxicology studies:

- A compound-related effect must be demonstrated. This in turn requires that
  - studies utilize sufficient numbers of experimental animals to maximize the probability of finding a real effect;
  - concurrent controls be run under conditions that ensure that the only variable being tested is the agent of concern; and
  - appropriate statistical analyses be performed.
- A dose-response relationship must be established, i.e., a significant, predictable relationship must be established between the appropriate dosimetry and the response measured.

- o The effect must have replicability.

Given these criteria, it is concluded that ELF fields have not been demonstrated to produce adverse reproductive and/or developmental effects in either mammalian or avian species. However, there are a small number of studies (especially with magnetic fields) that suggest some agent-related effects, but these studies must be replicated before any definitive statements can be made.

CHAPTER 9. Human Studies of Carcinogenic, Reproductive, and General Health Effects of ELF Fields

Recently published articles suggest an association between cancer and various presumed indicators of exposure to ELF electric and magnetic fields. Although other studies report no such association. Studies concerning ELF electric and magnetic fields and cancer in humans are based on residential and occupational exposure studies. They have been criticized because

- case and control groups may not have been adequately constituted to produce a valid estimate of the association between purported exposure to cancer;
- exposure characterization is generally poor or absent; and
- confounding variables increase uncertainly in purported causal relationships and disease.

A series of published reports on cancer, primarily leukemia, present results concerning associations with occupational status. Methodological issues involving these studies include the following:

- The quality of information on the duration, intensity, type, and frequency of field is generally absent.
- Worker exposure to electric and magnetic fields is typically confounded by exposure to a variety of other agents in the work place.
- Worker exposure to known carcinogens, such as medical treatment with ionizing radiation, was not examined nor were social class differences examined.
- Most articles cited are "Letters to the Editor" or meeting abstracts; hence, they generally have not received peer review for technical merit.

The conclusions are:

- o Results of studies on cancer and residential and occupational exposures to ELF electric and magnetic fields do not demonstrate that such fields are causally related to cancer risk.

- o Although valid questions of possible association between exposure to ELF electric and magnetic fields and reproduction have been raised, currently available scientific data do not demonstrate deleterious effects of such exposure during either prenatal or perinatal development.

- o The currently available scientific data on nonspecific, general human health effects of exposure to the ELF Communications System electric and magnetic fields do not establish that public health would be adversely effected.

CHAPTER 10. Potential Effects on Natural Biota of Operating an Extremely Low Frequency Communication System

The 1977 NAS report on potential biological effects of the Navy's ELF Communications System concluded that although some uncertainties existed, the risks were small enough to warrant proceeding with the project if biological studies accompanied operations of the facility. Chapter 10 addresses two questions:

- o Would the redesign of the ELF Communications System change the anticipated electromagnetic fields enough to invalidate the 1977 evaluation by NAS, and

- o Does the literature published since 1977 contain new evidence that ELF communications are likely to alter the ability of a species to carry out their normal function in an ecosystem ?

The approach was to differentiate between facts meeting the scientific criteria of reproducibility and independent verification versus unverified observations and speculations. It is noted that extrapolation of findings to potential ecological effects is tenuous at best because

- at least most of the effects produced in the laboratory do not appear to be specific to ELF exposure;

- there is no agreed upon hypothesis explaining the mechanism of action; and

- there is little evidence for a predictable dose-response relationship.

Laboratory studies were carefully considered with the expectation that the demonstration of an effect in the laboratory may well mean that it will occur in the wild. However, there are important caveats:

- In vitro or species-specific in vivo laboratory results are difficult to extrapolate to the ecosystem level.

- Detection of ELF electric or magnetic fields does not imply an adverse biological effect.

- Responses may be demonstrated only under special controlled conditions.

- Real-life circumstances may override subtle effects disclosed under controlled laboratory conditions.

- Some organisms or in vitro preparations are sensitive only to particular frequency and intensity windows.

- Heterogenous wild populations may show wide variations in individual susceptibilities to a treatment, especially at low levels.

- Responses may be undetectable at the ecosystem level.

Data obtained in the vicinity of high voltage overhead power transmission lines (60 Hz) are pertinent to the ecological assessment and, indeed, electric and magnetic fields associated with such lines (in the 60-Hz region) are typically considerably greater by 1 to 2 orders of magnitude than fields near the ELF Communications System. With the possible exception of honeybees, none of the studies on plants or animals in the vicinity of high voltage power transmission lines suggest an area of concern for the ELF Communications System. Honeybees exhibit effects when hives are kept in high (about 2 kV/m) electric fields, which exceeds the electric field strength associated with the ELF Communications System.

Data obtained from studies in the laboratory suggest that ELF electric and magnetic fields may affect animals either by

- o covert biochemical or physiological changes of which the animal is unaware but may alter its chance of survival in the wild. Examples of covert changes are mutagenesis, changes in activity levels of enzymes and hormones, changes in cell cycles, embryological effects, calcium efflux in nerve tissue, and alteration of the circadian system; or

- o overt behavioral response resulting from detection and reaction to the ELF fields.

"Detecting" and "reacting" to a stimulus are differentiated here because in vivo detection of electric or magnetic fields can occur at a lower field intensity than do changes in nerve tissue in vitro. Some receptor(s) may therefore act as transducers. In any case, although it is generally agreed that under some circumstances electric and magnetic fields will sometimes produce changes at the subcellular, cellular, organ, or whole organism level of complexity, the biological significance of such changes is speculative. The interaction of electric and magnetic fields with living material is viewed by all as an intriguing scientific problem with many practical ramifications. Additional research is recommended but, currently, adverse effects on natural biota as a result of operation of the Navy's ELF Communications System are considered unlikely and, in fact, the majority of species occurring at the site of the ELF Communications System are unlikely to detect even the operation of the system. However, biological mechanisms for detecting electromagnetic fields are poorly understood except in some electrosensitive fish.

Chapter 10 concluded that:

- o The ecological risk of operating the redesigned USN ELF Communications System is low. The risk is probably less than that projected in the National Academy of Sciences 1977 evaluation.
- o The complexity of ecological systems makes it impossible to rule out the possibility of some component of the ecosystem responding to electromagnetic fields generated by the ELF Communications System. The prediction of low risk is an assumption that should be verified through ecological research conducted in concert with operation of the ELF Communications System.
- o Research published since 1977 does not alter the conclusions drawn by the National Academy of Sciences in 1977 nor does it negate their recommendations for additional research on the effects of ELF electromagnetic fields on biological systems.
- o Ecological effects, if detected, in the vicinity of the operating ELF systems will be subtle not catastrophic; may require a long time to develop; and are of secondary importance to changes produced by the construction of the Communications System.

CONCLUSIONS

After a careful, comprehensive review of the literature on biological effects of ELF electric and magnetic fields, with particular emphasis on findings since 1977, the AIBS Committee unanimously agrees that

- o ELF electric and magnetic fields can, at least in some frequency and intensity combinations and under certain circumstances, cause a variety of effects at any of several levels of biological organization of plants and animals or in vitro preparations.

- o Additional research on coupling of living systems to ELF electric and magnetic fields, on mechanisms of interaction, and on responses of biological material to such fields will be necessary to gain a more nearly complete understanding of the biological significance, if any, of interactions of these fields with living systems.

With respect to the operating characteristics of the Navy ELF Communications System, the coupling of the System's electric and magnetic fields and living systems, and the possible mechanisms of interaction, the AIBS Committee unanimously concludes that:

- o It is unlikely that exposure of living systems to ELF electric and magnetic fields in the range of those associated with the Navy's ELF Communications System can lead to adverse public health effects or to adverse effects on plants and animals.

- o Because of certain ambiguities in the scientific literature, the Navy should continue to monitor the literature and respond appropriately to any significant new information.

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CHAPTER 2

COUPLING OF LIVING ORGANISMS TO ELF ELECTRIC AND MAGNETIC FIELDS

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INTRODUCTION

Exposure of a living organism to electric and/or magnetic fields is normally specified by the field strength measured or calculated with the subject removed from the system. The use of this field, designated the exposure field in this chapter, is convenient because it involves a quantity that is relatively easy to measure or calculate. The fields that actually act on an exposed organism include electric and magnetic fields acting on the outer surface of the body and electric and magnetic fields and current densities induced inside the body. These fields, designated dosimetric fields, can be different from the exposure field because of perturbations caused by the body of the exposed subject. They must, however, be determined in order to specify exposure at the level of living tissues.

In situations where exposure is limited to only one type of field, where exposure geometry is well controlled, and where only one type of organism is involved, different exposure protocols can be compared using exposure field strength, because the relationship between the exposure and dosimetric fields is approximately constant. However, it is more difficult to compare most exposure protocols because they differ in one or more of the following ways: different species were used, different exposure geometries were used, or different types of exposure fields were used. Quantitative comparisons of these protocols must be based on field strengths at the tissue level.

The ELF Communications System produces both electric and magnetic fields,

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and these fields are found both in the air and in the ground near the system. There are, therefore, a number of ways in which a living organism can couple to the fields from the system.

For example, if a person is standing on the ground under an antenna of the ELF Communications System, the electric field in the air around his/her body will act directly on the body's outer surface and will also induce an electric field inside it. The magnetic field produced by the System will exert forces on electrically charged particles in motion inside the body of the person and it will also induce an electric field inside the body. The System also generates electric current in the earth, and some of this current will be shunted through the person's body if it is in conductive contact with the ground at more than one point.

Most laboratory data relating to human exposure to ELF fields were obtained in laboratory experiments where animals were exposed to uniform, vetical, ELF electric fields coupled to their bodies through an air medium. Cleary, estimation of field strengths at the tissue level will be needed in order to relate these biological data to the multifaceted exposure received by a person near the System.

This chapter provides background information, theory, and references with which dosimetric fields in exposure situations relevant to the ELF Communications System can be estimated. An exhaustive review of the literature on ELF dosimetry was not appropriate to achieve this goal. The works cited in this chapter were selected because of their uniqueness or accessibility. Literature reviews of some parts of this subject have been published by Bridges and Preache (1981), Kaune and Phillips (1985) and Sheppard and Eisenbud (1977).

The following three sections discuss exposure to electric fields in the air, electric fields in the ground, and magnetic fields. The fourth section illustrates the ideas developed in this chapter by giving three specific examples: (1) a comparison of human exposure to the electric and magnetic fields produced by the ELF Communications System, (2) an analysis from a dosimetric perspective of the relevance of calcium-efflux-type experiments to the System, and (3) an estimate of the magnitude and distribution of currents shunted through the body of a person standing near an antenna or a ground terminals of the ELF Communications System.

ELECTRIC FIELDS IN THE AIR

The interaction of humans, animals, and other living organisms with electric fields applied through an air dielectric has received the most study of the subjects discussed in this chapter. Most of this work has been done in connection with electric-power transmission lines. Fortunately, with suitable scaling, these results can be applied to the electric fields that exist between the ELF Communication System's antennas and the ground.

Electric-Field Coupling to Spheroids

A useful method for estimating dosimetric electric fields acting on living organisms is to approximate the body of the subject as a homogeneous spheroid. This section presents formulas and values needed for making these estimates.

Barnes, McElroy, and Charkow (1967) described electric-field coupling to electrically homogeneous spheroids in the context of the exposure of humans and animals to the electric fields produced by high-voltage electric-power transmission lines; a subsequent analysis was given by Shiau and Valentino (1981). Cases where the external electric field is orientated either parallel or perpendicular to the symmetry axis of the spheroid are considered here. For either case, the electric field, E_1, induced inside a spheroid by an external field, E_0, can be written as follows (Fricke 1924)

$$E_1 = \frac{E_0}{1 - (1 - \sigma_1^\star / \sigma_0^\star)\,\Gamma}, \qquad (1)$$

where $\sigma_0^\star$ and $\sigma_1^\star$ are the complex conductivities of the media outside and inside the body, respectively, and Γ is a geometrical factor depending on the spheroid's shape and its orientation relative to the applied electric field. For the case of a living body exposed to an electric field through an air dielectric, $\sigma_0^\star = j\omega\epsilon_0$ and $\sigma_1^\star = \sigma_1 + j\omega\epsilon_1\epsilon_0$, where ω is angular frequency defined by $\omega = 2\pi f$, f is the frequency of the electric field, $j = \sqrt{-1}$, the imaginary unit, ϵ_0 is the permittivity of air (8.85×10^{-12} F/m), and σ_1 and ϵ_1 are the conductivity and dielectric constant of the spheroid, respectively.

In the ELF range, σ_1 has values from about 0.02 S/m for fatty tissues to 0.1 S/m for muscle and nonfatty tissue, 0.7 S/m for blood, and 1.5 S/m for clear physiological fluids such as cerebrospinal fluid, urine, and bile (Geddes and Baker 1967). Even though the ELF dielectric constants of most tissues are very large, it is still true that $\sigma_1 \gg \omega\epsilon_1\epsilon_0$ (Barnes, McElroy, and Charkow 1967; Kaune and Gillis 1981; and Schwan and Kay 1957), which means that $\sigma_1^\star \approx \sigma_1$ and $\sigma_1 \gg \omega\epsilon_0$. Therefore, Eq. (1) can be simplified to

$$E_1 = \frac{j\omega\epsilon_0}{\Gamma\sigma_1} E_0. \qquad (2)$$

The presence of j in this equation indicates that E_1 is shifted in electrical phase relative to E_0 by 90°. This phase shift arises because the body is capacitively coupled through an air medium to an antenna of the ELF Communications System.

Let 2h be the total length of the symmetry axis of a spheroid, and let R be its radius. For E_0 parallel to the symmetry axis:

$$\Gamma_h = \frac{hR^2}{2} \int_0^\infty \frac{dq}{(q + h^2)^{3/2} (q + R^2)}. \qquad (3)$$

For E_0 perpendicular to the spheroid's symmetry axis:

$$\Gamma_R = \frac{hR^2}{2} \int_0^\infty \frac{dq}{(q + h^2)^{1/2} (q + R^2)^2}. \qquad (4)$$

These integrals (Stratton 1941) can be simply evaluated in terms of elementary and transcendental functions. Figure 2.1 gives calculated values of Γ_h and Γ_R as a function of the aspect ratio, h/R, of a spheroid.

The surface electric field can also be calculated. Based on their analysis of tissue-impedance data, Barnes, McElroy, and Charkow (1967) proposed the following principle for the ELF range: An animal or human exposed to a 60-Hz electric field "will behave external to its boundary as a perfect conductor and internally as a pure resistance." This very useful principle allows the immediate conclusion that the external electric field will be perpendicular to the surface of the body of a living organism. The

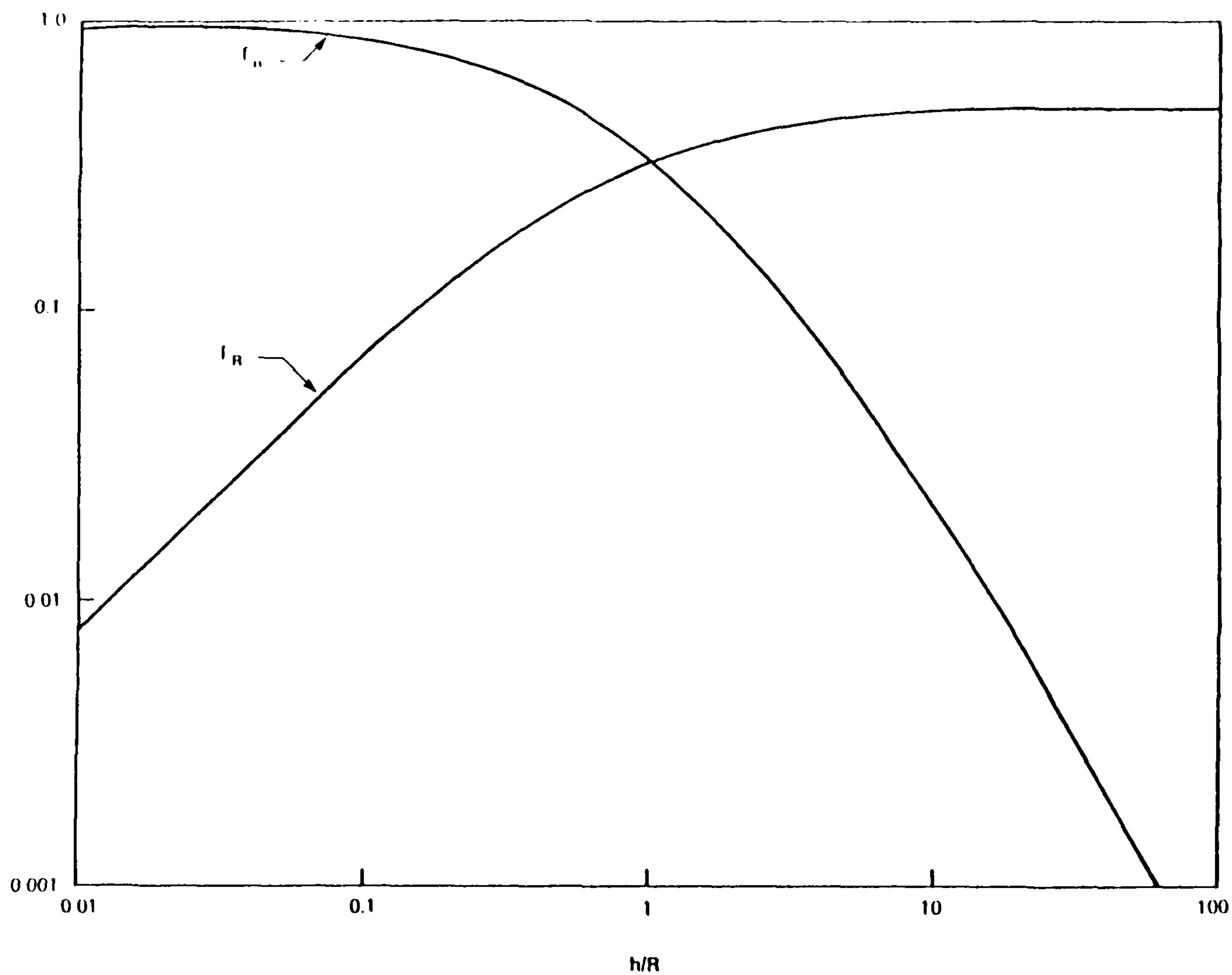

Figure 2.1 Γ as a function of the aspect ratio, h/R, for a spheroid exposed to a uniform ELF electric field. The symmetry and radial axes of the spheroid are h and R, respectively. Γ_h and Γ_R pertain, respectively, to the cases where the external electric field is parallel to or perpendicular to the symmetry axis of the body.

magnitude of this field, E_s, can be calculated using one of the two formulas below. For E_o parallel to the symmetry axis:

$$E_s = \frac{z/h^2}{[(\rho/R^2)^2 + (z/h^2)^2]^{1/2}} \frac{E_o}{\Gamma_h}. \quad (5)$$

For E_o perpendicular to the spheroid's symmetry axis:

$$E_s = \frac{\rho/R^2}{[(\rho/R^2)^2 + (z/h^2)^2]^{1/2}} \frac{E_o}{\Gamma_R}, \quad (6)$$

where ρ and z are the radial (i.e., perpendicular to the symmetry axis) and vertical (along the symmetry axis) coordinates, respectively, of the point on the surface of the spheroid where E_s is to be calculated.

There will be a current inside any conducting body that has an electric field present in its interior. The magnitude and direction of this current can be specified by the current density vector, $\bar{J}(\bar{r})$, defined at each point, $\bar{r}$, inside the body. $\bar{J}(\bar{r})$ points in the direction of current flow at $\bar{r}$ and has a numerical value equal to dI/dA, where dI is the current that would flow across an infinitesimal area element, dA, orientated perpendicular to $\bar{J}$. The current-density and electric-field vectors are related by Ohm's law, which is

$$\bar{J} = \sigma_1 \bar{E}_1. \quad (7)$$

There are advantages to using current density in discussing electric-field coupling through air to conducting bodies. In homogeneous bodies, the current density can be shown to be independent of the body's conductivity (Kaune and Gillis 1981). (This conclusion can be proved for spheroids by combining Eqs. (2) and (7) to get an expression for J that is independent of σ_1.)

Barnes, McElroy, and Charkow (1967) pointed out that the results of an analysis of spheroids exposed to uniform electric fields may also be directly applied to the case of a hemispheroid standing on a ground plane while exposed to a vertical ELF electric field. This form of the spheroidal analysis is of considerable use because most humans and animals exposed through air to the electric fields produced by the ELF Communications System antenna will be standing on the ground.

Several research groups have extended the spheroidal analysis to include ellipsoids (Bayer, Brinkmann, and Wittke 1977; Hart and Marino 1982;

Kolesnikov and Chukhlovin 1978; Lattarulo and Mastronardi 1981). Ellipsoids enable the bodies of humans and animals to be more accurately simulated in some cases. The only differences from the spheroidal analysis are in the formulae for Γ and the surface fields, E_s. Let the x, y, and z axes be designated as x_1 , x_2, and x_3, respectively, and the surface of the ellipsoid be defined by the equation $(x_1/a_1)^2 + (x_2/a_2)^2 + (x_3/a_3)^2 = 1$. For an exposure field, E_o, parallel to the k^{th} axis:

$$\Gamma_k = \frac{a_1 a_2 a_3}{2} \int_0^\infty \frac{dq}{(q + a_k^2)[(q + a_1^2)(q + a_2^2)(q + a_3^2)]^{1/2}} \qquad (8)$$

$$E_s = \frac{x_k/a_k^2}{[(x_1/a_1^2)^2 + (x_2/a_2^2)^2 + (x_3/a_3^2)^2]^{1/2}} \frac{E_o}{\Gamma_k}. \qquad (9)$$

The integral in Eq. (8) can be expressed in terms of incomplete elliptic integrals (Lattarulo and Mastronardi 1981).

Experimental Data for Humans and Animals

Deno (1977) published the first data on induced currents in anatomically detailed human models. His data consisted of measurements, made with a copper-covered human mannequin, of the currents induced in various parts of the body. Using these, he estimated average vertical current densities in humans standing on the ground while exposed to vertical 60-Hz electric fields (Deno 1979). These data may be extrapolated to other frequencies, f, in the ELF range by multiplying them by the ratio f/60 (Kaune and Gillis 1981).

Deno also developed a simple technique for measuring the external electric fields acting directly on the surface of the body. It can be shown (Kaune and Gillis 1981) that the accuracy of surface-electric-field measurements made with conducting models like Deno's mannequin is very good if the model accurately simulates the shape of a real human. Surface electric-field strengths measured at one frequency can be extrapolated without scaling to any other frequency in the ELF range (Kaune and Gillis 1981).

Kaune and Phillips (1980) used Deno's methods to measure surface electric fields and induced-current distributions in rats and pigs, from which they estimated axial (i.e., along the horizontal axis of the body) current densities.

One quantity of interest is the total current flowing between a grounded body and ground (i.e., the short-circuit current). Published short-circuit-current data are summarized in Table 2.1 for humans (Bracken 1976; Deno 1977), horses and cows (EPRI 1975), pigs (Kaune et al. 1978), guinea pigs (Kaune and Miller 1984), and rats (Kaune and Phillips 1980). Most of the measurements in these papers were taken at only one frequency and with one body weight. They have been extrapolated to other frequencies, f, and body weights, W, assuming a $fW^{2/3}$ dependence (Kaune and Gillis 1981). The human data were expressed by Deno (1977) in terms of body height rather than body weight. It is assumed that a body height of 1.7 m was equivalent to a body weight of 70 kg (ICRP 1975) in the preparation of Table 2.1.

TABLE 2.1.

SHORT-CIRCUIT CURRENTS INDUCED IN GROUNDED HUMANS AND ANIMALS BY VERTICAL ELF ELECTRIC FIELDS

The frequency and strength of the applied field are f (Hz) and E_0 (V/m), respectively. The weight of the subject is W (g).

Species	Short-Circuit Current (μA)
Human	$1.5 \times 10^{-7}\ fW^{2/3}E_0$
Horse	$8.5 \times 10^{-8}\ fW^{2/3}E_0$
Cow	$8.6 \times 10^{-8}\ fW^{2/3}E_0$
Pig	$7.7 \times 10^{-8}\ fW^{2/3}E_0$
Guinea Pig	$4.2 \times 10^{-8}\ fW^{2/3}E_0$
Rat	$4.0 \times 10^{-8}\ fW^{2/3}E_0$

Figure 2.2 gives surface-electric-field and current-density data derived from Deno's human measurements and Kaune and Phillip's animal data for a frequency of 76 Hz (midway between the two frequencies used by the ELF Communications System) and an electric-field strength of 120 V/m (about the maximum produced at ground level under an antenna).

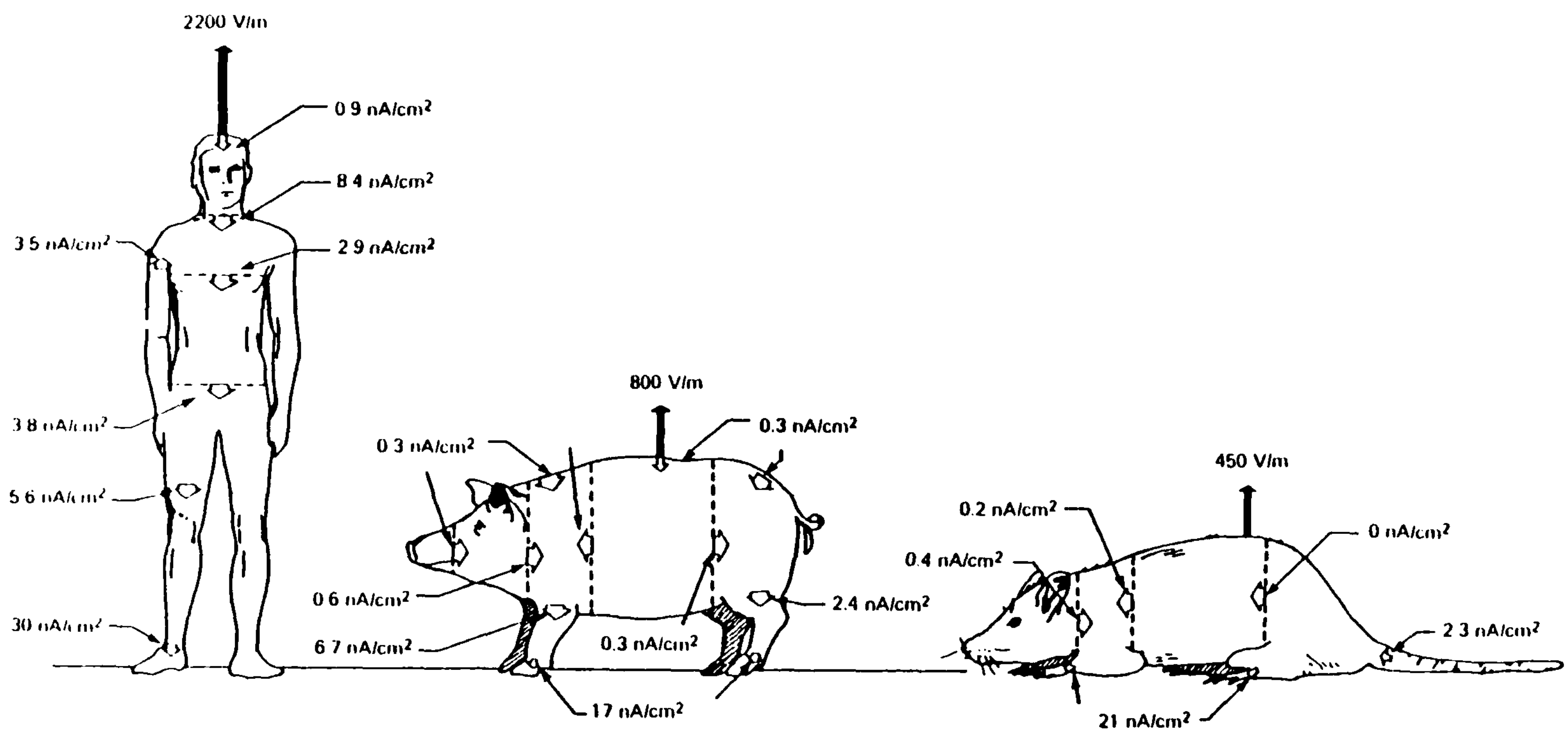

Figure 2.2 Grounded man, pig, and rat exposed to vertical, 76-Hz, 120-V/m electric field. Surface-electric-field and axial-current-density data are shown.

Figure 2.2 shows that the dosimetric fields to which the human is exposed are considerably larger than the corresponding quantities for the animal species, even though the exposure fields are the same. This difference means that exposure fields must be scaled to equalize dosimetric-field strengths in order to extrapolate biological data from one species to another. This process is complicated by the fact that actual value of the scaling factor depends on which dosimetric field is being scaled. For example, a scaling factor for the peak electric-field strength acting on the body would be about 4.9 to 1 for humans to rats while the scaling factor for axial current density in the neck would be about 20 to 1. Evidently, knowledge must be obtained about the site of action for a particular biological effect (i.e., the point in the body where the applied electric field acts to cause the effect) before extrapolation of data across species can be performed.

The surface-electric-field data given in Figure 2.2 are quite limited in that measurements were made at only a few points on the body. A simple way to calculate electric-field strength averaged over the entire body surface of a grounded subject has been described by Kaune (1981). This method requires only that the subject's short-circuit current and the surface area of its body be measured.

The current-density data given in Figure 2.2 are only one (the axial) of three components of the total current-density vector. This is a serious limitation in the animal data because it is certain that significant vertical current will also be present. Measurements in three-dimensional models of humans and animals are required to overcome this limitation.

Guy et al. (1982) and Kaune and Forsythe (1985) measured induced electric fields and current densities in grounded saline models of humans exposed to 60-Hz electric fields. Figure 2.3 summarizes some of Kaune and Forsythe's data for human models, assuming a frequency of 76 Hz and an exposure field strength of 120 V/m. It is expected that these authors will publish similar data for rats and pigs.

Summary

There are considerable data and theoretical methods that can be used in estimating the dosimetric fields in situations involving the exposure of humans or animals to ELF electric fields in air. First approximations can be

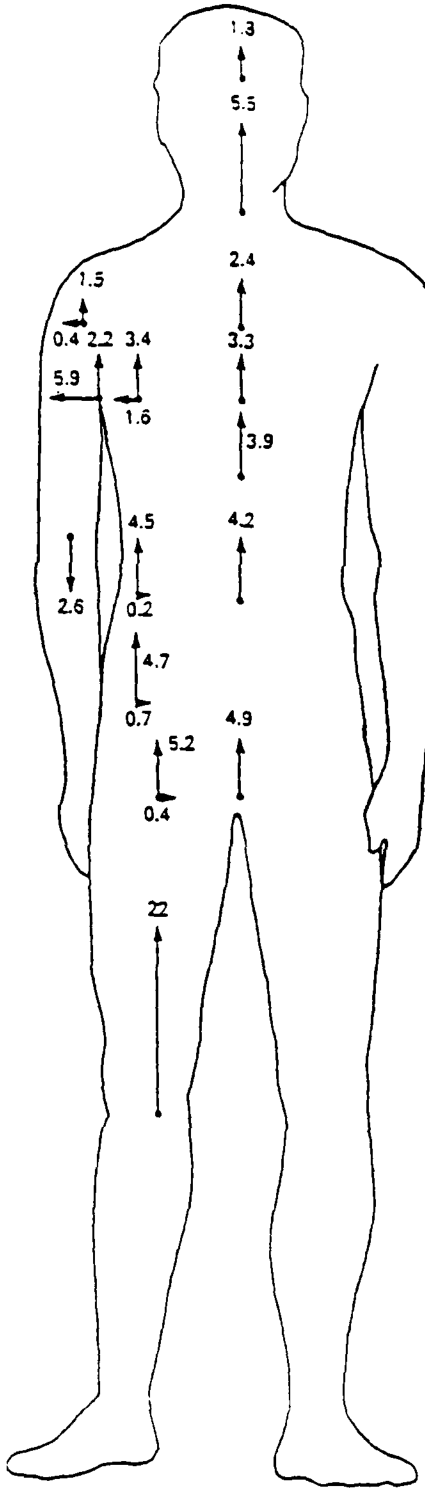

Figure 2.3 Current densities induced in a grounded saline phantom of a man standing on ground and exposed to a vertical 120-V/m, 76- Hz electric field. Current-density values are in nA/cm^2.

made using spheroidal or ellipsoidal techniques, and more refined analyses can be based on the experimental papers reviewed in this section.

ELECTRIC FIELDS IN THE GROUND

Organisms that reside in or on the ground will couple to electric fields in the ground. The next two sections discuss this type of exposure in more detail.

Organisms Residing in the Ground

Dosimetry for organisms living in the ground has received little attention in the literature, but many of the theoretical techniques developed for exposure of bodies to electric fields in air can be applied to this problem. For example, spheroids or ellipsoids can be used to model organisms that live in the ground. Let σ_0 and σ_1 be the conductivities of the soil and the organism, respectively. From Eq. (1), the electric field induced inside a spheroidal model of an organism in soil is

$$E_1 = \frac{E_0}{1 - (1 - \sigma_0/\sigma_1)\,\Gamma} . \qquad (10)$$

Table 2.2 gives some typical values for the conductivities of different kinds of soil (El-Kady and Vainberg 1983; Rudenberg 1945; Sverak 1982), and Table 2.3 gives calculated values of E_1 for various aspect ratios and soil and organism conductivities when the electric field in the soil is parallel to the symmetry axis of the spheroid. Table 2.4 gives similar values for spheroids oriented perpendicular to the applied electric field.

A long thin body shape is of particular interest because it simulates several types of organisms that live in the ground (e.g., worms and tree roots). The best spheroidal simulation of this body shape is with h/R large. The data in Table 2.3 (for h/R = 100) show that an external electric field parallel to the long axis of the body is coupled into it with almost no alteration for a wide range of soil and body conductivities. This result could perhaps have been predicted by noting that (1) a long thin object will hardly perturb a field that is parallel to its long axis and (2) components of electric field parallel to the boundary of the body have the same value on both sides of the boundary. Because this argument is evidently valid, it seems reasonable to generalize it to long thin bodies that are not spheroids.

TABLE 2.2.

AVERAGE SOIL CONDUCTIVIES

Type of Soil	Conductivity (S/m)
Wet Organic Soil	0.1
Clay	0.01–0.2
Lake Water	0.003–0.02
Sand, Moist Soil	0.001–0.02
Sandstone, Dry Soil	0.0002–0.01
Wet Crushed Stone	0.0003
Rock	0.001

Soil electric fields that are transverse to the axis of the body do not exhibit the same simple pattern. Fields coupled inside the body may be attentuated or enhanced, depending on the relative conductivities of the body and soil.

Many organisms living in the soil are surrounded by membranes (e.g., skin) characterized by electrical conductivities different from their bodies. Spheroidal models incorporating two (or more) layers can be developed to model these situations.

Organisms Standing on the Ground

As discussed in Chapter 1, there are two sources of electric fields in the ground. The first source is the time-varying magnetic fields that are generated by currents in the antennas of the ELF Communications System. The second source of electric fields in the ground is the ground terminals of the system.

The feet of a human or animal standing on ground may be at different potentials when there is a horizontal electric field present. This means that

TABLE 2.3

Electric Field, E_1, and Current Density, J_1, Induced in a Spheroidal Body Located in the Ground. The unperturbed electric field and current density in the soil are E_0 and J_0, respectively. E_0 is parallel to the symmetry axis of the spheroid, which has a length of 2h. The radius of the spheroid is R. The conductivities of the soil and spheroid are σ_0 and σ_1, respectively.

	h/R = 0.1		h/R = 1.0		h/R = 10		h/R = 100	
σ_1 / σ_2	E_1/E_0	J_1/J_0	E_1/E_0	J_1/J_0	E_1/E_0	J_1/J_0	E_1/E_0	J_1/J_0
0.01	6.77	0.068	1.49	0.015	1.02	0.010	1.00	0.010
0.05	5.49	0.274	1.46	0.073	1.02	0.051	1.00	0.050
0.1	4.44	0.444	1.43	0.143	1.02	0.102	1.00	0.100
0.5	1.76	0.878	1.20	0.600	1.01	0.505	1.00	0.500
1	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
5	0.225	1.13	0.429	2.14	0.925	4.62	0.998	4.99
10	0.114	1.14	0.250	2.50	0.846	8.46	0.996	9.96
50	0.023	1.16	0.058	2.88	0.502	25.1	0.979	49.0
100	0.012	1.16	0.029	2.94	0.332	33.2	0.959	95.9

TABLE 2.4.

Electric Field, E_1, and Current Density, J_1, Induced in a Spheroidal Body Located in the Ground. The unperturbed electric field and current density in the soil are E_0 and J_0, respectively. E_0 is perpendicular to the symmetry axis of the spheroid, which has a length of 2h. The radius of the spheroid is R. The conductivities of the soil and spheroid are σ_0 and σ_1, respectively.

	h/R = 0.1		h/R = 1.0		h/R = 10		h/R = 100	
σ_1/σ_2	E_1/E_0	J_1/J_0	E_1/E_0	J_1/J_0	E_1/E_0	J_1/J_0	E_1/E_0	J_1/J_0
0.01	1.07	0.011	1.49	0.015	1.94	0.019	1.98	0.020
0.05	1.07	0.054	1.46	0.073	1.87	0.094	1.90	0.095
0.1	1.07	0.107	1.43	0.143	1.79	0.179	1.82	0.182
0.5	1.04	0.518	1.20	0.600	1.32	0.662	1.33	0.667
1	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
5	0.782	3.91	0.429	2.14	0.338	1.69	0.333	1.67
10	0.615	6.15	0.250	2.50	0.185	1.85	0.182	1.82
50	0.227	11.3	0.058	2.88	0.040	2.00	0.039	1.96
1001	0.127	12.7	0.029	2.94	0.020	2.02	0.020	1.98

there will be a current flowing inside the body between the feet. The size of this current is determined by the potential differences between the feet--the step potentials--and the impedances in the circuit. A complete analysis of human or animal exposure to step potentials must first estimate the total current entering the body from the ground and then must determine the distribution of this current within the body.

There are other ways in which humans or animals can be exposed to the electric fields in the ground upon which they are standing. For example, suppose an animal touches a barbed-wire fence strung on wooden poles. The fence may be electrically grounded at some point, and current can flow from ground to the fence at this point and then return to ground through the animal's body. Another example is that of a man launching an aluminum canoe in a lake. The electrical potentials involved in these exposures can be designated as bridging potentials because the exposed subject and other conductors that may be in the circuit form a bridge-like structure which touches the ground at two or more points.

The problem of estimating the total current entering the body of a human or animal exposed to various forms of bridging potentials has received considerable attention from electrical engineers who design electric-power transmission and distribution systems (e.g., El-Kady and Vainberg 1983; IEEE 1976), and it was also treated in great detail during a 1977 review of the ELF Communications System conducted by the National Academy of Sciences (NAS 1977). The method to calculate this current recommended by these sources is illustrated in Figure 2.4 for the step-potential case. Generalization to other bridging-potential cases is straightforward. The following paragraphs discuss in more detail the elements of the circuit shown in Figure 2.4.

<u>Open-Circuit Voltage</u>. V_{oc} is the open-circuit voltage between the feet of the exposed subject. This voltage is related to the horizontal electric field, E_h, at the surface of the ground by

$$V_{oc} = E_h s \cos \theta, \qquad (11)$$

where s is the horizontal distance between the points of contact to the ground and θ is the angle between s and $\bar{E}_h$.

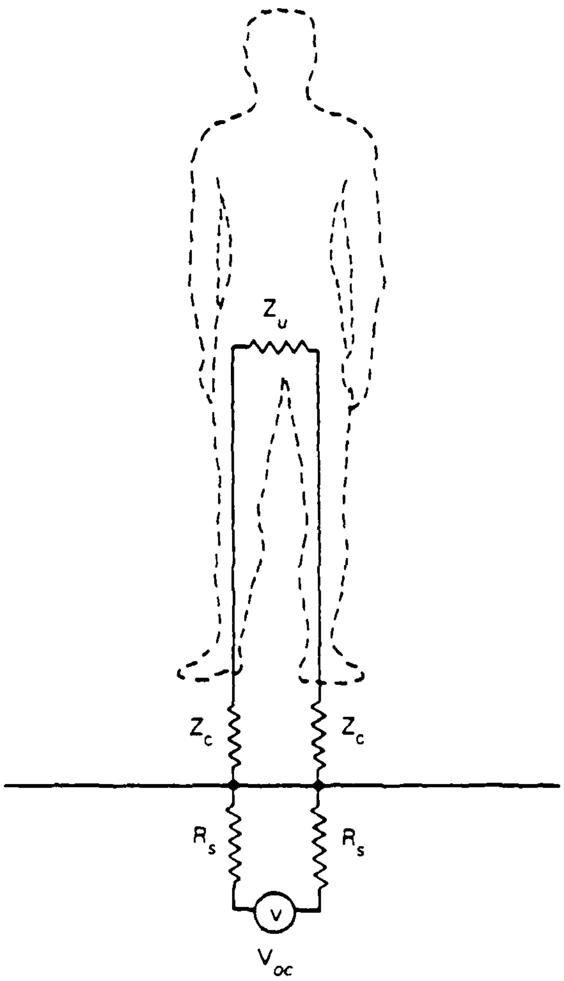

Figure 2.4 Equivalent circuit of a man standing on a ground which contains a horizontal electric field.

Spreading Resistance. The impedances designated R_s in Figure 2.4 are the source impedances encountered by current flowing from the earth into the feet of the subject. These impedances are resistive and are sometimes called spreading resistances. They can be roughly estimated by modeling the foot as a hemisphere inserted into the ground, with the result that

$$R_S \approx \frac{1}{\sigma_S(2\pi A)^{1/2}}, \qquad (12)$$

where σ_s is the conductivity of the soil and A is the area of contact between the foot and ground. For adult humans, $A \sim 0.025\ m^2$, so $R_s \sim 2.5/\sigma_s$ (Baughn 1977).

Contact and Internal Body Impedances. The contact impedance between each foot and ground is designated Z_c in Figure 2.4. Z_c is difficult to quantify because it is highly variable and because it depends on many factors, including type of footwear, moistness of feet and footwear, weight of subject, and presence of open wounds or abrasions on the subject's feet. Most measurements of these impedances appear to have also included the internal impedance, Z_b, of the body. Because of this, because it does not seem possible to separate Z_c from Z_b in most of the published literature, and because only the total body impedance, $Z_t = 2Z_c + Z_b$, must be known for step-potential calculations, Z_c and Z_b will be discussed together.

Bridges (1981) and Hammam and Baishiki (1983) have recently published papers that review data on Z_t for humans. These authors emphasize that the skin resistance is normally the dominant contributor to Z_t. However, it appears to be customary in step- and bridging-potential calculations to assume that the contact impedance is zero. Those proposing this justify its use because it is conservative, which it is, but perhaps the more fundamental reason is that it is very difficult to decide what other value to use for Z_c. If the contact impedances are set equal to zero, then $Z_t = Z_b$. For step-potential exposure, Z_b can be estimated as the sum of the impedances of the two legs, which can, in turn, be modeled as right-circular conical sections. The resistance of such a section is $4L/(\sigma\pi d_1 d_2)$, where L is the length of the leg, d_1 and d_2 are the diameters of the ankle and upper thigh, respectively, and σ is the average conductivity of the leg. Estimated values for the adult male are $L \sim 0.75$ m, $d_1 \sim 0.08$ m, $d_2 \sim 0.2$ m, and $\sigma \sim 0.1$ S/m. With these values, $Z_b \sim 1.2$ kΩ. This value is close to the value of 1000 Ω often used in step potential calculations (IEEE 1976).

It appears that it is almost always the case that the contact impedances are large compared to the internal body impedance, for if this were not true, adults would receive electrical shocks from car batteries, and children would be shocked by the batteries that are used in some toys.

Bridges (1981), in an interesting paper, reviews selected human-impedance data. In Figure 1 of his paper, hand-to-hand impedance data measured on human cadavers within 24 h after death are plotted. These data show clearly that the body impedance decreases for applied voltages above about 20 V. For voltages $>$1000 V, measured impedances are about 1 to 2 kΩ, whereas for voltages less than 20 V, they are $>$ 5 kΩ. Bridges points out that only in "contrived laboratory conditions has it been possible to measure values of body resistance (at least for low level voltage sources) much below a few thousand ohms." Therefore, it would seem appropriate to use some nonzero value for Z_c, especially because the open-circuit voltages involved in bridging-potential exposures are small.

The maximum impedance that can exist between the human foot and ground is determined by the capacitance between these parts. This value is about 50 pF (EPRI 1975) for conventional footwear, which corresponds to a reactance of 40 MΩ at 76 Hz.

A few body-impedance data are available for animals. Some representative values are $\sim$5 kΩ between two of the feet of a pig (Kaune et al. 1978) and 730 Ω between the front and rear hooves of a dairy cow (Norell et al. 1983).

Once the various impedances in Figure 2.4 have been estimated, the total current, I_b, entering the body of a subject exposed to a step potential can be calculated using the formula

$$I_b = \frac{V_{oc}}{2R_s + Z_t}. \tag{13}$$

An example of a calculation using this equation is given in the last section of this chapter.

It seems to be generally assumed, presumably because of their small values, that contact and tissue impedances are largely resistive at 60 Hz. Bridges (1981) measured the phase of the total body impedance of rhesus monkeys and found that it was fairly small but definitely not zero. The error introduced in Eq. (13) by treating these impedances as resistances is probably negligible.

The next step in a complete analysis of step-potential currents is to estimate how the current entering the body is distributed within the body. This step is bypassed in analyses of bridging-potential risks by using data relating electric-shock hazard to the total current passing through the human body. Most of these data were obtained for currents entering, and often exiting, the human body through the hands, so the appropriateness of their use to assess risks arising from step potentials is doubtful. What really is needed is a description of the current densities passing through the body, especially in the vicinity of the heart (Bridges 1981). Unfortunately, there are very few, if any, data, either experimental or theoretical, on the distribution within the body of currents entering through the feet.

However, there are data available on the distribution of current induced by external electric fields within the human body. A method to use these data to estimate current distributions arising from step potentials is described in the third example given in the last section of this chapter.

INTERACTION OF LIVING ORGANISMS WITH ELF MAGNETIC FIELDS

As discussed earlier in this chapter, the bodies of humans, animals, and other living organisms cause very large perturbations in any ELF electric field to which they are exposed. In order to assess perturbations in an applied ELF magnetic field caused by the body of a living organism, the magnetic permeabilities of the tissues of the body must be compared to that of air, and the skin depths in these tissues must be calculated and compared to the size of the body of the organism. Living tissues have almost no magnetic properties, so $\mu \simeq \mu_0 = 4\pi \times 10^{-7}$ H/m, where μ and μ_0 are the permeabilities of the tissues and air, respectively. The skin depth, δ, is given by $\delta = (2/\omega\mu\sigma)^{1/2}$ (Smythe 1968). A typical value for the conductivity of living tissues is 0.2 S/m. Skin depth, calculated with these values, is > 50 m. Because $\mu \simeq \mu_0$ and because δ is much greater than the size of any living organism considered here, it may be concluded that the body of a living organism will not significantly perturb an applied ELF magnetic field. This fact greatly simplifies exposure specification because there is no difference between the exposure and dosimetric magnetic fields.

The following sections discuss in more detail the ways in which an ELF magnetic field can couple to a living organism.

Induced Electric Fields

Faraday's law of induction states that time-varying magnetic fields generate electric fields through induction. Therefore, a living organism exposed to the magnetic fields produced by the ELF Communications System will also be exposed to an induced electric field from this source.

The electric field induced by a magnetic field causes current to flow in any conductive body. This current, in turn, produces a second magnetic field that combines with and modifies the original magnetic field. By Lenz's law (Reitz and Milford 1960), this modification always reduces the strength of the initial magnetic field. The skin-effect calculation carried out at the beginning of the section essentially gauges the significance of this modification. The currents produced by a magnetically induced electric field are called eddy currents and circulate in closed loops that tend to lie in planes perpendicular to the direction of the magnetic field.

More insight can be gained by considering the case of a homogeneous spheroid centered at the origin of a rectangular coordinate system and oriented with its symmetry axis parallel to the z axis. For exposure to a uniform magnetic field parallel to the z axis, the electric field, $\bar{E}_m$, induced inside the spheroid at a point (x, y, z) is

$$\bar{E}_m = \frac{j\omega B_o}{2}(y\hat{x} - x\hat{y}) \qquad \left(\begin{matrix}\bar{B}_o \text{ parallel} \\ \text{to z axis}\end{matrix}\right), \tag{14}$$

where B_o is the magnetic flux density and $\hat{x}$, $\hat{y}$, and $\hat{z}$ are unit vectors in the x, y, and z directions, respectively. It is easily shown that the maximum induced electric field occurs where the surface of the body intersects the x-y plane and that its magnitude is $E_{max} = \omega B_o R/2$. For magnetic fields perpendicular to the spheroid's symmetry axis,

$$\bar{E}_m = \frac{j\omega B_o}{h^2 + R^2}(R^2 z\hat{y} - h^2 y\hat{z}) \qquad \left\{\begin{array}{c}\bar{B}_o \text{ parallel} \\ \text{to x axis}\end{array}\right\} \qquad (15)$$

$$\bar{E}_m = \frac{j\omega B_o}{h^2 + R^2}(-R^2 z\hat{x} - h^2 x\hat{z}) \qquad \left\{\begin{array}{c}\bar{B}_o \text{ parallel} \\ \text{to y axis}\end{array}\right\}. \qquad (16)$$

The maximum electric field in Eq. (15) occurs at the points $(0, \pm R, 0)$ or $(0, 0, \pm h)$ for prolate or oblate spheroids, respectively. In Eq. (16), the maximum value of E_m occurs at the points $(\pm R, 0, 0)$ or $(0, 0, \pm h)$ for prolate or oblate spheroids. The maximum field strength, for either equation, is $\omega B_o hR[\max(h,r)]/(h^2 + R^2)$, where max (h,r) is equal to the larger of h and R. It is straightforward to generalize Eqs. (14) through (16) to homogeneous ellipsoids (Hart and Marino 1982).

Gandhi, De Ford, and Kanai (1984) calculated induced current densities in the torso of a human exposed to an ELF magnetic field. These authors developed a technique that simulates an exposed object with a multidimensional lattice of impedance elements. They only considered a two-dimensional simulation, but there appears to be no fundamental problem in extending the method to three dimensions. The method offers a simple and apparently powerful way to analyze the coupling of humans and animals to ELF magnetic fields. However, until the results of more calculations become available, the state of the art is to simulate an exposed organism as a spheroid or ellipsoid.

Direct Magnetic Interactions

As noted earlier, ELF magnetic fields penetrate inside living organisms without significant perturbation. These fields will exert a force, called the Lorentz force, on any charged particle which is in motion within the body. This force, $\bar{F}$, is related to the particle's velocity, $\bar{v}$, and its electrical charge, q, by the equation

$$\bar{F} = q\bar{v} \times \bar{B}, \qquad (17)$$

where $\bar{B}$ is the magnetic flux-density vector.

The most prevalent types of motion in matter are the motion of electrons in atoms and the intrinsic spins of the electrons, protons, and neutrons that make up matter. This motion leads to the existence of magnetic dipole moments that may be permanent (paramagnetism and ferromagnetism) or induced by the applied magnetic field (diamagnetism). A magnetic dipole interacts with a uniform magnetic field in such a way that it experiences a torque but no net force. This torque is in a direction to align the dipole parallel to the magnetic field, but this alignment is resisted by random thermal motion. Let Θ be the angle between a dipole and the magnetic field, $\bar{B}$. For an assembly of similar dipoles in a magnetic field, the average value of $\cos\Theta$ can be written approximately as $\langle \cos\Theta \rangle = mB/(3kT)$ if $mB/(3kT) \ll 1$ (Reitz and Milford 1960), where m is the magnitude of the dipole moment, k is Boltzmann's constant, and T is the absolute temperature. Complete alignment of the magnetic moments would be characterized by $\langle \cos\Theta \rangle = 1$, whereas $\langle \cos\Theta \rangle = 0$ would indicate no alignment.

Magnetic moments associated with electronic orbital motion (i.e., orbital angular momentum) and electron spin are equal, within about an order of magnitude, to the Bohr Magneton (9.27×10^{-24} J/T). The analogous quantity for nuclear magnetic moments is the nuclear magneton (5.05×10^{-27} J/T. At body temperature (310° K) and at the maximum ELF Communications System magnetic-field level of about 6 μT, $\langle \cos\Theta \rangle \sim 10^{-9}$ and $\sim 10^{-12}$ for electronic and nuclear magnetic moments, respectively. Obviously, the effect of the System's field on magnetic dipoles that are part of the subject's body is very small. Of course, every single dipole is subject to this effect and, conceivably, some sort of physiological process that is sensitive to the average response of a great many of these dipoles might be affected by even a 6-μT field.

Magnetic dipoles placed in a nonuniform magnetic field do experience a net force. Some scientists have therefore suggested that spatially nonuniform magnetic fields may have more potential to affect living organisms.

Charged particles are also carried by the bulk motion of various parts of the body. For example, charged ions are carried by blood flow. These ions are both positively and negatively charged and will experience Lorentz forces in opposite directions. This results in separation of the two polarities of electric charge and, therefore, in the generation of electric potentials. It has been shown that these potentials can be detected as artifacts in the electrocardiograms of rats (Gaffey and Tenforde 1981), although at magnetic-field intensities much larger than those produced by the ELF Communications System.

EXAMPLES

This section gives three examples that illustrate the application of the methods introduced in this chapter. In the first of these examples, human exposure to the maximum ground-level electric and magnetic fields produced by the ELF Communications System are compared. The second example is a discussion of the relevance of the so-called calcium-efflux studies, which were done at frequencies substantially different from the base frequencies of the System. In the concluding example, the magnitude and distribution of body currents resulting from step potentials near an antenna of the ELF Communications System are estimated.

Comparison of Human Exposure to Electric and Magnetic Fields

The common element in electric- and magnetic-field exposure is the electric fields induced inside the bodies of the exposed organisms. The induced electric fields must therefore be estimated in order to compare these two types of exposure.

The calculated maximum ground-level electric field produced by the antennas of the ELF Communications System is about 120. From Figure 2.2, the estimated current densities induced in the head and abdomen of a grounded human exposed to a 76-Hz, 120-V/m electric field are about 1 and 4 nA/cm^2, respectively. Assuming an average tissue conductivity of 0.2 S/m, these current densities correspond to induced electric fields in the head and abdomen of 0.05 and 0.2 mV/m, respectively.

We will estimate induced electric-field levels resulting from the exposure of a human to the calculated maximum 6-μT (0.06-G) magnetic field produced at ground level by the ELF Communications System using the spheroidal techniques described earlier. As a first effort, consider only the head of a human, which can be modeled as a sphere with a radius of about 9 cm. The maximum magnetic field produced by the System will be found directly under its antenna and will be horizontal. Using Eqs. (15) or (16), with h = R, the magnitude of the induced electric field is $E_m = \omega B_0 \rho /2$, where ρ is the distance measured perpendicular to B_0 from the center line of the head to the point where E_m is to be calculated. With $B_o = 6\ \mu T$, the maximum induced electric field, which occurs at the surface of the head, is 0.13 mV/m. The average field induced in the head is 0.08 mV/m. These values are similar to the value of 0.1 mV/m which was the estimate of the field induced in the head by the System's electric fields.

Of course, the head is attached to the body. The whole body can be modeled using a spheroid, the total height and volume of which are selected to equal those of a typical man, that is 1.7 m and $\sim 0.07\ m^3$, respectively. The spheroid that fits this description has h = 0.85 m and R = 0.14 m. The maximum induced electric field, E_{max}, the abdominal plane (i.e., the horizontal plane through the center of the body) is

$$E_{max} = \omega B_o R \left(\frac{h^2}{h^2 + R^2} \right) \simeq 0.4\ mV/m. \tag{18}$$

The average electric field in this region is

$$E_{avg} = \frac{4\omega B_o R}{3\pi} \left(\frac{h^2}{h^2 + R^2} \right) = 0.2\ mV/m. \tag{19}$$

These values are comparable to the 0.2-mV/m electric field that was estimated to be induced in the abdomen of a human by the electric field from one of the antennas of the ELF Communications System. However, the internal field distributions resulting from these two sources are quite different. The internal electric field induced by the System's electric field is approximately vertical (Guy et al. 1982; Kaune and Forsythe 1985), whereas the internal field induced by the System's magnetic field is variable in magnitude and is tangent to horizontal circles with centers lying on the symmetry axis of the body.

The induced electric field, E_t, at the top of the spheroid is an estimate for the head. Using Eq. (15), $E_t = 0.05$ mV/m, which is similar to 0.08-mV/m, the average value calculated earlier for the head using the simple spherical model.

This example serves two purposes. First, it illustrates the kinds of calculations that can be done to compare exposure levels produced by the different kinds of fields produced by the ELF Communications System. Second, it shows that the maximum ground-level electric and magnetic fields produced by the System induce roughly equal electric fields inside a grounded man.

Relating Biological Experiments at Different Frequencies

Considerable biological data have been published from laboratory experiments conducted at frequencies different from the 72- and 80-Hz base frequencies used by the ELF Communications System. The following analysis will address, from a dosimetric perspective, whether the results of one group of these experiments, the so-called calcium-efflux experiments, have relevance to the System.

Bawin and Adey (1976) and Blackman et al. (1982) have reported that the "efflux" of calcium ions from chick-brain tissue is altered in response to exposure to ELF electric fields with frequencies in the approximate range of 6 to 16 Hz and at intensities of 6 and 40 V/m.

At first, it seems reasonable to suppose that these experiments have no relevance to the ELF Communications System because of their considerably lower frequencies. However, reflection shows that, although the conclusion may be true, the argument is invalid, because the frequency-shift modulation used by the System leads to the emission of electromagnetic energy at frequencies other than the 72- and 80-Hz base values of the system.

The basic System transmission unit is a "chip", which consists either of 4.5 cycles of a 72-Hz sine wave or 5 cycles of a 80-Hz sine wave. The ELF Communications System uses a pseudorandom chip pattern which is repeated a number of times so that signal-averaging techniques can be used to improve its reception.

For the purposes of the estimate given here, the ELF signal was assumed to consist of alternating 72- and 80-Hz chips. This pattern maximizes the number of the frequency shifts and is, therefore, a worst case for the generation of harmonic frequencies. The frequency spectrum produced by this chip pattern was calculated using Fourier-series analysis. The results are given in Table 2.5 for the frequency range 0 to 180 Hz, where the continuous-wave 72- and 80-Hz field strengths were both assumed to be 120 V/m, the approximate maximum level produced at ground level by the System. Similar calculations were made for several random chip patterns, with the result that power in the 0 to 16-Hz frequency range was reduced by about a factor of 2, which corresponds to a reduction in electric-field strength of about 30%.

TABLE 2.5.

CALCULATED ELECTRIC-FIELD STRENGTHS DIRECTLY UNDER THE ELF COMMUNICATIONS SYSTEM ANTENNA

The frequency-shift pattern was assumed to be alternating 72- and 80-Hz chips.

Frequency (Hz)	Electric Field (V/m)
4	0.06
12	0.20
20	0.37
28	0.60
36	0.95
44	1.59
52	2.98
60	7.11
68	35.9
76	108.0
84	35.9
92	7.14
100	3.03
108	1.66
116	1.04
124	0.71
132	0.51
140	0.39
148	0.30
156	0.24
164	0.19
172	0.16
180	0.13

As shown in Table 2.4, electric fields are generated with frequencies in the vicinity of 16 Hz. However, because their strengths (0.2 to 0.4 V/m) are relatively small compared to those used by Bawin and Adey (1976) and by Blackman et al. (1982), it is again tempting to conclude that calcium-efflux experiments do not bear on the ELF Communications System. But, as emphasized at the beginning of this chapter, such a conclusion must be based on an analysis of dosimetric rather than exposure field strengths. Joines and Blackman (1980, 1981) have given a dosimetric analysis for chick-brain exposure to radio frequencies. Using the geometrical assumptions of their analysis, an approximate analysis can be constructed for the ELF range using the techniques introduced in this chapter.

Joines and Blackman modeled the chick-brain preparation as a 0.414-cm-radius sphere of brain tissue surrounded by a 0.71-cm-radius spherical shell of culture medium. If the surrounding culture medium is first neglected, the electric field, E_c, induced inside the brain tissue by an external electric field, E_o, can be calculated using Eq. (1). For spheres, $\Gamma = 1/3$, so

$$E_c = 3 \frac{\omega \epsilon_o}{\sigma_c} E_o, \tag{20}$$

where σ_c is the electrical conductivity of chick-brain tissue.

The effect of the surrounding shell of medium can be taken into account by multiplying Eq. (20) by a factor D, given by

$$D = \frac{1}{(R_c/R_m)^3 + (1 + 2\sigma_m/\sigma_c)[1 - (R_c/R_m)^3]/3}, \tag{21}$$

where R_c is the radius of the chick-brain-tissue sphere, R_m is the outer radius of the spherical shell of culture medium, and σ_m is the conductivity of the culture medium. The derivation of this equation follows.

The potentials, ϕ_1 and ϕ_2, in the spherical shell and in the brain tissue, respectively, can be written in the general forms $\phi_1 = -E_o r[\alpha - \beta(R_m/r)^3] \cos\Theta$ and $\phi_2 = -\gamma E_o r \cos\Theta$ (Reitz and Milford 1960). The constants α, β, and γ are determined by the following boundary conditions: $j\omega\epsilon_o (\partial \phi_o/\partial r) = \sigma_m(\partial \phi_1/\partial r)$ at $r = R_m$, and $\phi_1 = \phi_2$ and $\sigma_m (\partial \phi_1/\partial r) = \sigma_c (\partial \phi_2/\partial r)$ at $r = R_c$ (Kaune and Gillis 1981). Carrying out this solution leads to Eq. (21).

The researchers doing the calcium-efflux experiments did not publish values for σ_m and σ_c. Cerebrospinal fluid, which bathes the brain in vivo, has an ELF conductivity of about 1.5 S/m (Geddes and Baker 1967). It seems likely that a similar medium was used for the in vitro experiments, so it is assumed that $\sigma_m \approx 1.5$ S/m. For σ_c, the value of 0.1 S/m for brain tissue (Bernhardt 1979) will be used. (The results of this analysis are almost independent of σ_c since $\sigma_c/\sigma_m \ll 1$.)

Electric-field strengths in chick-brain tissue, calculated using Eqs. (20)

and (21), are given in Table 2.6 for a frequency of 16 Hz and for the two electric-field strengths where effects on calcium efflux were reported by Blackman et al. (1982). Note that the actual dosimetric fields--the electric fields in the chick-brain tissue--are very small.

TABLE 2.6.

ELF ELECTRIC FIELDS INDUCED IN BRAIN TISSUE

Calculated values are given for calcium-efflux experiments with chick-brain tissue and for human exposure to certain frequency components of the electric fields produced by the ELF Communications System.

Preparation	Electric Field in air (V/m)	Frequency (Hz)	Electric Field in Brain Tissue (nV/m)
Chick Brain In Vitro	6	16	19
Chick Brain In Vitro	40	16	124
Human Brain Under ELF Antenna	0.06	4	2.6
Human Brain Under ELF Antenna	0.20	12	26
Human Brain Under ELF Antenna	0.37	20	81
Human Brain Under ELF Antenna	0.60	28	184

In order for calcium-efflux experiments to have relevance to environmental issues associated with the ELF Communications System, the electric fields produced by the System must be able to induce electric fields in the brain of an exposed organism that have frequencies near 16 Hz and are not too different in tissue-level field strenth from those used in the calcium-efflux experiments. Here human exposure will be considered.

From Figure 2.2, the approximate average current density induced in the human head is about 1 nA/cm^2 at 120 V/m and 76 Hz. Little is known about the distribution of this current within the head. The head, consisting of the scalp, skull, cerebrospinal fluid, various membranes, and the brain is a complex structure, and it seems unlikely that induced current will be distributed uniformly. However, because current knowledge provides little guidance in making a better estimate, the induced current density in the brain will be estimated as the average value quoted above. This estimate can be scaled to the harmonic field strengths and frequencies listed in Table 2.5 by multiplying it by the ratio of the field strengths and by the ratio of the frequencies (Kaune and Gillis 1981), and it can be converted to an electric-field strength by dividing by 0.1 S/m. The results are given in Table 2.6 for the harmonic frequencies closest to the 16-Hz frequency where effects on calcium efflux have been observed.

It is remarkable that the calculated tissue-level electric fields for calcium-efflux experiments and for maximal human exposure to the ELF Communications System actually overlap. Of course, there are a number of uncertainties and approximations in the quantitative values given in Table 2.5. Nevertheless, the similarity of values in this table makes it impossible to argue on dosimetric grounds that calcium-efflux experiments have no relevance to the System.

Step Potentials Near The ELF Commumnications System

Maximum horizontal electric-field strengths produced in the ground by the antennas of the ELF Communications System were calculated by the Navy to be about 0.15 V/m and 0.07 V/m at the Wisconsin and Michigan sites, respectively. However, as discussed in Chapter 1 of this report, the approximations made in these calculations were sufficiently coarse so that, in our judgement, the resulting maximum values must be regarded as quite uncertain. Until more experimental data are available, we therefore consider it prudent to use a value of 1 V/m for the maximum horizontal electric-field strength produced near the surface of the ground by the antennas of the ELF Communications System. Using Eq. (11), the estimated maximum open-circuit voltage between the feet of a man standing near one of the antennas of the System is about 0.75 V.

Soil conductivities characteristic of the ELF Communications System are estimated to be in the range 10 to 100 mS/m (Baughn 1977), which correspond to spreading resistances, R_s, of 25 to 250 Ω. As discussed earlier in this chapter, the minimum resistance between the feet of an adult human is about 1000 Ω, but when contact resistance is included and the voltage applied to the body is less than about 20 V, a more realistic estimate of this quantity is about 5000 Ω.

Using $R_s \sim 25\text{-}250\ \Omega$, $R_b \sim 1000\text{-}5000\ \Omega$, and Eq. (13), it is estimated that the maximum current that can flow through the body, from one foot to the other, is in the approximate range 100 to 700 μA (with the lower value being the more likely). By comparison, the short-circuit current that could flow to ground from the body of a human standing directly under an antenna of the ELF Communications System (E_0 = 120 V/m and f = 76 Hz) is $I_{sc} \sim 2.4$ μA. This calculation shows that the electric field in the ground near an antenna can produce *in the human body, under certain conditions*, much more current than can the electric field between the antenna and ground.

The distribution within the body of current entering and exiting through the feet will next be estimated using published data (Kaune and Forsythe 1985) on current densities induced by an external electric field in a homogeneous human model grounded through only one foot. Let I be the short-circuit current flowing through the grounded foot. By using symmetry considerations, these data can be used to construct the current-density distribution 180° later in electrical phase inside a model that has a current -I flowing to ground through the other foot.

The next step is to add (superimpose) the two current-density distributions described in the previous paragraph to give a third distribution which has a current I flowing through the one foot and a current -I flowing through the other foot. These are the only currents that leave the body since the electric fields in the air around the original two bodies, being 180° out of phase, approximately cancel when they are superimposed. It can be concluded, therefore, that the current distribution resulting from this superimposition is approximately equal to that resulting from a step-potential exposure, because the two systems approximately satisfy the same boundary conditions.

Figure 2.5 shows the results of carrying out this procedure on the human phantom data of Kaune and Forsythe (1985). A current of 100 μA was assumed to enter the body through the left foot. The data in this figure show that there are relatively intense current densities (hence, electric fields) produced in the lower pelvis by step-potential exposure, and that current densities rapidly descrease higher in the body.

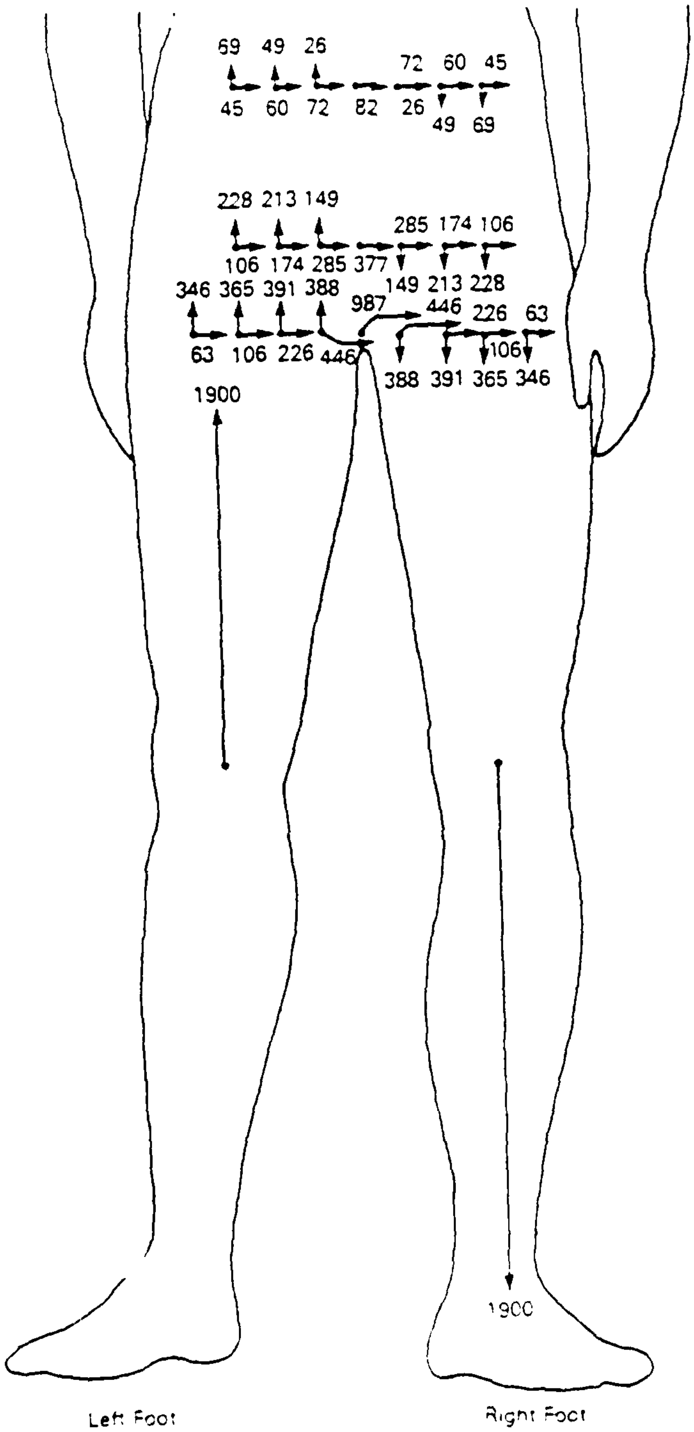

Figure 2.5 Current densities in a homogeneous man model exposed to an electric field in the ground on which he is standing. The total current entering the man through his left foot is 100 .. A. Current-density values are given in nA/cm^2.

SUMMARY

The purpose of this chapter was not to reach conclusions about environmental issues related to the ELF Communications System. Rather, the goal was to present physical methods that, when combined with biological data from laboratory and field experiments with non-human species, can serve as the basis for estimating risks incurred by humans exposed to ELF electric and magnetic fields.

Unfortunately, the ability to estimate internal electric fields resulting from the exposure to external electric and magnetic fields is still rather limited. Exposure to external fields in the air has received the most attention, and a considerable number of techniques and data are available for homogeneous models. However, virtually nothing quantitative is known about the effects on induced-current distributions of the nonhomogeneous electrical structures of living organisms. For example, it might be predicted that induced current would concentrate in the cardiovascular system because blood is a considerably better conductor at ELF frequencies than most other tissues. However, for this to happen, current would have to pass through the walls of the blood vessels and, as far as is known, no data are available on the electrical properties of these tissues. It can reasonably be expected that knowledge of ELF electric- and magnetic-field dosimetry will be greatly expanded in the next few years.

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CHAPTER 3

POSSIBLE BIOPHYSICAL MECHANISMS OF ELECTROMAGNETIC INTERACTIONS WITH BIOLOGICAL SYSTEMS

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INTRODUCTION

The body of scientific literature describing biological effects of radio frequency radiation is increasing rapidly. The variety and complexity of these reports as well as the numerous reports indicating complex relationships with wave characteristics (e.g., frequency, modulation, amplitude) suggest that more than one mechanism of interaction may be at work. Of particular interest are the reports indicating frequency and amplitude "windows." This subject has been recently reviewed by Postow and Swicord (1985) and covers observations from the extra low frequency to the millimeter frequency range. Of the many reports describing frequency and amplitude windows the objectives are varied, but together the reports do not form a cohesive set of studies that provide a structure for serious theoretical (mechanistic) analysis. There have been, however, several attempts to propose physical explanations for these window-type responses (Davydov 1979; Frohlich 1980; Grodsky 1975; Kohli et al. 1981; Lawrence and Adey 1982). These mechanisms have been reviewed by Taylor (1981). Some proposed mechanisms suggest interaction with complex membrane structures requiring cooperative phenomena or Bose-Einstein-type condensation of energy into a single mode. Others propose interaction with large molecular systems through vibrational modes or nonlinear interactions that result in local disturbances.

Neither the responses of a biological system to temperature elevation (thermal or microthermal responses) nor indirect sensory responses of animals, caused, for example, by the movement of body hair in an intense electric field, have been included here. Such responses and their health consequences are fairly obvious. What is not so obvious is the underlying mechanism of those reported biological effects that occur at low levels of exposure or depend on modulation or frequency characteristics of the field.

An early-reported extremely low frequency (ELF) effect was the change in brain calcium efflux observed using cerebral hemispheres of chicks (Bawin, Karzmarek, and Adey 1975). Increased calcium efflux was noted in brain hemispheres of chicks exposed to a 147-MHz carrier frequency that was modulated with a 16-Hz square wave. The effect was dependent on the ELF modulation frequency, which would not be expected if the mechanism were thermal. Later experiments on the same system indicated that not only did the effect exhibit an ELF frequency window, but it also exhibited a power window. Too much power seemed to over-drive the system, and no difference in the control and experimental subjects was observed.

The power window observation does not, in and of itself, rule out a thermal mechanism. Such window responses can be observed from competing thermal effects. For example, cell metabolism may be observed to increase initially with temperature elevation and then drastically decrease due to cell death. However, a thermal mechanism does not appear to be indicated for the calcium efflux experiments due to the low levels of exposure and to the periodic nature of the response.

Many other examples of modulation-dependent, frequency-dependent, or low amplitude phenomena have been reported in the literature. These include electrophysiological effects (Bawin, Gavalas-Medici, and Adey 1975; Bawin, Karzmarek, and Adey 1975; Gavalas et al. 1970; Servantie, Servantie, and Etienne 1975; Takashima, Oronal, and Schwan 1979), immunological effects (Byus et al. 1984; Lyle et al. 1983), teratological effects (Delgado et al. 1982; Ubeda et al. 1983), effects on cell and genetic function (Goodman, Bassett, and Henderson 1983; Moore 1979; Ryaby et al. 1983), and the beneficial effect reported in animals and humans of the promotion of the healing of bone fractures (Brighton, Pfeffer, and Pollack 1983; Brighton et al. 1981; Chrisbel, Cerf, and Pilla 1981; Spadaro and Becker 1979). In the context of current knowledge and understanding of biophysical and biomolecular processes, those reported observations seem impossible and thus are discounted by a large segment of the scientific community.

What needs resolution is whether fundamental physical arguments that can support these empirical observations exist or whether the observations are a collection of irreproducible (or reproducible) coincidences. This chapter presents a brief description of the physical arguments of those theoreticians who have examined this subject. Because there is no cohesive data base for analysis, these arguments are somewhat vague, and in some cases, may seem exotic due to the complex nature of the biomolecular or electrochemical system.

COOPERATIVE MODELS

Grodsky (1975) proposed a cooperative model to explain the release of bound calcium from excitable membranes that are exposed to ELF or ELF-modulated radio frequency signals. A general example of a cooperative model is as follows, consider a two-dimensional array of small magnets that is located in the x-y plane, with all of the north poles pointing in the positive z direction. In this configuration, all magnets are aligned in the same direction. The system is in the lowest energy state, and to have one magnet "flip," i.e., point its north pole in the z direction, requires energy. However, once one magnet has flipped--perhaps by some random event--then less energy is required for the neighboring magnets to flip. The process continues with each new neighbor requiring less energy to flip.

The magnet example and the Grodsky model parallel the concept of the Ising model to a certain degree. Originally formulated for ferromagnetism, the Ising model has also been applied to biological problems (Thompson 1972). Grodsky envisions two two-dimensional parallel sheets: the first is the phospholipid sheet in the plasma membrane and the second is a lattice of calcium sites. The phospholipid layer is a lattice of dipole-like sites where at each site an entity (pointing either up or down) combines with its nearest neighbor to control the binding of the calcium sites in the parallel sheet. The calcium site sheet is more sparsely populated than the phospholipid-dipole sheet. Changing the state of a single dipole-like entity would thus not immediately affect the occupation of the calcium site but could potentially lead to such an event. The energy required to change N neighboring dipole-like sites is not simply n times the energy to change one site. The changing of dipole-like states would closely follow a cooperative model, in which the second (and further) site(s) are more easily reoriented, requiring less energy.

There are four states of the Grodsky model that can be depicted by giving a direction to both the phospholipid dipole-like states and the calcium binding sites. Each site (dipole or binding) can point either up or down. Those directions, for example, can represent conditions of attraction or repulsion. The four states of the two sheets would then be (1) both pointing up, (2) both pointing down, (3) pointing toward each other, and (4) pointing away from each other. Shifts between these four bands, or energy states, thus provide resonant conditions. Grodsky suggests that the lowest resonant frequency state will possess the highest average amplitude, be the most likely to be excited, and will fall into the 1- to 30-Hz frequency range.

Thus the Grodsky model suggests four bands of frequencies that may or may not overlap. The lowest frequency of the lowest band is the most susceptible to resonance stimulation. Thus, small perturbations from an ELF signal may resonate with the structure, resulting in a number of altered states and, consequently, the release of bound calcium. Similar cooperative models could be applied to other membrane properties or to interactions with large macromolecular systems or subsystems.

FROHLICH MODEL

Frohlich (1968, 1978, 1980) described how order or organization exists in many different forms in a system. Order is not confined to spatial order, and order of motion can exist in thermal equilibrium. These "other" forms of order provide a basis for physical theories of frequency-selective responses (windows) that occur in a random 37°C thermal environment. One such system of order stems from membrane structure. A membrane, which is about 10^{-8} m thick, maintains a potential on the order of 10 to 100 mV. It is further noted that any oscillation of the membrane perpendicular to its surfaces will generate an oscillating electric dipole. The frequency of these oscillations will be the natural resonances of the system, which will be determined by the speed of sound (acoustic velocity) in the membrane. Frohlich assumed the sound velocity to be about 10^{3} m/s. The width of the membrane, 10^{-8} m, determines the wavelength and will be equal to an odd multiple of half-wavelengths (resonance for a violin string). Thus, the lowest natural vibrational mode will have a frequency on the order of 50 GHz. Frohlich's calculations agree with these predictions. He suggests that similar types of resonant structures will exist in large molecular systems such as protein and DNA (Frohlich 1980). It is further assumed that damping is not unduly high in these systems. Numerous oscillating polar systems of this type will interact with one another, generating a series of normal modes of the system. Frohlich suggests that the energy for the maintenance of these oscillations is supplied by metabolic processes. The model implies that very little energy is required to excite the various modes. Thus, coherent electric vibrations can exist in the biological system, provided that the energy supplied to systems of normal modes exceeds some critical value, so that a Bose condensation occurs, coherently exciting a single mode, presumably the lowest. (Bose condensation, or Bose-Einstein condensation, refers to a system of indistinguishable particles capable of oscillating in many different modes; all particles will tend to occupy the lowest energy level, i.e., the mode with the lowest frequency.) Frohlich offered the highly frequency-dependent biological effects of millimeter waves such as the effect reported by Grundler, Keilmann, and Strube (1982) the rate of yeast growth, as supportive of not only the presence of these modes but as evidence of the excitation of these modes by external sources.

MOLECULAR INTERACTIONS AND VIBRATIONAL MODES

The reported genetic effects of ELF (Goodman, Bassett, and Henderson 1983) or millimeter wave (Grundler, Keilmann, and Strube 1982) exposure that exhibit window or resonant frequency responses could be the result of direct interaction of the electromagnetic field with the membrane, inhibiting or enhancing membrane control function, or the direct interaction of the applied field with the chromosome or DNA molecule. Calculations have been made that indicate that the DNA molecule may show strong resonant aborption at microwave frequencies (Kohli et al. 1981). Those calculations considered longitudinal and transverse vibrational modes (acoustic or optical) in dehydrated double-strand DNA of varying chain lengths (number of base pairs). The calculated resonant modes were chain-length dependent, with the longitudinal acoustic vibrational modes being the most likely in the lower microwave frequency range. Van Zandt, Kohli, and Prohofsky (1982) recently extended this work to consider critically damped absorption of DNA in aqueous solutions.

The theoretical work of Lu, Prohofsky, and Van Zandt (1977) on DNA absorption is not confined to the microwave region but extends well into the infrared region where the theoretical prediction has been experimentally demonstrated (Small, Pebicolas, and Warner (1971). Swicord et al. (1983) have reported considerably enhanced absorption in the x-band region from highly concentrated aqueous solutions containing DNA with a wide distribution of chain lengths. Edwards et al. (1984) reported resonance absorption in solutions containing DNA strands of a uniform length both for circular and linearized plasmids. The observed frequency of the resonant mode agrees with the predictive theory (Edwards et al. 1984). Fundamental and harmonic resonant frequencies that are related to odd multiples of a half wavelength of the excited sound wave for linearized strands and multiples of the wavelength for circular DNA are observed. Resonances are not observed below a few hundred megahertz. At the lower frequencies, the resonant length of the molecule is too long, and the mode relaxes before energy can travel from one end to the other. Thus, a standing wave is not esta ..ed.

The authors have not investigated the response at frequencies below a few megahertz where the damping due to the aqueous solution might be considerably reduced. The Prohofsky model suggests a means of strongly coupling energy into a large molecule. Even though these modes may have a short lifetime, the continuous, coherent excitation of the mode would, in effect, maintain the molecule in an excited state. Whether this long term pumping and continual excitation would result in disruption of function has yet to be demonstrated. Long term (100 ps or longer) excitation of a molecule implies isolation from the thermal environment. Prohofsky (E. Prohofsky pers. comm. 1983) has suggested that his model of absorption can explain the observations of Grundler et al. (1983). The length of a nucleosome in the yeast chromosome is such that resonant absorption will occur at about 40 GHz. Small variations in frequency could result in rapid shifts into and out of resonance for the same or different nucleosomes.

SOLITONS

A pulse-type solution for certain nonlinear partial differential equations is called a "soliton" and has been used recently in solid-state physics, hydrodynamics, and elementary particle theory. Solitons are localized disturbances that are able to propagate through the nonlinear medium unattenuated. They are not wave trains; thus, dispersion does not occur. The soliton (solitary wave) was first described by Scott-Russell (1844) more than a century ago when he observed the unusual behavior of a wave generated by, separating from, and proceeding in front of a barge in a shallow canal.

Several applications of soliton dynamics have been made to biological systems. The most notable example is the application to the alpha-helical protein first considered by Davydov (1982) and then reviewed and expanded by Scott (1982).

The Davydov model relies on the nonlinearity of hydrogen bonding that potentially couples the basic structure of the alpha-helical protein with the three "spines." This excitation of amide-I vibrations, which under linear analysis would rapidly disperse, are coupled to longitudinal sound waves and are propagated as a soliton. However, the amide-I and nonlinear sound wave must be strongly coupled, and the amide-I vibrations must exceed a threshold value in order to generate the local disturbance or soliton. Davydov points out that the probability of a soliton causing a photon emission, or vice versa, is very small. It seems reasonable to argue that excitation of the molecule by a photon would result in nonlocalized (e.g., vibrational) modes that would not directly cause a localized disturbance. However, one could postulate that coherent excitation of vibrational modes, as modeled by Prohofsky and Van Zandt could lead to large amplitude excitations even in a highly damped system. Such large excitations could then possibly result in localized excitations, disturbances, or solitons.

Lawrence and Adey (1982) have suggested that solitons provide an explanation of the way in which signals are conducted through membranes. A chemical event, the arrival of a protein molecule, takes place at a membrane receptor or channel site. A soliton is created in proteins associated with membrane channels and propagates along the protein and through the membrane. The soliton then supplies energy for the second chemical event on the inside of the cell. It is further suggested that these processes may be affected by the presence of external fields, thus causing a bioelectromagnetic response.

DIPOLES AND DIELECTROPHORESIS

The classical interaction of electric fields with polar molecules (molecules whose centers of positive and negative charge are separated) has biological materials has been discussed at length by Grant, S South (1978) and Pethig (1979). Molecules may be permanently polarized (permanent dipole moment), water being the most classical example, or the polarization may be induced (induced dipole moment) by the external field. The induced polarization can lead to classical or quantum mechanical absorption processes and is involved, for example, in the Prohofsky model of field interaction with the DNA molecule discussed above.

The center of mass of permanent or induced polar molecules will not move in a uniform electric field due to the equal but opposite forces applied to the centers of positive and negative charge. However, if the field is nonuniform, then the centers of positive and negative charge will experience unequal forces, and thus, the molecule or particle will tend to move in the direction of increasing field strength. If the nonuniform field is static (not time varying), all polarized as well as charged particles will move in the field. In a time-varying field, only the polarized particles will move any significant distance. Charged particles will follow the direction of the field and thus oscillate back and forth in position. Polarized particles will rotate with the direction of the time-varying field and thus will always experience a net force in the direction of increasing field strength. This movement of polarized particles has been termed dielectrophoresis (Pohl 1978).

Cells contain charged molecules within or on the membrane. These molecules are capable of rapid movement. An externally applied electric field will cause a separation of charges on the membrane and thus induce a dipole moment or polarize the cell. Pohl et al. (1981) have used the phenomena of dielectrophoresis to study the electrical response of cells at low frequencies. This is accomplished by placing cells between two electrodes suspended in a high resistance medium (e.g., 10^5 ohm/cm). About 5 V is applied to the narrowly spaced (about 250 mm) electrodes. The dielectrophoretic yield (the number of particles collected at either electrode per unit time) is then obtained as a function of frequency. The spectral response varies for different types of cells and varies with cell viability.

Pohl et al. (1981) futher claimed that cells generate their own internal oscillating low frequency electric fields. They demonstrated this phenomenom by what they term microdielectrophoresis. Low and high dielectric constant powders are suspended in solution with a cell, and the cell is observed microscopically. An oscillating field generated by the cell will cause the high dielectric particles to move toward the cell. By counting the ratio of high to low dielectric particles around the cell, one can obtain a relative measure of the strength of the cell-generated electric field. A ratio of one indicates that no oscillating field is present. Again Pohl et al. (1981) reported differences due to cell viability and they also reported that the dielectrophoretic effect "peaks during the meiotic phase indicating that the electric field is associated with cell division." Pohl et al. further suggested that these experimental observations are manifestations of the electrical oscillations predicted by Frohlich (1968, 1980). It should be noted that Frohlich's original predictions involved the millimeter wave frequency range, and Pohl's observations most likely involved frequencies on the order of 100-kHz or below.

MAGNETIC FIELD INTERACTIONS

Although most theories of interaction deal with induced or permanent dipole responses to electric fields, recent work suggests that magnetic fields, through nuclear spin coupling, affect the dielectric properties (including dielectric loss) of cells. Jafary-Asl et al. (1982) reported resonant absorption peaks in the dielectric spectra of yeast cultures in solution at frequencies corresponding to the proton nuclear magnetic resonance (NMR) frequencies. A very sharp resonance (about 1-Hz bandwidth) was observed in the dielectric spectra a little above 2-kHz when a magnetic field of 50 μT was applied. The resonant frequency increased proportionally with the applied field from 100 to 200 μT.

Jafary-Asl et al. (1982) first observed a resonant relationship of cell properties and magnetic fields in studies of dielectrophoresis (see discussion of dielectrophoresis above). Jafary-Asl et al. observed a pronounced drop in the dielectrophoretic yield of live yeast cells at about 2-kHz. This corresponds to the proton NMR resonance frequency in the earth's magnetic field. This result is both interesting and perplexing. It is difficult to explain how effects on the state of the nucleus of the hydrogen atom are magnified to affect the macroscopic behavior of cells. The possible existence of such a relationship does, however, provide the basis for a theoretical explanation of a frequency window in biological responses.

Recent information (Blackman et al. 1984; Abraham R. Liboff pers. comm. 1984) has suggested that DC magnetic fields may interact and determine an ELF resonant frequency in another manner. Blackman, Karzmarek, and Adey (1984) reported at the Bioelectromagnetic Society meeting in July 1984 that the 16-Hz resonant frequency observed in previously reported effects of calcium efflux from excised chick brain (Bawin, Karzmarek, and Adey 1975; Blackman et al. 1979, 1980) was determined by the earth's magnetic field. The original work (Bawin et al. 1975) showed that exposed brain sections exhibited increased concentrations of preloaded calcium in the medium (interpreted as increased calcium efflux) that were dependent on the modulation frequency of the 147-MHz radiation. Modulation frequencies in the 9- to 20-Hz region were effective with maximal efflux being measured at 16 Hz; frequencies both higher and lower were ineffective. Subsequent (Blackman et al. 1979, 1980, 1982) studies demonstrated that the effect was independent of the carrier wave (147-MHz) and could indeed be observed at the ELF frequency of 16-Hz.

Blackman et al. (1984) noted that a DC magnetic field externally applied parallel or antiparallel to the earth's magnetic field alters the frequency at which the peak resonance calcium efflux response is observed. Doubling the DC magnetic field increases the frequency by a factor of 2 to 30 Hz. When the net magnetic field is reduced to zero, no difference between exposed and controls is observed. It has been suggested (Blackman et al. 1984; Abraham R. Liboff pers. comm. 1984) that this phenomenom is the result of cyclotron-type resonance of specific molecules. The relationship between the DC magnetic field (B) and the frequency (f) of the oscillating field for cyclotron-type resonance is given by $f=(1/2\pi)(e/m)B$, where (e/m) is the charge to mass ratio of the particle being affected or accelerated. Liboff (Abraham R. Liboff pers. comm. 1984) noted that some of the Blackman et al. (1984) results suggested cyclotron resonance e/m ratios that were very close in value to the e/m ratios for potassium and sodium. (It should also be noted that some of the Blackman et al. results did not apparently correspond to the cyclotron resonance of any common ions.)

Liboff recently collaborated with Thomas (J. Thomas pers. comm. 1984) on behavioral responses to 60-Hz fields. No alteration in behavioral response had been noted from exposure to 60-Hz magnetic fields (and the normal earth's magnetic field). Liboff postulated from the Blackman et al. (1984) results that changes might be observed if the DC (earth's) magnetic field were increased by a factor of four. The equipment available did not allow them to generate a field of that value. Further calculations by Liboff suggested that lithium, an element important in neuronal processes, should experience cyclotron resonance at 60-Hz in a magnetic field of about 0.27 G. Because that is less than the earth's normal magnetic field, a pair of coils were oriented to oppose the earth's normal field. This exposure condition resulted in alteration of behavior (loss of time estimation) of the exposed animals.

ELECTROCHEMICAL EFFECTS

In recent years, pulsed electromagnetic fields have been used in clinical practice to accelerate or facilitate the healing of nonunions as well as the growth of soft tissue. This subject has been reviewed by Spadaro (1982). Clinical empirical observations have not led to an understanding of the basic mechanism whereby pulsed electromagnetic fields aid in such healing processes. Several recent studies, however, have examined the effect of various pulse characteristics in an attempt to maximize the biological response and to gain an understanding of the mechanism. These studies indicate that a window effect does occur (i.e., there are certain pulse characteristics that seem to promote healing of separated bones and others that do not) (Chrisbel, Cerf, and Pilla 1978).

A number of in vivo and in vitro studies have been conducted in attempts to better understand the basic mechanisms involved. One example is the work of Goodman, Bassett, and Henderson (1983) in which two pulse forms that are in clinical use, a single pulse repeated at 72-Hz and a 15-Hz repetitive pulse train, were used to study effects on RNA transcription patterns in salivary gland chromosomes of a dipterian. The response varies for the two exposure situations with the 72-Hz single pulse causing the largest change in RNA transcription. Goodman and Henderson (n.d.) have recently performed experiments on RNA transcription using continuous wave exposures at 72, 222, and 4400 Hz. Again, effects on transcription were observed, which suggest that there are fundamental frequency components of the pulse system previously used that are important.

The term "electrochemical effects" has been applied to these low frequency and pulse modulated effects that appear to be electric field modulation of cell membrane function. This subject has been discussed by Beltrame et al. (1980) and Pilla, Sechaud, and McLeod (1983), with the latter giving three examples of electromagnetic field interactions with electrochemical processes. The first example involves the interaction of the applied field with the majority ions in the bulk solution far from large macromolecules or membranes. It is argued that for large concentrations of ions, a small electric field can generate currents on the order of diffusion currents, and thus, these terms are not to be neglected and may indeed affect chemical processes. Beltrame et al. (1980) give examples of how small perturbing electric fields (or induced electric fields) can cause perturbations in ion movement near the membrane or in ion transport across the membrane. The examples given (Beltrame et al. 1980; Pilla, Sechaud, and McLeod 1983) are most general but still suggest that nonrandom externally applied fields could possibly affect electrochemical or membrane function.

DISCUSSION AND CONCLUSIONS

In considering theoretical ELF mechanisms, there are perhaps several ways in which electric or magnetic fields can interact with biological systems. The possiblity of such interaction is readily accepted because biological systems are constructed from charged molecular systems. The difficulty is in understanding how small perturbations of local molecular electrostatic fields can significantly alter biological function. Unfortunately, no proposed theories to date clearly explain how electric or magnetic fields can cause the experimentally observed effects in biological systems.

Most of the models discussed directly address the issue of ELF effects. The example of cooperativity, the Grodsky model, was developed in response to the calcium efflux results. However, the model has always been too vague and thus impossible to test experimentally. In light of recent findings suggesting that a DC magnetic field determines the resonant frequency, the Grodsky model seems even less attractive. The general idea of cooperativity should not be discounted, however, and may play a central role in combination with some other interactive model.

The concept of cyclotron resonance proved to be useful for Liboff in predicting ELF experimental results. This demonstrates the important role played by the local DC magnetic field. This result, however, may raise more questions than it answers. For example, the lithium ion would not be expected to move unencumbered through the intercellular media. Water molecules would most likely be bound to the lithium ion, resulting in a larger effective mass, which would alter the charge-to-mass ratio used in Liboff's calculations. Is the Liboff predication correct due to coincidence or is the relation between ions and surrounding molecules different from what has been expected? Also, would one expect a significant amount of energy to be pumped into the (lithium) ion, increasing the magnitude of its random velocity, or as Liboff has suggested, cause helical motion which increases transport through the membrane? The latter suggestion seems too speculative, because any induced radial motion would be large compared to membrane structure. Perhaps the presence of these external fields brings order to the randomly moving system of ions and molecules. This is a result of imposed preferred directions of motion and result in an increased mean free path of the ion or molecule. This could increase the probability of the ion colliding with a receptor site on the membrane and thus increase the metabolic processes resulting from such collisions. Additionally, one can now conceive of how the system may be overdriven creating the power window. Too large a field could disturb the resonant condition for order. None of the theories discussed above adequatly address the power window observation. Most of them allow for speculation of such windows due to their general nature.

The concept of externally imposed order (the external field encouraging the system to order randomly distributed energy) may have application to interactions with large molecular structures, such as membranes, or macromolecules, such as DNA. This concept is not too far removed from Frohlich's suggestions concerning Bose-Einstein condensation. In fact, this point is probably the only one applicable to ELF of the Frohlich theory. Despite the suggestion of Pohl (1981) that his low frequency observations are a demonstration of Frohlich's predictions, Frohlich's calculations deal only with millimeter wave phenomena.

The theoretical prediction of field interactions with the DNA molecule by Van Zandt, Kohli, and Prohofsky (1982) is perhaps the only theoretical model that has been confirmed by experimental measurements. The experimental work was performed at frequencies above 400 MHz, and thus, its applicability to ELF effects is in question. A resonant length at ELF frequencies would be comparable to the entire length of the DNA molecule in a chromosome, which would be on the order of 1 cm. Conceptually, it is possible to excite such a molecule, but it seems rather speculative. Again, no relation between the theoretical or experimental results on absorption and reported genetic effects has been established.

Two concepts--electrochemical processes and solitons--definitely have applicability for ELF effects, but are too general at this point and have no experimental confirming evidence. These processes, however, may complement or be involved in a number of proposed mechanisms. Therefore, the mechanisms discussed above should not be considered singly. Electrochemical processes may be the driving force for cooperative processes, and classical dielectric relaxation may, for large amplitude pulsed fields, provide the energy for creating solitons.

At most, the mechanisms suggest that field interactions resulting in a biological response are physically conceivable. Further, it is reasonable to expect these responses to be frequency- and amplitude-dependent, and in some cases, they may depend on the presence of a combination of electric and magnetic fields. Still, the key word is may. The connection between mechanisms and observed biological effects has not been made. Thus, no useful predictive theory currently exists in the assessment of hazards of electric or magnetic fields.

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CHAPTER 4

BIOLOGICAL EFFECTS OF ELF MAGNETIC FIELDS

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INTRODUCTION

Time-varying magnetic fields in the ELF range below 300 Hz originate from both natural and man-made sources (Grandolfo and Vecchia 1985). The largest time-varying atmospheric magnetic fields result from intense solar activity and thunderstorms, and can reach intensities of 0.5 μT during a major magnetic storm. Diurnally varying fields with maximum intensities of 0.03 μT are present in the atmosphere as the result of solar and lunar influences on ionospheric currents. Also present in the atmosphere are weak magnetic fields associated with the Schumann resonance phenomenon, in which fields produced by lightning discharges propagate at ELF frequencies within the resonant cavity formed by the earth's surface and the lower boundary of the ionosphere.

Man-made sources of ELF magnetic fields are numerous, and they exhibit a wide range of intensities from less than 0.1 μT to levels approaching 0.1 T in certain industrial settings. The sources of these fields include (1) AC power transmission lines and generators; (2) AC electrical and electronic devices used in industry, research facilities, and households; (3) video display terminals; (4) ELF communication systems; (5) induction heating processes such as welding and electrosteel production; and (6) medical applications of AC and pulsed fields for therapy of bone fractures and electromagnetic blood flow measurements. The magnetic field intensities to which humans are exposed from the first four of these sources are generally less than 50 μT, with the exception of fields near the surface of certain types of rotating equipment (e.g., drills and circular saws) and household items (e.g., hair driers and electric shavers). These rotatory devices produce local fields in their immediate vicinity as high as 2 mT, but the magnetic field strength decreases rapidly as a function of distance from the surface (Gauger 1984). Human exposure to magnetic fields from high-voltage transmission lines and ELF communication systems is estimated to occur at levels less than 15 μT in the immediate vicinity of these installations (Scott-Walton et al. 1979; Valentino 1984). The ELF magnetic fields from video display terminals at typical operator locations (Stuchly, Lecuyer, and Mann 1983) and the ambient field levels at most locations within a household environment (Caola, Deno, and Dymek 1983; Male, Norris, and Watts 1984) are generally less than 0.3 μT. By far the highest level of human exposure to ELF magnetic fields occurs in the industrial and medical technologies listed above as items 5 and 6. In a survey of electrosteel and welding industries in Sweden, the local magnetic fields near 50-Hz ladle furnaces were found to reach intensities of 8 mT, and intensities up to 70 mT were measured near induction heating devices associated with steel production" (Lovsund, Oberg, and Nilsson 1982).

In medicine, pulsed magnetic fields with ELF repetition rates and peak intensities of approximately 2 mT are being used for the treatment of bone fractures and arthroses (Bassett, Mitchell, and Gaston 1982; Bassett, Pawluk, and Pilla 1974; Watson and Downes 1978). Solenoidal transducers that produce ELF magnetic fields with typical intensities of 5 to 10 mT are commonly used as a means of monitoring arterial blood flow during prolonged surgical procedures (Kolin 1952; Mills 1977). The rapidly switched gradient fields used in nuclear magnetic resonance (NMR) imaging devices also produce human exposure to time-varying magnetic fields (Budinger and Lauterbur 1984; Margulis et al. 1983). This medical technology is in an early stage of development, and the magnetic field characteristics of future hospital-based NMR devices remains an active area of research.

A summary and critical evaluation of the literature describing biological effects of ELF magnetic fields will be given in this chapter. Various aspects of this subject have been summarized in recent review articles and monographs (Adey 1983; Budinger 1981; Sheppard and Eisenbud 1977; Tenforde 1979; Tenforde 1985a). The principal topics that will be discussed in this chapter are magnetic field interaction mechanisms, effects on vision (magnetophosphenes), the nervous system and animal behavior, and a summary of biological effects reported on diverse cellular, tissue and animal systems. A brief discussion will also be given of recent reports on cancer risk in humans exposed to ELF magnetic fields.

ELF MAGNETIC FIELD INTERACTION MECHANISMS

The fundamental physical interaction mechanisms of ELF electric and magnetic fields with living matter have been reviewed in Chapter 2. For the specific case of ELF magnetic fields, the primary physical interaction mechanism is the induction of electric fields and currents in tissue in accord with Faraday's law. In its general form, Faraday's law can be written as

$$\oint \vec{E}\cdot d\vec{l} + - d/dt \iint \vec{B}\cdot d\vec{S}, \qquad (1)$$

where the line integral is around a closed curve and the surface integral is taken over the surface bounded by the closed curve. In eqn. (1), $\vec{E}$ is the electric field intensity, $d\vec{l}$ is a differential length element directed along the curve over which the line integral is taken, $\vec{B}$ is the magnetic flux density, and $d\vec{S}$ is a differential surface area element directed normal to the surface. For the specific case where $\vec{B}$ is spatially uniform, eqn. (1) can be written as

$$E_{av} = (1/L)\ \vec{S} \cdot \frac{d\vec{B}}{dt} \qquad (2)$$

where E_{av} is the magnitude of the average electric field tangent to the closed curve, L is the total length of the curve, and $\vec{S}$ is the surface area vector. If the closed curve is a circular loop of radius R, and the orientation of the loop is perpendicular to $\vec{B}$, then eqn. (2) simplifies to

$$E_{av} = (R/2)\ S \cdot \frac{dB}{dt} \qquad (3)$$

For a sinusoidally varying field with a frequency f, eqn. (3) becomes

$$E_{av} = \pi f R B. \qquad (4)$$

From Ohm's law, the average current density J_{av}, induced in a material with an average conductivity k_{av}, is given by

$$J_{av} = k_{av} E_{av}. \qquad (5)$$

Equations (1) - (5) can be used to calculate the magnitude of a time-varying ELF magnetic field that would be expected to perturb the function of critical biological tissues such as the heart and the central nervous system. Using data from several sources, Bernhardt (1979) has estimated that the endogenous current densities associated with electrical activity of the brain and heart have lower limits of 1 and 10 mA/m^2, respectively, and perturbations of normal biological functions might be expected to occur in the presence of ELF magnetic fields that induce tissue currents above these levels. Consider for illustration a 60-Hz sinusoidal magnetic field that is normally incident on a circular loop of tissue with a radius of 0.06 m, comparable to the human heart, and an average conductivity of 0.2 S/m (Schwan and Kay 1956). From eqn. (5) the amplitude of the magnetic flux density that would induce a current density of 10 mA/m^2 is 4.4 mT. A similar calculation for brain tissue with an average conductivity (Bernhardt 1979) of 0.1 S/m and a loop radius of 0.1 m, comparable to the human cranium, leads to the prediction that a current density of 1 mA/m^2 is induced by a 60-Hz magnetic field with an amplitude B_0 of 0.53 mT. Because ELF magnetic fields with intensities higher than 5 mT are present in the vicinity of certain types of instruments and industrial processes, the induction of tissue fields at levels that could potentially perturb biological functions is therefore possible.

ELF magnetic fields can also interact with biological tissues through orientational effects on paramagnetic substances with permanent magnetic moments (e.g., the magnetite inclusions in magnetotactic bacteria) and with macromolecular assemblies in which the summed diamagnetic anisotropy is large (e.g., the photopigment molecules of retinal photoreceptors). In considering the possible role of magneto-orientation phenomena in the biological interactions of time-varying magnetic fields, it is important to recognize that the frictional resistance to motion in biological tissues is high, and thus serves to damp out even low-frequency oscillations associated with time-varying magnetic orientational forces. This is illustrated by the fact that the orientation of diamagnetically anisotropic retinal photoreceptor outer segments in a 1-T static field occurs with a characteristic time of 4 s in water (Hong, Mauzerall, and Mauro 1971). A time-varying field with a frequency exceeding approximately 1 Hz would therefore be unable to induce a "flickering" rientational phenomenon in this system because the frictional drag force would not allow the motion of the retinal rods to keep pace with the oscillating field. A similar conclusion can be drawn for the interaction of paramagnetic entities such as magnetotactic bacteria with an ELF time-varying magnetic field. With the possible exception of quasi-static fields with frequencies in the range 0 to 1 Hz, it is therefore probable that magneto-orientation phenomena play little if any role in the interaction of ELF magnetic fields with living systems. Similar conclusions can be drawn for the translational forces experienced by paramagnetic substances in an ELF magnetic field spatial gradient, and for the electromechanical force exerted by the electric fields induced in tissue by externally-applied ELF magnetic fields.

Another possible interaction mechanism of ELF magnetic fields that has recently been proposed is the distortion of counterion distributions at cell surfaces (Polk 1984). The effect of introducing an inhomogeneity into the counterion atmosphere at the surface of a living cell, or along the length of a large organic macromolecule such as DNA, has not as yet been investigated experimentally. However, this interaction mechanism possesses the interesting property that the magnitude of the effect becomes frequency-independent when the frequency of the applied magnetic field is much greater than the dielectric counterion relaxation frequency. The existence of biological effects that are independent of the field frequency has recently been suggested on the basis of an increased rate of DNA synthesis that was observed in human fibroblasts exposed to sinusoidal magnetic fields with frequencies ranging from 15 Hz to 4 kHz, and intensities of 2.3 to 560 μT (Liboff et al. 1984). The lack of dependence of this effect on the time rate of change of the field, and hence on the induced current density calculated from Faraday's law, was tested for values of dB/dt that ranged from approximately 1.8×10^{-4} T/s to 1.8 T/s. The extent to which this phenomenon may relate to other bioeffects of ELF magnetic fields remains to be studied.

An important factor to be considered in the response of biological systems to ELF magnetic fields is the waveform of the applied field. Numerous types of magnetic field waveforms have been used in biological studies, including both sinusoidal and square-wave fields, and pulsed fields with burst repetition rates that lie in the ELF frequency range. For both square-wave and pulsed fields, two parameters of key importance are the rise and decay times of the signal, which determine the maximum time rates of change of the field and hence the maximum instantaneous current densities that are induced in living tissue. For example, a sharply rising square-wave magnetic field pulse will induce a peak current density in tissue that exceeds the value achieved with a sinusoidal field having the same r.m.s. intensity and fundamental frequency. Another factor that must be considered for waveforms with a rapid rise time is the skin depth. Magnetic fields with a rise time less than 10 ns will be attenuated at an air/tissue interface due to the finite skin depth and reflection losses. Pulses with such short rise times, however, are seldom used in biological studies.

A factor of major importance in determining the response of living systems to ELF magnetic fields with any type of wave form is the fundamental field frequency. The phenomenon of magnetophosphenes, which is discussed in the next section of this chapter, is limited to time-varying magnetic fields with frequencies less than approximately 70 Hz. The mechanism underlying the loss of sensitivity at higher frequencies has not been elucidated, but it is conceivable that the visual system cannot process and respond to induced electrical currents with frequencies above approximately 70 Hz. This hypothesis is supported by the fact that flicker fusion occurs in response to repetitive photic stimuli with frequencies above approximately 30 to 40 Hz. Although the frequency dependence of the biological response to time-varying magnetic fields has not been well characterized for systems other than the visual apparatus, it is conceivable that a similar dependence may exist in tissues such as the central nervous system and heart in which the endogenous electrical activity has dominant frequencies that are less than 50 Hz.

Another aspect of ELF magnetic field interactions with living systems that merits discussion is the possible existence of "windows" of sensitivity in the frequency and/or intensity domains. The existence of window phenomena in biological tissues has been demonstrated for several types of electromagnetic fields, including millimeter waves, ELF electric fields, and radiofrequency radiation with amplitude modulation in the ELF range (Postow and Swicord

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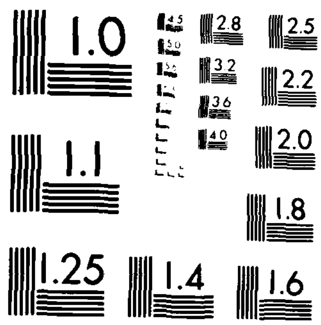

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1985). A comprehensive discussion of these ELF field effects is given in the chapter 3. During the past two years, several reports have appeared in the literature suggesting that window phenomena may occur with ELF magnetic fields. The existence of windows of sensitivity in both the frequency and the intensity domain have been claimed in reports of teratogenic effects on chicken embryos exposed to weak, pulsed magnetic fields with repetition rates in the low-frequency range (Delgado et al. 1982; Ubeda et al. 1983). A window of frequency sensitivity extending from 3 to 50 Hz has been reported in studies on the mitogen-induced blastogenic response of human lymphocytes exposed to ELF square-wave magnetic fields (Conti et al. 1983). It has also been reported recently that a window of frequency sensitivity may exist in calcium ion efflux from chick brain tissue exposed to ELF magnetic fields (Blackman et al. 1984). The interpretation of these windowed responses to ELF fields is obviously complex, and numerous suggestions have been made of nonlinear physical mechanisms such as cooperative phenomena involving membrane dipoles, limit-cycle behavior of chemical oscillators, and solitons as possible nonthermal processes by which the effects of extremely weak electromagnetic fields could be amplified in biological systems (Postow and Swicord 1985).

In the specific case of window phenomena associated with ELF magnetic fields, a further interpretive complication is posed by the apparent dependence of these effects on the strength and direction of the geomagnetic field within the exposed biological specimen (Blackman et al. 1984; Rozzell 1984). The suggestion has been made that low-field magnetic resonance effects could occur in living matter, as indicated by dielectric measurements on yeast cells and by measurements of bacterial growth and enzyme activity under magnetic resonance conditions using fields with intensities comparable to the geomagnetic field (Jafary-Asl et al. 1982). In such weak fields, several biologically relevant electrolytes such as potassium and chloride ions may exhibit resonant frequencies in the ELF range. However, further experimental tests of this possible interaction mechanism, as well as the various nonlinear interaction mechanisms mentioned above, must be undertaken before their relevance to ELF magnetic field bioeffects can be assessed.

One final point that merits attention is the fact that totally linear mechanisms such as induced Faraday currents may give rise to apparent window phenomena. For example, at very low field frequencies (approaching DC) the induced current densities in tissue may be too low to elicit an effect, while at high frequencies the biological system may be unresponsive to the applied stimulus even though the induced currents are large. In this context, it is possible that the frequency range of 7 to 70 Hz over which magnetophosphenes have been observed with suprathreshold field intensities might be considered as a window of visual sensitivity without invoking interaction mechanisms other than induced Faraday currents.

MAGNETOPHOSPHENES AND RELATED VISUAL STUDIES

One of the most extensively studied magnetic effects in living systems is the induction of magnetophosphenes, in which a flickering illumination within the visual field occurs in response to stimulation by pulsed or oscillating magnetic fields with frequencies less than 100 Hz (Barlow, Kohn, and Walsh 1947; Budinger, Cullander, and Bordow 1984; d'Arsonval 1896; Dunlap 1911; Lovsund, Oberg, and Nilsson 1979a, 1979b, 1980; Lovsunnd, Nilsson, and Oberg 1981; Lovsund et al. 1980; Magnusson and Stevens 1911; Seidel, Knoll, and Eichmeier 1968; Thompson 1909-1910). In subjects with normal vision, the maximum visual sensitivity to sinusoidal magnetic fields has been found at a frequency of 20 Hz (Lovsund et al. 1980). At this frequency the minimum field intensity required to elicit phosphenes is approximately 10 mT (Lovsund et al. 1980), which lies well above the range of ELF magnetic field levels generally encountered by man as discussed earlier in this chapter. The magnetophosphene visual sensation is completely reversible upon removal of the external magnetic field, and there have been no reports of harmful effects on the visual system.

Table 1 presents a summary of principal research findings on the properties of magnetophosphenes that have been reported since the discovery of this phenomenon by d'Arsonval in 1896. The locus of the magnetic field interaction that leads to phosphenes has been shown to be the retina on the basis of several lines of evidence: (1) magnetophosphenes are produced by time-varying fields applied in the region of the eye, and not by fields directed toward the visual cortex in the occipital region of the brain (Barlow, Kohn, and Walsh 1947); (2) pressure on the eyeball abolishes sensitivity to magnetically-induced phosphenes (Barlow, Kohn, and Walsh 1947);

Table 1. Magnetophosphene Studies

Reference	Principal Findings
d'Arsonval 1896	Initial report of magnetophosphenes produced by a 42-Hz field
Thompson 1909-1910	Described magnetophosphenes produced by a 50-Hz field as a colorless, flickering illumination that is most intense in the peripheral region of the eye
Dunlap 1911	Demonstrated that magnetophosphenes produced by a 25-Hz field are more intense than those produced by a 60-Hz field of comparable intensity
Magnusson and Stevens 1911	Demonstrated the production of magnetophosphenes by pulsed DC fields as well as by time-varying fields with frequencies from 7 to 66 Hz; observed strongest magnetophosphenes with fields oscillating at 20 to 30 Hz
Barlow, Kohn, and Walsh 1947	Demonstrated threshold field intensity of 20 mT (r.m.s.) at 30 Hz, and showed that the threshold for magnetophosphenes is relatively insensitive to background illumination as compared to electrophosphenes; characterized "fatigue" phenomenon with a magnetic 60-Hz field applied for 1 min, which was followed by a refractory period of 40 s during which a second phosphene could not be elicited; demonstrated that magnetic fields must be applied in the region of the eye to produce phosphenes, and that sensitivity is abolished by pressure applied to the eyeball
Seidel, Knoll, and Eichmeier 1968	Observed comparable light patterns associated with visual stimuation by ELF electric and magnetic fields, but found different probabilities of occurrence of certain types of phosphene patterns
Lovsund et al. 1979-1981	Analyzed threshold field intensity for production of magnetophosphenes over frequency range of 10 to 45 Hz; demonstrated maximum sensitivity to a 20-Hz field; studied effects of dark adaptation, background illumination, and visual defects on sensitivity to magnetophosphenes; compared threshold stimuli required to produce electrophosphenes and magnetophosphenes; characterized changes in electrophysiological responses of isolated frog retinas exposed to ELF magnetic fields
Budinger, Cullander, and Bordow 1984	Found minimum time rate of change of pulsed magnetic field to be 1.3 to 1.9 T/s to produce magnetophosphenes

(3) the threshold magnetic field intensity required to elicit phosphenes in human subjects with defects in color vision was found to have a different dependence on the field frequency than that observed for subjects with normal color vision (Lovsund et al. 1980); and (4) in a patient in whom both eyes had been removed as the result of severe glaucoma, phosphenes could not be induced by time-varying magnetic fields, thereby precluding the possibility that magnetophosphenes can be initiated directly in the visual pathways of the brain (Lovsund et al. 1980).

Although the available evidence strongly implicates the retina as the site of magnetic field action leading to phosphenes, it is not as yet clear whether the photoreceptors or the neuronal elements of the retina are the sensitive substrates that respond to the field. In a series of experiments on in vitro frog retinal preparations, Lovsund, Nilsson, and Oberg (1981) have made extracellular electrical recordings from the ganglion cell layer of the retina immediately following termination of exposure to a 20-Hz, 60-mT field in the presence or absence of broad-spectrum background light. It was found that the average latency time for response of the ganglion cells to a photic stimulus was increased from 87 to 92 ms ($p < 0.05$) in the presence of the magnetic field. In addition, the ganglion cells that exhibited electrical activity during photic stimulation ("on" cells) ceased their activity during magnetic field stimulation (i.e., they became "off" cells). The converse behavior of ganglion cells was also observed. These observations indicate that stimulation of the retina by light and by a time-varying magnetic field elicits responses in similar post-synaptic neural pathways.

An important electrophysiological finding by Lovsund, Nilsson, and Olberg (1981) was the observation that the electrical response of frog retinal ganglion cells to both photic stimuli and time-varying magnetic fields was blocked when either sodium aspartate or cobalt chloride was added to the Ringer's solution in the eyecup preparation. These compounds inhibit the transfer of information from the photoreceptors to the neuronal elements of the retina. The electrophysiological observations on chemically blocked retinal preparations appear to implicate the photoreceptors per se as the locus of the magnetic field stimulation. The origin of magnetic field responses within the receptors is consistent with the hypothesis of Knighton (1975) that a transretinal electric current may act to polarize the photoreceptor synaptic membrane, and thereby alter the post-synaptic transmission of electrical information. One experimental observation made by Lovsund, Nilsson, and Oberg (1981) which appears to be inconsistent with this hypothesis was the ability of an applied magnetic field to induce phosphenes in a patient with Retinitis pigmentosa, in whom the photoreceptors and pigment epithelium were defective but the bipolar and ganglion cell layers of the retina were conserved. The disparity in these observations, however, may be attributable to a smaller number of functional photoreceptors within the otherwise degenerated retina of the Retinitis patient. In this context, it is of interest to note that Kato, Saito, and Tanino (1983) found that electrophosphenes could be generated in patients with pigmentary retinal dystrophy, but a substantially larger stimulus intensity was required over the entire frequency range of 7 to 80 Hz than with subjects that had normal vision. Lovsund, Nilsson, and Oberg (1981) have also speculated that sensitivity to time-varying magnetic fields may exist within both the photoreceptor and the neuronal elements of the retina, but that the former are stimulated with greater ease.

RESPONSES OF NERVOUS TISSUES AND ANIMAL BEHAVIOR TO ELF MAGNETIC FIELDS

Several studies have been made of the electrical response of neurons to stimulation with time-varying magnetic fields. As discussed by Bernhardt (1979), the current densities induced by the field must exceed 1 to 10 mA/m^2 in order to have an appreciable effect on nerve bioelectric activity, and a threshold extracellular current density of about 20 mA/m^2 has been found experimentally with Aplysia pacemaker neurons stimulated by an ELF electric field (Wachtel 1979). In a subsequent study with Aplysia (Sheppard, Burton, and Adey 1983), an induced current density of approximately 5 mA/m^2 produced by a 10-mT, 60-Hz sinusoidal field was ineffective in altering the spontaneous neuronal electrical activity. Ueno, Lovsund, and Oberg (1981) were also unable to alter the amplitude, conduction velocity, or refractory period of evoked action potentials in lobster giant axons by applying ELF magnetic fields with intensities of 1.2 T at 5 to 20 Hz, 0.8 T at 50 Hz, and 0.5 T at 100 Hz. However, using magnetic flux densities in the range from 0.2 to 0.8 T, Kolin, Brill, and Bromberg (1959) were able to stimulate frog nerve-muscle preparations at field frequencies of 60 and 1000 Hz. Oberg (1973) and Ueno et al. (1978) were also able to stimulate contractions in frog nerve-muscle preparations by using pulsed magnetic fields with pulse durations less than 1 ms. In addition, the excitation of frog sartorius and cardiac muscles (Irwin et al. 1970) and the sciatic nerves of dogs and rabbits (Maass and Asa 1970) has been reported to occur in response to pulsed magnetic fields. Based on electromyographic recordings from the human arm, Polson, Barker, and Freeston (1982) were able to characterize the pulsed magnetic field parameters that elicited a neural response. From data presented in their report, the threshold value of dB/dt necessary to stimulate the major nerve trunks of the arm is approximately 10^4 T/s.

From these studies, it appears that sinusoidal ELF magnetic fields with intensities in the range generally used in the laboratory or encountered by humans in occupational settings are insufficient to alter the bioelectric properties of isolated neurons. However, direct magnetic stimulation of nerve and muscle tissues can be achieved by using pulsed fields with a large time rate of change of the magnetic flux density. It should also be borne in mind that the effects of ELF sinusoidal fields on complex, integrated neuronal networks such as those within the central nervous system may be considerably greater than the effects that occur in single neurons or nerve bundles. This amplification of a field effect could occur through a summation of the small responses evoked in individual neuronal elements (Valentinuzzi 1965). An additive response mechanism may also underlie the production of magnetophosphenes through the stimulation of multiple neuronal elements of the retina by ELF magnetic fields (Valentinuzzi 1962).

During the past two decades, a large number of studies on animal behavioral responses to ELF magnetic fields have been reported (Andrianova and Smirnova 1977; Becker 1979; Beischer, Grissett, and Mitchell 1973; Brown and Skow 1978; Caldwell and Russo 1968; Clarke and Justesen 1979; Creim et al. 1984; Davis et al. 1984; Delgado, Monteagudo, and Ramiriz 1983; de Lorge 1972, 1973a, 1973b, 1974, 1979, 1985; Friedman, Becker, and Bachman 1967; Gibson and Moroney 1974; Graham et al. 1984; Grissett 1971; Grissett and de Lorge 1971; Mantell 1975; Medvedev, Urazaev, and Kulakov 1976; Ossenkopp and Shapiro 1972; Papi, Meschini, and Baldaccini 1983; Persinger 1969; Persinger and Foster 1970; Persinger and Pear 1972; Smith and Justesen 1977; Tucker and Schmitt 1978). A chronological listing of these reports and a summary of the principal findings are given in Table 2. Several studies in which the behavior of honeybees and birds was observed to be altered in the presence of combined ELF electric and magnetic fields (Greenberg, Bindokas, and Gauger 1981; Greenberg et al. 1981; Larkin and Sutherland 1977; Southern 1975) have not been included because of the difficulty in attributing these effects to either the electric or magnetic field component. In the case of bees, it appears that ELF electric fields may induce step-potential currents in the hive that have harmful effects when the field intensity exceeds approximately 2 kV/m (Greenberg et al. 1981b). However, altered behavioral patterns of honeybees have also been reported to occur in 60-Hz magnetic fields in the absence of an external electric field (Caldwell and Russo 1968). The mechanism underlying the observed disruption of avian migration by the 72 to 80 Hz electric and magnetic fields from an ELF communication test system is not known (Larkin and Sutherland 1977; Southern 1975). However, there are numerous reports that weak DC magnetic fields comparable in strength to the earth's field may influence the migration patterns of birds (Tenforde 1985b), and very weak oscillating magnetic fields have also been claimed to affect avian orientation (Papi, Meschini, and Baldaccini 1983). One possible mechanism of interaction of low-intensity magnetic fields with bees and avians may result from magnetic forces exerted on the deposits of magnetite crystals that have been identified in these species (Gould, Kirschvink, and Deffeyes 1978; Walcott, Gould, and Kirschvink 1979). From a theoretical perspective, it is unlikely that a time-varying ELF field could orient or produce significant motion of the magnetite inclusions, as discussed earlier in this chapter. The time-varying force produced by an ELF field may, however, trigger somatosensory responses. Currently, there is no convincing evidence to suggest that such an interaction occurs, nor that a similar interaction mechanism exists in mammalian species.

In assessing the effects of ELF magnetic fields on the behavior of mammalian species, the 24 publications listed in Table 2 that bear on this subject are nearly equally divided between positive findings and observations of no behavioral effects in mammals. A careful examination of this list, however, leads to the interesting conclusion that in 8 of the 14 investigations in which no behavioral effect was observed, the time rate of change of the applied magnetic field was sufficient to induce peak

Table 2. Behavioral Effects of Exposure to Time-Varying ELF Magnetic Fields

Reference	Subject	Exposure Conditions*	Results
Friedman et al. 1967	Human	0.1 and 0.2 Hz, 0.5 to 1.1 mT; acute exposures	Increased reaction time in 0.2-Hz field
Caldwell and Russo 1968	Honeybee	60 Hz, 2.2 to 30 mT; 10-min exposures	Altered exploratory behavior
Persinger 1969	Rat	0.5 Hz, 0.3 to 3.0 mT, rotating field; exposure during entire gestational period	Decreased open-field activity and increased defecation when tested postnatally at 21 to 25 days
Persinger and Foster 1970	Rat	0.5 Hz, 0.3 to 3.0 mT, rotating field; exposure during entire gestational period	Decreased avoidance of aversive electrical shock when tested postnatally at 30 days
Grissett and deLorge 1971	Monkey	45 and 75 Hz, 0.3 mT; fields applied in 10A daily sessions of 1 h duration	No effect on reaction time
Grissett 1971	Monkey	45 Hz, 1.0 mT; continuous exposure for 42 days	No effect on reaction time
Persinger and Pear 1972	Rat	0.5 Hz, 0.3 to 3.0 mT, rotating field; exposure during entire gestational period	Suppressed rate of response to a conditioned stimulus preceding an aversive shock when tested postnatally at 70 days
Persinger et al. 1972	Rat	0.5 Hz, 0.3 to 3.0 mT, rotating field; exposure of adult animals for 21 to 30 days	Increased ambulatory activity after removal from field
Ossenkopp and Shapiro 1972	Duck eggs	0.5 Hz, 2 to 10 and 10 to 30 mT, rotating field; exposure for entire prenatal period	Increased ambulation and defecation rate when tested postnatally

* The magnetic fields were sinusoidal unless otherwise indicated.

Table 2. Behavioral Effects of Exposure to Time-Varying ELF Magnetic Fields (continued)

Reference	Subject	Exposure Conditions*	Results
DeLorge 1972, 1973, 1974, 1979, 1985	Monkey	10, 15, 45, 60, and 75 Hz, 0.8 to 1.0 mT; fields applied in 4 to 13 daily sessions of 2 to 8 h duration	No consistent influence on motor activity, reaction time, interresponse time, overall lever responding, or match-to-sample performance
Beischer et al. 1973	Human	45 Hz, 0.1 mT; 22.5-h exposure	No effect on reaction time
Gibson and Moroney 1974	Human	45 Hz, 0.1 mT; 24-h exposure	No consistent effect on cognitive or psychomotor functions
Mantell 1975	Human	50 Hz, 0.3 mT; 3-h exposure	No effect on reaction time
Medvedev et al. 1976	Human	50 Hz, 10 to 13 μT; acute exposures	Increased latency of sensorimotor reactions
Smith and Justeson 1977	Mouse	60 Hz, 1.4 to 2.0 mT; 2-min aperiodic exposures over 2 days	Increased locomotor activity and aggression-related vocalization
Andrianova and Smirnova 1977	Mouse	100 Hz, 10 mT; acute exposures	Heightened motor activity;
Brown and Scow 1978	Hamster	10-5 Hz, 0.8-26 μT; 26-h schedule of high (14 h) to low (12 h) field switching over period of 4-5 months	Modified circadian rhythm in locomotor activity
Tucker and Schmitt 1978	Human	60 Hz, 1.06 mT over whole body, or 2.12 mT over head region; repetitive acute exposures	No perception of field
Becker 1979	Termites	50 Hz, 0.05 μT in shielded room; exposures up to several weeks	Stimulation of gallery building activity

* The magnetic fields were sinusoidal unless otherwise indicated.

Table 2. Behavioral Effects of Exposure to Time-Varying ELF Magnetic Fields (continued)

Reference	Subject	Exposure Conditions*	Results
Clark and Justesen 1979	Chicken	60 Hz, 2.4 mT; aperiodic exposures during 1-h interval for 10 days	Increased variability of response tor electric shock stimulus when 60-Hz magnetic field used as conditional stimulus
Delgado et al. 1983	Monkey	9 to 500 Hz, 0.1 mT (applied to cerebellum); 9-h daily exposures for maximum of 19 days	Modification of threshold for excitation of motor neurons
Papi et al. 1983	Pigeon	0.034, 0.043 and 0.067 Hz, 60 µT peak intensity; exposures up to 4 h	Initial disturbance of orientation, but no effect on homing performance
Graham et al. 1983	Human	60 Hz, 40 µT; acute exposures	No perception of field
Creim et al. 1984	Rat	60 Hz, 3.03 mT; 1-h exposure	No field-associated avoidance behavior
Davis et al. 1984	Mouse	60 Hz, 2.33 mT; 3-day continuous exposure	No change in memory retention, locomotor activity, or sensitivity to a neuropharmacologic

* The magnetic fields were sinusoidal unless otherwise indicated.

intracranial current densities at or above the endogenous level of approximately 1 mA/m^2. In contrast, only one or the 10 positive findings of behavioral alterations in mammals (Andrianova and Smirnova 1977) involved the use of an ELF magnetic field capable of inducing intracranial currents at this level. In examining the possible reasons for this apparent disparity, it is important to assess the potential influence on animal behavior of extraneous factors such as mechanical vibration and audible noise that may accompany the activation of magnet coils. The importance of these factors has been well demonstrated by Tucker and Schmitt (1978), who found that perceptive individuals could sense the presence of a 60-Hz magnetic field through auxiliary clues. When these investigators developed an exposure chamber that provided extreme isolation from vibration and audible noise, none of the more than 200 individuals tested could detect 60-Hz fields with intensities of 1.1 mT over the whole body or 2.1 mT over the head region. The sensitivity of behavioral indices to adventitious factors such as changes in barometric pressure has also been discussed by de Lorge (1973b), who emphasized that the correlation of such variables to positive findings of apparent ELF field effects must be examined.

Another aspect of ELF magnetic field effects that should be considered in the context of behavioral alterations is the recent report of a correlation between the incidence of suicides and the intensity of residential 50-Hz magnetic fields from power-line sources (Perry et al. 1981). Based on coroner and police records from various urban and rural regions within a 5000-km2 area in the Midlands of England, a statistically significant increase in suicide rate was found among individuals who lived in residences where the 50-Hz field intensity exceeded 0.15 μT at the front entrance. A subsequent statistical analysis of the same data indicated that the cumulative probability ratio for the incidence of suicide increased above the null effect level of unity for residential 50-Hz magnetic field intensities exceeding 15 nT (Smith 1982). However, oscillations occurred in the cumulative probability ratio as a function of increasing magnetic field intensity, and at 0.2 μT the ratio for the "urban" study group was consistent with the absence of any 50-Hz magnetic field effect. From an epidemiological perspective, the lack of a clear-cut dependence of the suicide incidence on magnetic field intensity suggests that the apparent correlation between these variables may be purely fortuitous. An extension of the studies initiated by Perry et al. (1981) using a significantly larger population of individuals will be required before any firm judgment can be made regarding the proposed correlation between suicide incidence and ELF magnetic field exposure.

ELF MAGNETIC FIELD EFFECTS ON CELLULAR, TISSUE AND ANIMAL SYSTEMS

A large number of literature reports have appeared during the last two decades describing effects of ELF magnetic fields on a wide variety of cellular and organized tissue systems. These reports have been listed in chronological order in Table 3, and a brief summary is given of the principal research findings in each study. The following types of investigations have not been included in Table 3 for the reasons stated below: (1) Studies of ELF magnetic field effects on the visual system (magnetophosphene induction), nervous tissues and animal behavior, and carcinogenic risk have been excluded because these subjects are discussed elsewhere in this chapter. (2) Reports lacking adequate documentation of field exposure conditions (e.g., frequency, waveform, intensity, and duration of exposure) have been excluded. Similarly, studies have not been included in which the biological measurements were qualitative rather than quantitative, as in certain medical reports on bone fracture reunion following therapy with pulsed magnetic fields. (3) Reports of research that involved combined exposures to ELF electric and magnetic fields have not been included because of the obvious difficulty in delineating the relative effects of the two types of fields. An example of such studies is the investigation conducted at the Naval Aerospace Medical Research Laboratory on the development and physiology of rhesus monkeys chronically exposed to 72- to 80-Hz electric and magnetic fields that were designed to simulate the field parameters of a proposed naval ELF submarine communication system (Grissett 1980). In two separate experiments, an increased rate of growth was observed in the exposed group of juvenile male monkeys, which has been hypothesized to result from an increased production of testosterone in response to direct electrical stimulation of the testicles through contact with the energized cage bars. This possible explanation for the accelerated growth phenomenon was tested by measurements of serum testosterone, but the results were inconclusive (Lotz and Saxton 1984).

Table 3. Effects of Exposure to ELF Magnetic Fields at the Cellular, Tissue, and Animal Levels (continued)

Reference	Test Specimen	Exposure Conditions*	Results
Odintsov 1965	Mouse	50 Hz, 20 mT; 6.5-h single exposure or 6.5-h daily for 15 days	Increased resistance to Listeria infection
Druz and Madiyevskii 1966	Rat	3 Hz, 0.1 to 0.8 T, and 50 Hz, 0.05 to 0.2 T; 1-min exposures	Change in hydration exposures capacity of brain, kidney, and liver tissues
Riesen et al. 1971	Guinea pig brain mitochondria in vitro	60 Hz, 10 mT; 10- to 110-min exposures	No effect on respiration (oxidative phosphorylation)
Riesen et al. 1971	Rat brain synaptosomes in vitro	60 Hz, 5 to 10 mT; 30-min exposure	Decreased uptake of norepinephrine at 0°C, but not at 10°, 25°, or 37°C
Tarakhovsky et al. 1971	Rat	50Hz, 13 to 14 mT; exposure for 1 month	Changes in serum chemistry, hematocrit, and tissue morphology
Krueger et al. 1972	Chicken	45 Hz, 0.14 mT, and 60 Hz, 0.12 mT exposure for 1 month	Reduced growth rate in young animals
Ossenkopp et al. 1972	Rat	0.5 Hz, 0.05 to 0.30 or 0.3 to 1.5 mT, rotating field; exposure during entire gestational period	Increased thyroid and testicle weights at 105 to 130 days of age; no change in thymus or adrenal weights relative to controls
Beischer et al. 1973	Human	45 Hz, 0.1 mT; 22.5-h exposure	Elevated serum triglycerides; now effects on blood cell counts or serum chemistry

* The magnetic fields were sinusoidal unless otherwise indicated.

Table 3. Effects of Exposure to ELF Magnetic Fields at the Cellular, Tissue, and Animal Levels (continued)

Reference	Test Specimen	Exposure Conditions*	Results
DeLorge 1973	Monkey	15 and 45 Hz, 0.82 to 0.93 mT; fields applied in 5 to 8 daily sessions of 2-h duration	No alteration in blood cell counts or serum chemistry (including triglycerides)
Toroptsev et al. 1974	Guinea pig	50 Hz, 20 mT; 6.5-h single exposure or 6.5-h daily for 24 days	Pathomorphological changes in testes, kidneys, liver, lungs, nervous tissues, eyes, capillaries, and lymphatic systema
Udintsev and Moroz 1974	Rat	50 Hz, 20 mT; 1 to 7 days exposure	Increase in adrenall 11-hydroxy corticosteroids
Mizushima et al. 1974	Rat	50 Hz, 0.12 T; 3-h exposure	Anti-inflammatory effects of field on carrageenan-induced edema and adjuvant-induced arthritis
Beischer and Brehl 1975	Mouse	45 Hz, 0.1 mT; 24-h exposure	No change in liver triglycerides
Mantell 1975	Human	50 Hz, 0.3 mT; 3-h exposure	No hematological changes
Udintsev et al. 1976	Rat	50 Hz, 20 mT; 1-day exposure	Increased lactate dehydrogenase activity and change in distribution in heart and skeletal muscles
Batkin and Tabrah 1977	Mouse neuroblastoma	60 Hz, 1.2 mT; 13-day exposure	Decreased tumor growth rate
Sakharova et al. 1977	Rat	50 Hz, 20 mT; 1-day exposure	Increased catecholamines in tissue

* The magnetic fields were sinusoidal unless otherwise indicated.

Table 3. Effects of Exposure to ELF Magnetic Fields at the Cellular, Tissue, and Animal Levels (continued)

Reference	Test Specimen	Exposure Conditions*	Results
Kartaskev et al. 1978	Yeast	0.1 to 100 Hz, 0.025 to 0.40 mT; 20- to 30-min exposure	Changes in rate of anaerobic glycolysis
Kolesova et al. 1978	Rat	50 Hz, 20 mT; single 24-h exposure and 6.5-h daily for 5 days	Development of insulin deficiency
Tabrah et al. 1978	Tetrahymena pyriformis	60 Hz, 5 to 10 mT; exposures up to 72 h	Cell division delay, reduced growth rate, increased oxygen uptake
Persinger et al. 1978	Rat	0.5 Hz, 0.1 T to 1.0 mT, rotating field; 10-day exposure	No significant changes in thyroid follicle numbers, mast cells, adrenal and pituitary weights, body weight, or water consumption
Persinger and Coderre 1978	Rat	0.5 Hz, 0.01 T to 1.0 mT, rotating field; 5-day exposure	No significant change in thymus mast cell numbers in animals exposed prenatally and post-natally or exposed as adults
Udintsev et al. 1978	Rat	50 Hz, 20 mT; 0.25-, 6.5- and 24-h exposures	Changes in iodine uptake by the thyroid and thyroxine uptake by tissues
Udintsev and Khlynin 1979	Rat	50 Hz, 20 mT; 1-day exposure	Metabolic changes in testicle tissue
Kronenberg and Tenforde 1979	Cultured mouse tumor cells	60 Hz, 2.33 mT; 4-day exposure	No effect on cell growth rate
Chandra and Stefani 1979	Mouse mammary carcinoma	60 Hz, 0.16 T; 1-h daily exposures for 1 to 4 days	No effect on tumor growth rate

* The magnetic fields were sinusoidal unless otherwise indicated.

Table 3. Effects of Exposure to ELF Magnetic Fields at the Cellular, Tissue, and Animal Levels (continued)

Reference	Test Specimen	Exposure Conditions*	Results
Goodman et al. 1979; Greenebaum et al. 1979, 1982	Slime mold	75 Hz, 0.2 mT; 400-day exposure	Lengthened nuclear division cycle and altered respiration rate (decreased O uptake)
Kolodub and Chernysheva 1980	Rat	50 Hz, 9.4, and 40 mT; 5 h daily for 15 days	Altered brain metabolism at higher field intensity, including decreased rate of respiration, decreased levels of glycogen, creatine phosphate and glutamine, and increased DNA content
Fam 1981	Mouse	60 Hz, 0.11 T; 23 h daily for 7 days	Decreased body weight and increased water consumption; hematology, organ histology, and reproduction not affected
Aarholt et al. 1981	Bacteria	16.66 and 50 Hz, 0 to 2.0 mT; 10- to 12-h exposure	Decreased growth rate
Ramon et al. 1981	Bacteria	60 and 600 Hz, 2 mT; 17 to 64-h exposure	Decreased growth rate and cytolysis
Toroptsev and Soldatova 1981	Rat	50 Hz, 20 mT; 1- to 24-h exposures	Pathomorphological changes in brain
Koledub et al. 1981	Rat	50 Hz, 9.4 to 40 mT, daily 3-h exposures for up to 6 months	Changes in carbohydrate metabolism in the myocardium
Sakharova et al. 1981	Rat	50 Hz, 20 mT, 1-day exposure	Changes in catecholamine content and morphology in brain, heart, liver, spleen, and circulatory system

* The magnetic fields were sinusoidal unless otherwise indicated.

Table 3. Effects of Exposure to ELF Magnetic Fields at the Cellular, Tissue, and Animal Levels (continued)

Reference	Test Specimen	Exposure Conditions*	Results
Delgado et al. 1981 1982	Chicken embryo	10, 100, and 1000 Hz; 0.12, 1.2 and 12 T; 0.5-ms rectangular pulses; 2-day exposure	Morphological abnormalities in nervous tissue, heart, blood vessels, and somites
Soldatova 1982	Rat	50 Hz; 20, 40, and 70 mT; 6.5 h daily for 5 days, or 24-h continuous exposure	Pathomorphological changes in brain tissue
Sander et al. 1982	Human	50 Hz, 5 mT; 4-h exposure	No changes in ECG, EEG, hormones, blood cell counts, or blood chemistry
Lubin et al. 1982	Mouse osteoblast cultures	Single bidirectional pulses at 72 Hz, or 4-kHz bursts of bidirectional pulses with 15-Hz repetition rate; 2 mT peak intensity; 3-day exposure	Reduced cAMP production in response to parathyroid hormone
Shober et al. 1982	Mouse	10 Hz, 1 mT; 1-day exposure	Decreased sodium ion content of liver
Norton 1982	Cultured chicken embryo sternum	4-kHz bursts of bidirectional pulses with 15-Hz repetition rate; 2-mT peak intensity; four 6-h exposures during 2 days	Increased hydroxyproline, hyaluronate, and DNA synthesis; decreased glycosoaminoglycans; increased lysozyme activity
Conti et al. 1983	Cultured human lymphocytes	1, 3, 50, and 200 Hz; 2.3 to 6.5 mT; square-wave pulses; 3-day exposure	Inhibition of lectin-induced mitogenesis by 3- and 50-Hz fields

* *The magnetic fields were sinusoidal unless otherwise indicated.*

Table 3. Effects of Exposure to ELF Magnetic Fields at the Cellular, Tissue, and Animal Levels (continued)

Reference	Test Specimen	Exposure Conditions*	Results
Goodman et al. 1983	_Drosophila_ salivary glands	Single bidirectional pulses at 72 Hz, or 4-kHz bursts of bidirectional pulses with 15-Hz repetition rate; 2-mT peak intensity; 5- to 90-min exposures	Increased RNA transcription
Jolley et al. 1983	Rabbit pancreas	4-kHz bursts of bidirectional pulses with 15-Hz repetition rate; 2-mT peak intensity;18-h exposure	Reduced Ca^{++} content and efflux; reduced insulin release during glucose stimulation
Ramirez et al. 1983	_Drosophila_ eggs	0.5-ms square-wave pulses at 100 Hz, 1.76 mT peak-to-peak intensity; or 50-Hz, 1.41-mT sinusoidal field; 2-day exposure	Decreased viability of eggs
Ubeda et al. 1983	Chicken embryos	0.5-ms bidirectional pulses at 100 Hz (4 different waveforms); 0.4- to 104-µT peak intensity; 2-day exposure	Teratogenic changes in nervous system, circulatory system, and foregut
Archer and Ratcliffe 1983	Cultured chicken tibiae	1 Hz, 15- to 60-mT square-wave pulses; 7-day exposure	Decreased collagenous and noncollagenous protein synthesis; no alteration in glycosoaminoglycan DNA synthesis
Liboff et al. 1984	Cultured human fibroblasts	15 Hz to 4 kHz; 2.3 to 560 µT; 18- to 96-h exposures	Increased DNA synthesis

* The magnetic fields were sinusoidal unless otherwise indicated.

Table 3. Effects of Exposure to ELF Magnetic Fields at the Cellular, Tissue, and Animal Levels (continued)

Reference	Test Specimen	Exposure Conditions*	Results
Cain et al. 1984	Cultured mouse calvarium	Single bidirectional pulses at 72 Hz, or 4-kHz bursts of bidirectional pulses with 15-Hz repetition rate; 2.5-mT peak intensity; exposure for 1 to 16 h	Inhibition of cAMP production and Ca^{++} release in response to parathyroid hormone
Winters and Phillips 1984a, 1984b	Cultured human colon tumor	60 Hz, 0.14 mT; 1-day exposure	Increase in growth rate, number transferrin receptors, and expression of tumor-specific antigens

* The magnetic fields were sinusoidal unless otherwise indicated.

Despite the large number of test specimens that have been examined for sensitivity to ELF magnetic fields, it is difficult at present to draw firm conclusions concerning the biological effects of these fields at the cellular and tissue levels as a result of several factors: (1) A wide range of intensities, frequencies, waveforms, and exposure durations have been used. Many of the earlier studies utilized sinusoidal fields oscillating at 15 to 80 Hz, but research during the last few years has focused increasingly on the biological effects of square-wave or pulsed fields with complex waveforms. Among the studies conducted with purely sinusoidal fields, the field intensities have ranged from approximately 1 μT to 1 T, and the exposure durations have varied from 10 min to 1-4 weeks of either continuous or intermittent exposures. (2) Although the vast majority of the published literature describes positive bioeffects of ELF magnetic fields, none of the findings listed in Table 3 have been verified by means of independent replication in other laboratories. (3) A number of apparent inconsistencies can be found in the comparison of data acquired on similar (but not identical) test specimens. For example, exposure to a low-intensity ELF magnetic field was reported to produce an elevation in the serum triglyceride levels of human subjects (Beischer, Grissett, and Mitchell 1973), but comparable effects were not observed in monkeys (de Lorge 1974).

Regardless of the inadequacies that exist in the available database, the existing literature reports summarized in Table 4 indicate that several aspects of the biochemistry and physiology of cells and organized tissues may be perturbed by exposure to ELF magnetic fields. The reported biological effects for which there is a growing body of evidence include:

- altered cell growth rate (Aarholt, Flinn, and Smith 1981; Batkin and Tabrah 1977; Goodman, Greenebaum and Marron 1979; Greenebaum, Goodman, and Marron 1979, 1982; Ramon, Ayas, and Streeter 1981; Tabrah et al. 1978; Winters and Phillips 1984a, 1984b);

- decreased rate of cellular respiration (Goodman, Greenebaum, and Marron 1979; Greenebaum, Goodman, and Marron 1979, 1982; Kolodub and Chernysheva 1980);

- altered metabolism of carbohydrates, proteins, and nucleic acids (Archer and Ratcliffe 1983; Goodman, Bassett, and Henderson 1983; Kartaskev, Kalyuzhin, and Migalkin 1978; Kolodub and Chernysheva 1980; Kolodub, Chernysheva, and

Table 4. Epidemiological Studies on the Potential Relationship of Residential and Occupational Exposure to ELF Magnetic Fields and Cancer

Reference	Subjects	Correlation Between Increased Cancer Incidence and Residential or Occupational Exposures
Wertheimer and Leeper 1979	Children (<19 yr) residential fields (344 cases; 344 controls)	(+)
Fulton et al. 1980	Children (<20 yr); residential fields (119 cases; 240 controls)	(-)
Tomenius et al. 1982	Children (<18 yr); residential fields (716 cases; 716 controls)	(+)
Wertheimer and Leeper 1982	Adults; residential fields (1179 cases; 1179 controls)	(+)
Wiklund, Einhorn, and Eklund 1981	Adults; telecommunication workers; (Swedish Cancer Registry with 385,000 cases for 1961-1973)	(-)
Milham 1982	Adults; male workers in 11 occupations *involving electric* and/or magnetic fields (Survey of 438,000 deaths in Washington State men from 1950-1979)	(+)
Wright et al. 1982a, 1982b	Adults; male workers in 10 electrical/electronic occupationsB (Cancer Surveillance Program in Los Angeles County, 1972-1979)	(+)
McDowall 1983	Males aged 15-74; workers in 10 electrical/electronic occupations (Survey of occupational mortality in England and Wales, 1970-1972	(+)
Coleman, Bell and Skeet 1983	Males aged 15-74; workers in 10 electrical/electronic occupations (South Thames Cancer Registry from 1961-1979)	(+)
Vagero and Olin 1983	Males and females aged 15-64; workers in electrical/electronic occupations (Swedish Cancer Registry with 385,000 cases from 1961-1973)	(+)

Evtushenko 1981; Liboff et al. 1984; Norton 1982; Udintsev and Khlynin 1979; Udintsev et al. 1976);

- endocrine alterations and altered hormonal responses of cells and tissues (Cain, Luben, and Adey 1984; Jolley et al. 1983; Kolesova, Voloshina, and Udintsev 1978; Lubin et al. 1982; Riesen et al. 1971; Sakharova, Ryzhov, and Udintsev 1977, 1981; Udintsev and Moroz 1974; Udintsev, Serebrov, and Tsyrov 1978);

- altered immune response to antigens and mitogens (Conti et al. 1983; Mizushima, Akaoka, and Nishida 1975; Odintsov 1965);

- morphological and other nonspecific tissue changes in adult animals, frequently reversible with time after exposure (Druz and Madiyevskii 1966; Sakharova, Ryzhov, and Udinstev 1981; Shober, Yank, and Fischer 1982; Soldatova 1982; Toroptsev and Soldatova 1981; Toroptsev et al. 1974);

- teratologic and development effects (Delgado et al. 1981, 1982; Kreuger et al. 1972; Ossenkopp, Koltek, and Persinger 1972; Ramirez et al. 1983; Ubeda et al. 1983).

In view of the generally positive findings of effects on many tissue and organ systems, it is interesting to note that, with the exception of one isolated report (Tarakhovsky et al. 1971), all of the published studies on hematological parameters in exposed animals have shown no consistent field-associated effects (Beischer, Grissett, and Mitchell 1973; de Lorge 1974; Fam 1981; Mantell 1975; Sander, Brinkmann, and Kuhne 1982). The apparent lack of sensitivity of the hematological system to ELF magnetic fields is in distinct contrast to the well documented effects of ionizing radiation and high-intensity microwave fields on this particular physiological system.

Eighteen of the investigations with ELF sinusoidal fields have involved the exposure of rodents to 50- and 60-Hz fields with intensities ranging from 0.01 to 0.8 T (Chandra and Stefani 1979; Druz and Madiyevskii 1966; Fam 1981; Kolesova, Voloshina, and Udintsev 1978; Kolodub and Chernysheva 1980; Kolodub, Chernysheva, and Evtushenko 1981; Mizushima, Akaoka, and Nishida 1975; Odintsov 1965; Sakharova, Ryzhov, and Udintsev 1977, 1981; Soldatova 1982; Tarakhovsky et al. 1971; Toroptsev and Soldatova 1981; Toroptsev et al. 1974; Udintsev and Moroz 1974; Udintsev and Khlynin 1979; Udintsev, Serebrov, and Tsyrov 1978; Udintsev et al. 1976). With the exception of one report in which tumor growth rate was observed not to be influenced by brief exposure to a

60-Hz, 0.16-T field (Chandra and Stefani 1979), all of these studies report positive findings of cellular and tissue effects from ELF magnetic fields. The maximum current densities induced in the experimental subjects by the applied field exceeded approximately 10 mA/m^2 in these studies, and were therefore at or above the upper limit of the endogenous currents that are normally present within the body (Bernhardt 1979). It is also notable that positive findings of biological effects were obtained in all of the 11 studies listed in Table 3 in which square waveforms and pulsed fields with repetition frequencies in the ELF range were used (Archer and Ratcliffe 1983; Cain, Luben, and Adey 1984; Conti et al. 1983; Delgado et al. 1981, 1982; Goodman, Bassett, and Henderson 1983; Jolley et al. 1983; Lubin et al. 1982; Norton 1982; Ramirez et al. 1983; Ubeda et al. 1983). During the rising portions of the various square-wave and bidirectional pulsed fields that have been used experimentally, a high time rate of change of the magnetic flux density is present and current densities exceeding 10 mA/m^2 are induced in the exposed tissues. These various laboratory studies thus suggest that the induction by ELF fields of electric currents in tissues and extracellular fluids that exceed the normal physiological levels may lead to perturbations of cellular and tissue functions. It has been suggested that the currents induced by such fields may exert an electrochemical effect at the cell surface that, in turn, influences the membrane transport and intracellular concentration of calcium ions (Jolley et al. 1983; Lubin et al. 1982). Because of the important role played by calcium ions in metabolism and growth regulation, this proposal should be given careful consideration in the context of ELF magnetic field effects at the cellular and tissue levels.

Three of the studies listed in Table 3 involved short-term exposures of human subjects to ELF magnetic fields (Beischer Grissett, and Mitchell 1973; Mantell 1975; Sander, Brinkmann, and Kuhne 1982). With the exception of one unconfirmed report of an elevation in serum triglycerides in the exposed subjects (Beischer, Grissett, and Mitchell 1973), none of these investigations revealed adverse effects of ELF magnetic fields with intensities comparable to or exceeding the levels generally encountered by man. Particularly notable in this regard is the report by Sander, Brinkmann, and Kuhne (1982), who observed that a 4-h exposure of human subjects to a 50-Hz, 5-mT field produced no changes in serum chemistry, blood cell counts, blood gases and lactate concentration, electrocardiogram, pulse rate, skin temperature, hormones (cortisol, insulin, gastrin, thyroxine), and various neuronal measurements including visually evoked potentials recorded in the electroencephalogram.

ELF MAGNETIC FIELDS AND CANCER INCIDENCE

During the last five years, several investigations have been carried out to assess whether correlations exist between exposure to ELF electric and/or magnetic fields and the incidence of reproductive alterations and carcinogenesis (Coleman, Bell, and Skeet 1983; Fulton et al. 1980; McDowall 1983; Milham 1982; Nordstrom, Birke, and Gustavsson 1983; Tomenius, Hellstrom, and Enander 1982; Vagero and Olin 1983; Wertheimer and Leeper 1979, 1980, 1982, 1984; Wiklund, Einhorn, and Eklunl 1981; Wright, Peters, and Mack 1982a, 1982b). These studies are discussed in detail in the Chapter 9 and Michaelson (1985). Because of the large number of investigators who claim to have found an apparent association between cancer risk and residential or occupational exposure to power-frequency magnetic fields, a brief discussion and critique of these specific studies are also given here.

Ten reports on this subject published since 1979 are summarized in Table 4. The initial publication by Wertheimer and Leeper (1979) reported an apparent correlation between the incidence of leukemia in children living in the Denver, Colorado area and exposure to power-frequency magnetic fields from high-current primary and secondary wiring configurations in the vicinity of their residences. A later epidemiological survey by Tomenius, Hellstrom, and Enander (1982) of childhood leukemia incidence in the County of Stockholm produced results that were consistent with the Wertheimer and Leeper (1979) study.

In a study conducted in Rhode Island, Fulton et al. (1980) concluded that there was no statistically significant correlation between the incidence of childhood leukemia and residential exposure to magnetic fields from power lines. Wertheimer and Leeper (1980) were critical of the study by Fulton et al. (1980) on the basis that the control and case groups had not been matched for interstate migration, for years of occupancy of residences, or for the ages of the children at the time their residential addresses were determined from birth records and hospital medical records. In a subsequent analysis of the data obtained by Fulton et al. (1980), Wertheimer and Leeper (1980) excluded cases and controls aged eight and above in order to define a complete residential history for the remaining subjects (53 cases and 71 controls). In this subset of the total population studied by Fulton and his associates, Wertheimer and Leeper found a weakly significant correlation ($p \sim 0.05$) between the incidence of leukemia and residential high-current power line configurations.

A total of four brief epidemiological reports were published during 1982 and 1983 in the format of letters to journal editors (Coleman, Bell, and Skeet 1983; McDowall 1983; Milham 1982; Wright, Peters, and Mack 1982a, 1982b) all of which showed an apparent association between the incidence of leukemia in males and occupational explosure to ELF electric and magnetic fields. Two of these studies were conducted in the United States (Milham 1982; Wright, Peters, and Mack 1982a, 1982b) and two in England (Coleman, Bell, and Skeet 1983; McDowall 1983). In a study using the Swedish Cancer-Environment Registry as an epidemiological data base, a slightly higher total incidence of cancer was reported among male and female workers in the electrical manufacturing industry as compared to the general population (Vagero and Olin 1983). In an epidemiological study of telecommunications workers that was also based on the Swedish Cancer-Environment Registry, Wiklund, Einhorn, Eklund (1981) found no increased risk for this occupational group as compared to the Swedish population as a whole.

Overall, 8 of the 10 recent epidemiological studies discussed above have reported an apparent association between cancer incidence and residential or occupational exposure to ELF fields from electric power sources. However, there were a number of methodological deficiences in these studies that limit the soundness of their conclusions. Several specific problems are the following: (1) In all of the studies thus far reported, the magnetic field dosimetry was at best qualitative. In studies of residential ELF magnetic fields, the neglect of local fields from appliances may have led to incorrect conclusions concerning the peak and average exposure of individuals to power-frequency fields and the harmonic frequencies that emanate from electrical devices used within the home. (2) The sample populations in many of the epidemiological studies were small, and the reported increases in cancer incidence by a factor of 2 or less might be expected to occur on the basis of chance alone. In these studies, it would have been informative if the authors had presented data on several nonexposed occupational groups in which the sample size was comparable to that of the exposed groups. (3) Control groups were frequently chosen in a nonblind manner involving subjective criteria, and the control population was often not matched with the exposed groupd on the basis of age, sex, race, socioeconomic class, or urban/rural residential status. (4) Several of the studies used weak statistical methods such as the calculation of proportionate mortality ratios, which can lead to extremely misleading conclusions for population subgroups in which the overall incidence of disease is low with the exception of one disease class such as cancer (or some specific form of cancer such as leukemia). (5) The existence of confounding factors such as smoking habits and exposure to industrial pollutants of known carcinogenic potential (e.g., aryl hydrocarbons) were ignored in all of the epidemiological studies that have attempted to relate ELF fields and cancer incidence.

In view of the numerous deficiencies in the epidemiological studies conducted to date, it is currently not possible to conclude that a definite association exists between the exposure of individuals to ELF magnetic (or electric) fields and their relative risk of contracting leukemia or other forms of cancer. In addition, the field levels to which humans are generally exposed are sufficiently low that it is difficult to conceive plausible mechanisms that might underlie a causal relationship between cancer incidence and ELF magnetic field exposure. To put this issue into clearer perspective, it is instructive to consider the internal potentials and currents induced in humans as the result of motion through the earth's magnetic field. A straightforward calculation based on Faraday's law indicates that the motion of a human bending forward at the waist within the geomagnetic field will induce instantaneous internal currents comparable to those produced by exposure to an external 60-Hz sinusoidal field with an intensity of approximately 0.1 to 0.2 μT. This magnetic field intensity is comparable to the ambient power-frequency fields in many residences and occupational settings. Such considerations indicate clearly the need for careful dosimetry in any attempt to detect a relationship between power-frequency magnetic fields and cancer. The conduct of prospective epidemiological studies with carefully matched control groups would also be of great value in assessing the validity of conclusions drawn from many of the retrospective studies that have been carried out during the past few years.

SUMMARY

Although a wide variety of biological effects resulting from exposure to ELF magnetic fields have been reported in studies on cellular, tissue, and animal systems, the only phenomenon consistently replicated is the induction of magnetophosphenes. The minimum field intensity required to induce magnetophosphenes using a sinusoidal time-varying field is 10 mT, and this level is significantly greater than the ELF magnetic field intensities to which humans are routinely exposed. It is also notable that many of the other reported bioeffects of ELF magnetic fields in cells, tissues, and animals were observed with field intensities and waveforms that induced circulating currents above the naturally occurring levels in biological objects.

A large number of investigations have been carried out during the past two decades to assess the biological effects of ELF magnetic fields with intensities comparable to, or in some cases lower than, those to which humans are routinely exposed. These studies have led to both positive and negative findings of ELF magnetic field effects, and there is little consistency among reports from different laboratories. An example of the difficulty in interpreting these studies is provided by the many reports on animal behavior in ELF magnetic fields. A majority of the investigations carried out with low field intensities have indicated the occurrence of behavioral alterations, whereas nearly all of the studies conducted with higher field intensities have provided no evidence for field-associated effects on animal behavior.

Currently, many of the reported effects of very low intensity ELF magnetic fields on cellular, tissue, and animal systems must be viewed with caution, either because of a lack of independent verification of the experimental findings, or because the reported field effects may have resulted from the presence of confounding variables. This type of consideration also pertains to the recent epidemiological reports of an apparent correlation between cancer incidence and residential or occupational exposure to ELF magnetic fields. Numerous deficiencies have been noted in the dosimetric and epidemiological procedures that were used in these studies, and no definitive conclusions concerning the possible relationship between ELF magnetic field exposure and cancer risk can be drawn from the evidence that is currently available.

Several recent publications on ELF magnetic field interactions with living systems have indicated that the biological response may depend in a very sensitive manner on the waveform and frequency of the applied field. For example, studies using pulsed magnetic fields with fast rise times have led, in nearly all instances, to findings of perturbations in biological functions. Several recent reports of research using various waveforms have also indicated that the frequency of the applied field may be critically important for eliciting a biological response, and that "windows" of sensitivity may exist within the ELF frequency range. A number of theoretical models have been proposed to explain these observations, although none of these models has as yet been subjected to direct experimental verification. It is evident that future research efforts with ELF magnetic fields must focus to an increasing extent on mechanistic studies, with particular emphasis being placed on elucidating the underlying basis for the reported sensitivity of biological systems to fields with specific waveforms and frequency characteristics.

CONCLUSIONS

The basic goal of this chapter has been to summarize and to analyze in a critical manner the extensive literature that exists on the responses of animal, tissue, and cellular systems to ELF magnetic fields. The underlying motivation for preparing this review was the present need for an assessment of the potential influence on biological systems of the low-intensity fields associated with the proposed Naval ELF Submarine Communication System. In this section, the conclusions of the preceding literature review will be related in a concise manner to the ELF Communication System.

The characteristics of the magnetic fields produced by the proposed ELF Communication System are described in detail in the Appendix to this report. The predicted field intensity within the ELF antenna right-of-way is anticipated to be 6 μT, although levels up to 14 μT could occur near line sags or in areas with a high ground topography relative to the overhead line. At avian migrational altitudes above the antenna lines the field intensities are projected to be less than 1 μT, and even lower intensities will be present at ground level in areas outside of the antenna right-of-way. Based on recent measurements near the Wisconsin and Michigan test sites, the ELF antenna fields in the frequency band from 72 to 80 Hz appear to be comparable in magnitude to the 60-Hz ambient fields emanating from electrical wiring, appliances and equipment. The frequency spectrum of the ELF Communication System has been measured at the Wisconsin test facility, and the signal strength in the subharmonic frequency range was lower by 40-60 dB than the signal level at the center frequency (76 Hz). Similarly, the higher harmonic frequency spectrum exhibited levels that were down by 50-60 dB relative to the center frequency signal.

In the context of analyzing the potential biological effects of the extremely low-intensity magnetic fields produced by the ELF Communication System, two general conclusions can be made on the basis of the literature review provided in this chapter:

- Although numerous behavioral, physiological and biochemical effects of ELF magnetic fields have been reported on the basis of laboratory studies, very few of these experiments were carried out using low field intensities comparable to those associated with the ELF Communication System. The reports which indicate that measurable perturbations of biological processes occur as a consequence of exposure to extremely low intensity fields must currently be viewed with caution until the results have been established by independent replication in other laboratories.

- Recent epidemiological studies suggest that a correlation may exist between cancer incidence and exposure to the power-frequency magnetic fields present in residential and industrial environments. These studies are clearly relevant to the issue of potential biological effects from the magnetic fields that will be present in areas within the proximity of the right-of-way of the ELF Communication System. However, as discussed in this report, the methodological and dosimetric deficiencies of the published epidemiological studies are numerous, and the available evidence that a correlation exists between cancer incidence and ELF magnetic field exposure cannot be regarded as conclusive. A critical need exists for carefully designed epidemiological and laboratory studies to clarify this issue.

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CHAPTER 5

CELLULAR STUDIES OF EFFECTS OF ELF ELECTRIC AND MAGNETIC FIELDS

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INTRODUCTION

This chapter is concerned with developments since 1977 in the area of extremely low frequency (ELF) field interaction with cellular systems, especially as studied by in vitro preparations. Since 1977, there have been an extensive expansion of the literature on calcium ion changes in tissue, new data on biochemical measurements for cellular or physiological systems, expanded data on physiological responses of cells grown in culture, new data on neurophysiological responses, and most recently, intriguing information on biological responses to static or time-varying magnetic fields.

Various cellular systems were studied in vitro to determine the nature of cellular responses to electric and/or magnetic fields. The studies provide several clear examples of interactions between biological systems and extremely low frequency fields. Although control of exposure is superior for in vitro studies and portions of organisms can be studied in isolation from other influences, the manifestation of effects in the intact animal system requires in vivo studies.

The primary goal of in vitro studies is characterization of the interaction at the biophysical, biochemical, or macromolecular levels of cellular or tissue organization. This "mechanistic approach" provides two

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major benefits: the possibility that further experiments can be designed with the guidance of an established hypothesis and the determination of intensity-response and frequency-response characteristics. There is as yet no adequately detailed physical or chemical theory for biologically significant interactions between fields of environmental origin and internal body tissues. Indeed, the peripheral interactions with environmental electric fields of several kilovolts per meter that are thought to involve excitation of peripheral sensory systems are also largely unexplained. Thus, reported effects are viewed skeptically, even when data collection techniques appear credible.

Because of technical limitations, time, or cost considerations, data from whole animal studies may not determine intensity-response and frequency-response characteristics. In some cases, phenomena seen in vitro require large field strengths to be observed. Establishment of a threshold for these effects, or demonstration that in vivo experimental techniques could not achieve the requisite conditions, also serves a useful end in delimiting possible means of interaction. For example, it is readily apparent that weak ELF fields could not introduce significant transmembrane potentials in the cells of tissues exposed in vivo (National Academy of Sciences 1977, Appendix D), thereby eliminating many possible interactions from consideration.

There is also value in hypotheses based on biological principles that do not address physical coupling. For example, attention often is focused on interactions at the cell membrane surface, which is undoubtedly the site of many important cellular processes and undoubtedly the prime site for a field interaction. Yet, as recent data suggest, focusing on intracellular biochemical events may yield biological insights, even though the physical coupling at the membrane surface remains unexplained.

Generally, experiments conducted in vitro are acute, with field exposures that last from seconds to hours. Very strong electric field levels can be applied without the constraints incurred for exposure of whole animals to capacitively coupled electric fields and without the possibly confounding effects of peripheral sensory stimulation (e.g., of mechanoreceptors by hair vibration or stimulation of the olfactory and hearing senses by corona-generated ozone or noise). Biochemical manipulations of tissue enable discrimination of the site of an effect, such as on a biochemical apparatus located at the interior or exterior surfaces of the plasma membrane or at intracellular sites. Furthermore, a detailed picture of the biochemical pathways involved may be obtainable

However, there are many reasons why an effect seen in vitro may not be expressed in a study of whole animals or vice versa. For example, exposure to the intact organism is likely to involve greater variability in field strength due to movement or changes in posture. Also, compensatory or amplifying interactions with biochemical and neurophysiological systems may be absent in preparations of selected tissues.

SUMMARY OF NATIONAL ACADEMY OF SCIENCES REVIEW OF IN VITRO STUDIES

The Committee on Biosphere Effects of Extremely-Low-Frequency Radiation report on Project Sanguine/Seafarer (National Academy of Sciences 1977) reviewed a number of studies involving cellular preparations, with particular interest in the reports of altered calcium ion efflux from chick brains and changes in mitotic cycle and protoplasmic streaming in *Physarum*. These studies have each been continued since 1977 with fruitful results.

At that time, the Committee noted that the "binding of calcium ions may provide a sensitive index of interaction with environmental fields" (National Academy of Sciences 1977, p. 47). It was noted (1) that there were no studies confirming the work by Bawin, Kaczmarek, and Adey (1975) and Bawin and Adey (1976), (2) that even the calcium efflux studies with ELF sinusoidal signals of about 10 V/m (in air) were at field levels in excess of the proposed Seafarer antenna fields, and (3) that the frequencies studied were lower than Seafarer transmission frequencies.

The Committee carefully evaluated the *Physarum* study and concluded that, in the absence of an effect on growth and physiology, the data gave no reason for concern (National Academy of Sciences 1977, p. 41), and the Committee noted elsewhere (National Academy of Sciences 1977, p. 188) that the effects were not confirmed and "questionable," although further research was encouraged (National Academy of Sciences 1977, p. 41).

Convincing in vitro evidence for genetic effects was not found, and all genetic studies involved fields vastly stronger than the proposed Seafarer fields. The committee concluded that on "both theoretical and experimental grounds we believe that ELF fields are not likely to constitute a genetic hazard" (National Academy of Sciences 1977, p. 148).

Cell culture studies were evaluated (including some magnetic field exposures), but none was relevant to Seafarer, nor was any scientifically significant with regard to weak ELF field effects (National Academy of Sciences 1977, pp. 184-188). The conclusion was that neither electric nor magnetic fields can be "expected to have perceptible effects on cell growth and division." The magnetotactic response of bacteria was found important and interesting, but perhaps irrelevant in considering AC fields.

WAVEFORMS OF ELECTRIC AND MAGNETIC FIELDS

ELF studies have been conducted with sinusoidal or pulsed fields and with amplitude-modulated (AM) radio frequency (RF) fields in addition to the proposed ELF Communications System transmission, which is a frequency-shifted sinusoidal waveform designated MSK (minimum-shift-keyed). Of these waveforms, the single frequency sinusoid has the simplest frequency spectrum, the MSK signal involves a narrow spectrum of ELF frequencies near 76 Hz, the modulated RF involves only one ELF frequency, but the pulsed signals involve a spectrum of frequencies with an upper limit determined by the pulse rise and decay times. Amplitudes for the sinusoidal and MSK waveforms are readily interpreted. In the case of the modulated RF, the amplitude of the carrier wave gives an upper limit for the effective ELF component of the modulated wave, but because the site and mechanism of demodulation are unknown, the effective ELF amplitude is unknown. For pulsed electric or magnetic fields, there is a spectrum of amplitudes that depends critically on the electronic properties of the pulse generator and the circuit it is driving.

Investigators have used wide-ranging electric and magnetic field conditions, and the relevance of those studies to the ELF Communications System conditions should be examined individually. In view of the very weak magnitude of the proposed System fields, few studies mimic exposure conditions. For this and other reasons, the studies should be evaluated on the basis of their contributions to a general understanding of ELF biological interactions rather than for the precision of similarity to the exposure conditions of the proposed antenna system.

REVIEW OF IN VITRO STUDIES

Biochemical Processes at the Cellular Level

There is a growing data base of biochemical experiments with low frequency electric fields that examine biochemical effects of applied ELF electric fields, amplitude-modulated fields, and pulsed magnetic fields over a range of frequencies. Data are especially clustered for exposures at 100 kV/m (about the maximum practical limit for a laboratory animal exposure system), near 10 kV/m (similar to the maximum ground level transmission line electric field strength), or in the range of 10 to 100 V/m where experiments were conducted for explicit relevance to the Navy's ELF Communications System (National Academy of Sciences 1977; Naval Electronic Systems Command 1975).

Cytoskeletal and Histochemical Changes in Brain Tissue. Rabbits exposed to the 14-kV/m field of a 400-kV (50 Hz) substation exhibited cytoskeletal alterations of cerebellar Purkinje neurons and alterations in the concentration of two glial proteins (S-100 and glial fibrillary acidic protein (GFA)); large, deleterious changes in motor functions and severly stunted growth and development were also reported (Hansson 1981a, 1981b, 1982). Two control groups were used: (1) animals screened from the field by a Faraday cage and (2) animals kept outside the substation area entirely. Experiments conducted on rabbits and rats in the laboratory were reported to show the cytoskeletal and biochemical changes but not the gross effects on motor function, growth, and development (Hansson 1982). Cytoskeletal changes were reported to include abnormal endoplasmic reticulum that formed lamellar bodies, reductions or absence of certain mitochondria and hypolemmal cisterns, and reduced arborization of the dendritic branches.

Recently, Albert et al. (1984) gave a preliminary report on a study that showed similar changes in rats exposed for more than 2 months at 60 Hz, 65 kV/m (effective field strength). They found altered intracellular membrane structures that they called "pancakes." These may be the same as the lamellar bodies identified by Hansson, but Albert et al. indicated that they were not endoplasmic reticulum, as suggested by Hansson. Unlike Hansson's original report on rabbit tissue, the membraneous bodies were relatively rare, only a few per cell, and then in less than half the cerebellar cells of 4 of the 10 rats studied. Cytoskeletal changes were also found, although even more rarely, in hippocampal CA3 neurons. Extensive studies of synaptic density showed no significant changes. In addition to species and exposure differences, the studies differ in the delay of 17 to 27 days imposed from the end of exposure until animal sacrifice in Albert's laboratory. This was necessary because exposure took place in another laboratory (Battelle Northwest) and delays were required for transportation and acclimation. Albert et al. speculated that there may have been a reversal of the changes during the post-exposure period or that other factors such as species difference or exposure conditions accounted for the difference in the degree of effects.

In contrast, Portet et al. (1984) found no effects on the growth, development, or brain cell morphology of rabbits exposed under field strength conditions similar to those used by Hansson. However, the animals were exposed only during the final 2 weeks of gestation and the ultrastructural analysis of cerebellar Purkinje cells was conducted in only three of the exposed animals. It is possible that exposure for the briefer period and cytoskeletal examination of a smaller number of animals account for the negative findings of this study.

Thus, although two of the studies generally confirm exposure-related changes in the cytoskeleton, the extent and functional significance of the changes are not yet established. Further studies are required, and these should address the issues of reversibility, threshold, relation of protein changes to structural changes, and also include the protein assays for which Hansson cites more robust effects in comparison to the cytoskeletal changes. Unfortunately, it is doubtful that future studies could meaningfully address the possible relation between cellular changes and the severe developmental effects reported only in an unspecified fraction of the outdoor-exposed rabbits of the first study.

Possible reasons for the discrepancies found among exposure conditions and species in these studies include dependence on some unidentified cofactor in the environment, genetic make-up of the animals, or unidentified methodological differences. Resolution of discrepancies and further understanding of the genesis and functional significance of the cell changes are desirable.

Calcium Efflux in Brain and Other Tissues. There are now several in vitro studies and one in vivo study in which sinusoidal ELF or ELF amplitude-modulated RF fields were tested for an effect on calcium binding to excitable tissue (Adey, Bawin, and Lawrence 1982; Bawin and Adey 1976; Bawin, Kaczmarek, and Adey 1975; Bawin, Adey, and Sabbot 1978; Bawin, Sheppard, and Adey 1978; Blackman et al. 1979, 1982a, 1982b, 1983, 1984; Dutta et al. 1984; Lin-Liu and Adey 1982; Schwartz, Delorme, and Mealing 1983). All studies report an effect of ELF electric fields on the rate or amount of preloaded radioactive calcium released into a nonradioactive bathing solution. Two studies of pulse-modulated RF fields showed no effect (Shelton and Merritt 1981; Merritt, Shelton, and Chamness 1982). The tissues examined included cat and chick brain, synaptic vesicles (synaptosomes), frog heart, and cultured tumor cells. Bawin's work used both ELF fields (less than 100 V/m in air) and ELF modulated 147- and 450-MHz carrier waves. Blackman et al. worked at these frequencies and at 50 MHz to demonstrate independence from the carrier frequency and a frequency-dependent interaction effect among nearby samples in the exposure chamber (Blackman et al. 1980; Joines and Blackman 1981; Weill, Spiegel, and Joines 1984). Others have used only the AM-RF fields.

Similar--but not identical--effects are reported for both direct ELF and AM-RF exposures. These include a windowed dependence on field strength and frequency. The most recent Blackman et al. (1984) data involving ELF fields of 40-V/m p-p (14-V/m rms) also demonstrated a dependence on the static magnetic field, which in most uncontrolled circumstances is the geomagnetic field of about 0.4 G. The specific nature of the required field conditions presents a major complication in all studies of ELF field influence, and the situation could only be worse if the windowing were found to be specific to each tissue studied. It does, however, appear that the frequency responses in the calcium studies agree that there is a peak near 15 to 16 Hz. Such highly specific effects suggest a physical mechanism of some generality that would apply to most biological materials. The near ubiquity of calcium in many effects on cellular processes makes these findings significantly insightful about how many cellular events might be initiated. Adey (1976, 1981) has proposed a model based in part on these calcium efflux data, in which an initial interaction at the cell membrane surface is communicated intracellularly.

The magnitude of the alterations in efflux ranges from about 10 to 30 percent for either direct ELF fields or AM-RF fields. For AM-RF fields, the effective electric field strength is not known, although the upper limit is given by the magnitude of the carrier wave, which at 450 MHz, 10 W/m^2 produced an internal electric field estimated at 10 V/m (Adey 1976). Weill, Spiegel, and Joines (1984) measured the internal electric fields for the usual experimental condition in which multiple tubes are in close proximity. In an incident field of 10 W/m^2, the internal fields were 0.36, 0.58, and 1.32 V/m for carrier frequencies of 50, 147, and 450 MHz, respectively. The internal field is significantly reduced from the electric field in free space (61.4 V/m). Internal fields in the brain of an exposed cat also have been measured as 10 V/m (Bassen et al. 1977), and power levels were measured by Adey, Bawin, and Lawrence (1982). If the effective ELF level were known to be about 1 to 10 V/m, there would be little direct bearing on environmental exposures where tissue level fields are orders of magnitude less, but tne effective ELF field strength depends on the unknown efficiency of demodulation. Pickard and Rosenbaum (1978) showed that, due to ion transit times across the membrane, a transmembrane rectification mechanism for demodulation cannot occur for frequencies much above about 10 MHz. This was validated by experimental observations in excitable plant cells over a wide range of frequencies (Barsoum and Pickard 1982; Brunkard and Pickard 1984; Liu, Garber, and Cleary 1981; Pickard and Barsoum 1981), and recently Sheppard, Pickard, and Bawin (1984a) reported a similar absence of a transmembrane demodulation in *Aplysia* neurons exposed to a modulated 450-MHz field. Tenforde (1980) presented thermodynamic arguments to demonstrate that no significant heating of tissue occurs for the AM exposure condition, and certainly none occurs for ELF exposure in vivo (Sheppard and Eisenbud 1977) or under most in vitro experimental conditions.

Frequency Windowing. The calcium effect is seen only within selected ELF frequency ranges or "frequency windows. In the AM-RF studies, maximal effects occur at 16-Hz modulation and are not detectable at frequencies that differ by a factor of two nor is there any effect on the unmodulated carrier wave (Bawin, Kaczmarek, and Adey 1975). Blackman et al. (1979) found a similar frequency-windowing for chick brain studied with AM-RF at 147 MHz, and Dutta et al. (1984) found the same frequency window in calcium efflux from neuroblastoma cells exposed to AM fields at 915 MHz. In studies with direct ELF fields, a frequency window centered at 15 to 16 Hz also appears, and Blackman et al. (1983) also reported a harmonic series of effective frequencies ranging from an apparent fundamental at 15 Hz up to 105 Hz in steps of 15 Hz (15-V/m rms), except no signficant effect was observed at 30 Hz.

Amplitude Windowing. Amplitude windows in calcium exchange were first observed in the AM-RF exposures (Bawin, Adey, and Sabbot 1978; Bawin, Sheppard, and Adey 1978; Blackman et al. 1979; Sheppard, Bawin, and Adey 1979) and later in ELF studies where amplitudes of about 2- and 15-V/m rms were found effective (Blackman et al. 1983). Further evidence of the amplitude sensitivity observed in these studies comes from the work of Joines and Blackman (1981), who found that effects could be observed with a 50-MHz carrier only if the frequency dependence of the dielectric constant was considered. As a result of this analysis, it was estimated that the effective electric field strength was of the same magnitude as for the 147-MHz carrier.

Influence of the Static Magnetic Field. The most recent report by Blackman et al. 1984 suggested that the frequency maximum depends on the magnitude of the static magnetic field and is unaltered for antiparallel directions of the static magnetic field.

Influence of the Time-Varying Magnetic Field. The studies of a directly applied ELF field by Bawin and Adey (1976); Bawin, Adey, and Sabbot (1978); and Bawin, Sheppard, and Adey (1978) used a capacitively coupled parallel-plate exposure system so that no ELF magnetic field was applied. In contrast, Blackman et al. (1982a, 1982b, 1983, 1984) conducted exposures in the ELF range in a Crawford cell that was terminated by a 50-ohm resistor and thus created a small ELF magnetic field. Its influence on the difference in the sign of the data obtained from the two laboratories has been the subject of discussion and speculation. Recently Blackman et al. (1984) reported that no effect on calcium efflux was seen if the terminating resistor was removed, thereby eliminating the magnetic field, and reproducing the conditions of Bawin's experiment.

Influences of the Ionic Milieu. The calcium that is available for exchange resides in the very superficial layers of the exposed tissue. Because of the slow, 1.7-mm/h diffusion rate for calcium ions in brain tissue (Adey, Bawin, and Lawrence 1982), Bawin and her colleagues believed that measured effects involve mostly superficial Ca^{++} bound to the cell membrane surface (Bawin, Sheppard, and Adey 1978). Experiments to investigate the influence of changes in the ionic milieu (Bawin, Adey, and Sabbot 1978) disclosed a sensitivity to H^{+} concentration that suggested competition of Ca^{++} and H^{+} for binding sites, presumed to be along the glycoproteins that project from the lipid bilayer membrane into the extracellular space. Experiments with La^{++} bound to the cell membrane indicated a decreased efflux during exposure to the field, opposite in direction to the original Ca^{++} results. This may be a reflection of differences in binding competition of the La^{++}, Ca^{++}, and H^{+} ions in contrast to a system of just Ca^{++} and H^{+}. Because La^{++} blocks the transmembrane Ca^{++} channels, the data suggest an effect that is primarily at the cell surface.

Calcium Efflux in Synaptosomes. Lin-Liu and Adey (1982) found a frequency-dependent change in calcium binding to vesicles prepared from synaptic membrane. Effects were seen for 16-Hz modulated RF fields (30 W/m^2) but not for 60-Hz modulation, nor for the unmodulated RF carrier. In this study, unlike others, the rate of calcium efflux was observed by repeated measurements at 1-min intervals; other studies usually measured calcium exchange at a single time. The time constant for the efflux that followed exposure to 16-Hz AM-RF was 38 percent greater than for the control study and corresponded to a much smaller percentage increase in total efflux. Because efflux was measured in a calcium-free medium, calcium-calcium exchange was eliminated. Because the field-stimulated release occurred in the absence of calcium, and after most Na-Ca exchange was completed, it was suggested that the field-stimulated Ca^{++} release arose from membrane binding sites rather than from the intracellular sites usually associated with the slowly released pool.

Calcium Efflux in Cultured Cells. Dutta et al. (1984) reported results on Ca^{++} efflux with monolayer cultures of human neuroblastoma cells. An amplitude-windowed and frequency-windowed response was found using a 16-Hz modulated RF carrier of 915 MHz at 0.05 W/kg, but no response was seen at higher or lower carrier levels nor for the unmodulated carrier at 0.01 W/kg. The data show a sharp frequency dependence, with a 55 percent enhancement of efflux at 16 Hz, but only about 28 percent at 18 Hz and 35 percent at 14 Hz, and essentially no enhancement at 5 or 25 Hz. This is in agreement with the "tuning curve" initially presented by Bawin and Adey (1976) and a similar curve by Blackman et al. (1979). The absorbed energy, however, was quite different from that obtained with an incident field of 7.5 W/m^2 for which frequency-dependent results were seen in chick brain. However, at 1 W/kg, the effect on cultured cells was independent of the 16-Hz modulation. In addition to efflux data, data were obtained to indicate a significant field effect on uptake for 30-min exposures to 16-Hz modulated RF at a specific absorption rate (SAR) of 0.05 W/kg, but no effect at 0.1 W/kg.

Criticisms and Significance of the Calcium Efflux Effect. The calcium studies reviewed establish that weak fields could affect biomolecular structure in highly specific ways, although many serious issues remain: (1) clarification of the demodulation mechanism for AM-RF fields; (2) development of a quantitative model for transduction of fields less energetic than the (wideband) energy of thermal origin; (3) clarification of differences between the initial studies of Bawin et al. and those of Blackman et al., which involve ELF fields that differ in the presence (Blackman) or absence (Bawin) of a very weak ELF magnetic field that, in Blackman's laboratory, appears necessary; and (4) clarification of other contradictions in results from the Bawin and Blackman groups. Field effects of opposite sign (decrease versus increase) have been reported, but the two laboratories are in agreement on frequency and amplitude parameters.

The study of cultured neuroblastoma cells exposed to AM-RF fields much weaker than those used for other calcium efflux studies reproduced the 16-Hz frequency peak and introduced a modulation-independent effect. This work should be extended, including dosimetric contrasts with the other exposure techniques, evaluation of the magnetic field role, and possibly extension to a study of directly applied ELF fields.

In a review of these studies, Albert and Slaby (1985) cited technical issues (e.g., statistical techniques and reduction of raw data measured in counts per minute into efflux values) that are not fully detailed in the published reports. Albert and Slaby also criticized Blackman's studies because of unexplained shifts in sham values, and they were particularly interested in identifying the extracellular, membrane-bound, or intracellular sites for the field effect on efflux. Although Albert and Slaby stressed an intracellular source for the efflux (usually of interest in other research on calcium exchange), the studies with chick brain or other intact tissues involve particularly complicated calcium dynamics. This is because of the extracellular sites below the tissue surface from which calcium can slowly diffuse during the measurement period, thus adding to the slow release from intracellular pools. The calcium dynamics do not seem similar to those of the typical calcium exchange study in dispersed cells to which the ELF studies were compared. It should be noted that the critical comments by Albert and Slaby do not include reference to the work by Blackman et al. since 1980.

Because of the widespread, essential neuroregulatory role played by calcium ions in many membrane processes (including the well-known role of calcium in neurotransmitter release, its competitive binding to membrane macromolecules, or its role as a second messenger of intracellular changes involving protein phosphorylation), the action of weak ELF fields on calcium exchange from these tissues suggests, but does not demonstrate, the potential for profound changes in brain function. However, many of the effects are small and might not lead to readily observable changes in the function of intact tissues capable of adaptive changes. Because calcium is so intimately involved in many biochemical functions, it may be difficult to show that a given effect seen in vivo is uniquely related to the changes in calcium binding. To illustrate the qualitative difference in data obtained with fully functional systems, the in vivo study with cats (Adey, Bawin, and Lawrence 1982) indicated oscillatory changes rather than the monotonic divergence in efflux rates found in the synaptosome study.

Intracellular Biochemical Alterations

Lymphocytes derived from human tonsils were exposed to AM-RF fields at several modulation frequencies at 10 W/m^2 (Byus et al. 1984). Tests for changes in activity of c-AMP-dependent protein kinases were negative, but the c-AMP-independent kinases were affected in a modulation frequency-dependent manner. Significant effects were seen for 16-, 40-, and 60-Hz exposures (15 or 30 min). Maximum effects involved 50 percent or more reduction in activity for the 16-Hz exposures. However, prolonged exposure of 45 or 60 min, other modulation frequencies, and unmodulated fields were ineffective. These results and studies on bone exposed to pulsed magnetic fields (Luben et al. 1982) (showing effects on an adenylate cyclase membrane-related system) are biochemically distinct.

Pineal Melatonin Rhythm, Pineal Cell Activity

In studies of rats, guinea pigs, and pigeons exposed to static magnetic fields, or in some cases to changes in the orientation of static magnetic fields, several investigators (Semm 1982, 1983; Reuss, Semm, and Vollrath 1983; Welker et al. 1983) found electrophysiological evidence for changes in pineal cell firing rates, melatonin metabolism, and serotonin N-acetyl transferase (SNAT) activity of the pineal gland. Because the electric field studies described below do not seem to involve any artifactual sources of magnetic fields, it appears that either the pineal gland itself, or more likely, elements of the central or sympathetic nervous systems with neural input to the pineal gland, are affected by electric magnetic fields.

Anderson (1984) and Wilson et al. (1981) reported significant decreases in the nocturnal concentrations of the pineal gland neuroendocrine substance melatonin and in the activity of SNAT after in vivo exposure to 60-Hz electric fields at 65 kV/m (39 kV/m, effectively) for 30 days. Tests at intervals of from 1 to 3 weeks after the start of exposure indicated that 3 weeks were required to observe the onset of the change (Anderson et al. 1982). The effects on melatonin (depressed at 0200 hours during the active phase) and SNAT (also depressed) are opposite to the observed increase in 5-methoxy-tryptophol (5-MTOL), which was elevated at the same time of day. Because melatonin and 5-MTOL are alternative metabolites of serotonin, the data show a switch in the biochemical pathway in the field-exposed animals.

Wilson et al. (1981) speculated that the effects on the pineal gland may be mediated by increased excitability of nervous system components that are afferent to the pineal gland, especially in the absence of evidence for a humoral factor that might regulate serotonin metabolism in the pineal gland.

Possibly there is a primary transduction at the cellular level in pineal cells or in regions afferent to the pineal gland. These afferents include the retino-hypothalamic tract, suprachiasmatic nucleus, and other brain regions where signals are relayed to the pineal gland through the superior cervical ganglion. In this phenomenon, as also seen elsewhere, the effects do not seem to be linearly related to field strength. Data collected in a weak 60-Hz electric field of only 1.8 kV/m showed a simlarly depressed melatonin rhythm (Anderson et al. 1982; Anderson 1984).

The function of the pineal gland in maintaining circadian rhythms of the body is a vigorous area of current biological research interest, but the significance of these effects is not yet well understood. However, there is no question that circadian rhythms are important to health, and further definition of these field-related results is needed.

Neurophysiologic Studies

Several studies in which electric currents are applied to portions of the nervous system demonstrate an alteration in neuronal excitability. A frequency-dependent interference with the pacemaker activity of invertebrate neurons has been observed (Sheppard, Burton, and Adey 1982, 1983; Sheppard, French, and Adey 1980a, 1980b; Wachtel 1979), and a long-term alteration in the electrical response was seen in the rat hippocampal slice (Bawin et al. 1984). These studies were conducted at current densities greater than those found in the tissues of animals or humans exposed to environmental fields, but in some extreme cases the tissue electric fields are similar.

Effects on Aplysia Pacemaker Cells. Cell firing activity in pacemaker neurons of *Aplysia* was altered by extracellular currents with the greatest sensitivity at frequencies near the natural firing rate, which for these invertebrate neurons is about 1 Hz. Wachtel (1979) reported synchronizing effects at current densities of 20 mA/m^2, whereas Sheppard, French, and Adey (1980a, 1980b) found that at least 230 mA/m^2 rms was required. For media with a conductivity of about 5 S/m, the corresponding electric fields are 0.4 and 47 mV.

When exposed to either static, ELF sinusoidal, or low-frequency square wave magnetic fields of up to 16.2 mT (11.5-mT rms), preliminary data showed no effects on the beating patterns of the pacemaker cells (Sheppard, Burton, and Adey 1983). However, the interburst intervals of bursting pacemaker neurons were affected upon exposure to square wave and sinusoidal fields at 100 or 60 Hz. The calculated electric fields induced in the exposure chamber were about 8- or 5-mV/m rms at 100 or 60 Hz, respectively. Amplitudes for the square-wave-induced electric fields were about 300 mV/m, comparable to fields in some of the electric field studies with Aplysia.

A detailed model for extracellular current effects on neuronal excitability is not available and, although the general principles are clear, only approximate scaling to other neural systems is possible. If scaling is done on the basis of equal current densities, the high conductivity of the invertebrate medium and tissue (about 5 S/m) would result in the need for stronger tissue electric fields in the less conductive mammalian tissues. The equivalent field is at least 5 times greater for mammalian neural tissue with a conductivity of about 1 S/m or less; larger ratios apply for tissues (like bone) with lower conductivity. On the other hand, if scaled according to electric field strength, the effects reported for tissue-level fields of 1 V/m, down to about 10 mV/m, might also occur in mammalian tissues at similar strengths, depending on the nature of the coupling mechanism. Under extreme conditions of exposure to environmental fields (approaching 100 kV/m), levels in the body may reach about 100 mV/m (Kaune and Phillips 1980; Kloss and Carstensen 1983; Wachtel 1979, 1985).*

Wachtel (1979, 1985) estimated that the firing rate changes require a threshold extracellular current density of 20 mA/m^2. If about 1 percent of this current density is assumed to cross the membrane, the transmembrane component is 0.2 mA/m^2. This is 105 times less than the transmembrane currents associated with action potential currents or measured by voltage clamp techniques, and would produce sub-millivolt changes in membrane potential. In contrast, Sheppard and his coworkers found that a larger extracellular current density of at least 230-mA/m^2 rms was required, but estimated that only 5×10^{-6} of the extracellular current density crosses the membrane of the molluscan neuron (Sheppard, French, and Adey 1980a, 1980b; Sheppard et al. 1984). This indicates a

*Kaune and Phillips (1980) estimated 5.5 mA/m^2 of current in the neck of a grounded person exposed to a 10-kV/m (60 Hz) vertical field. Assuming a tissue conductivity of 0.5 S/m, the resulting internal field is about 10 mV/m.

transmembrane value of about 1-μA/m^2 rms, also too small to be have a significant direct effect on membrane potential. By contrast, neurophysiologists regularly cause significant membrane potential changes in these cells by injection of currents of 0.1 nA or more, which corresponds to a current density of about 800 μA/m^2 crossing the cell body membrane of a cell 200 μm in diameter.

Effects on Synaptic Function in Brain Tissue Slices. Changes in tissue excitability of mammalian brain tissue were reported by Bawin et al. (1984). The excitability of hippocampal neurons was tested in vitro by measuring the size of the response to an excitatory test pulse applied during control or field conditions. Extracellular fields of about 1-V/m rms at 5 or 60 Hz (Bawin et al. 1981a, 1981b, 1984) produced a long-lasting potentiation of the tissue excitability that lasted for many minutes. In contrast to these persistent changes, another field effect has been discussed in this tissue. In this case, the effect on the neurons is observed only during field presentation and is attributed to polarization of the nerve cells by extracellular fields of more than 5 V/m (Bawin et al. 1984; Jefferys 1981; Taylor and Dudek 1982). Although all these studies are conducted at current densities and electric field strengths greater than would be found in the tissues of animals or humans exposed to environmental fields, they reveal a sensitivity to fields that are weak in comparison with signals used for laboratory stimulation of brain tissue and are of the strength and frequency of electroencephalogram (EEG) fields. Although the brain slice studies involve fields many orders of magnitude larger, observations of changes in monkey behavior and EEG have been reported and interpreted as evidence that weak prolonged exposure to environmental fields affects brain processes (Gavalas et al. 1970; Gavalas-Medici and Day-Magdaleno 1976). Bawin, Gavalas-Medici, and Adey (1973) also found changed EEG rhythms in operantly conditioned cats exposed to AM-RF over an extended period. In both mammalian and invertebrate neurophysiological studies, the results indicate no tissue damage, but the functional changes that occurred may be related to nervous system effects observed in studies of intact animals.

Synaptic Function in Animals Exposed In Vivo. Jaffe et al. (1980)

reported on several tests of synaptic function performed on rat sympathetic cervical ganglia excised from animals after 30-day exposures to a 60-Hz effective field strength of 65 kV/m. The postsynaptic compound action potential (elicited by a single pulse), its rate of rise and fall, conduction velocity in the nerve, frequency response, post-tetanic response, and response after fatigue induced by prolonged high-frequency (20 Hz) stimulation were all unaffected. However, a clearly significant, replicable effect was seen in a test of synaptic function, the "conditioning-test ratio response." In this test, presynaptic fibers were stimulated with above-threshold stimuli, and the ratio of a pair of action potentials was observed as a function of the interval between the pair of stimulating pulses. A greater amplitude of response among exposed animals was seen for a range of interpulse intervals. Other tests on sciatic nerve (chosen as an example of myelinated nerve) and vagus nerve (unmyelinated) were negative for evidence of a field effect. Jaffe, Laszewski, and Carr 1981 observed a slight effect on fatigue recovery in slow twitch muscles was observed, but in other tests of the same neuromuscular apparatus and in all tests involving a fast twitch muscle of the same animals, no significant effects were found (although a trend was evident in one replication of the study of fast twitch muscle).

These data may prove important in estimating the quality and magnitude of effects on the nervous system following whole-body exposure. The results showed changes in neuronal function that were highly selective and persisted for at least several tens of minutes following the end of the exposure and dissection of the tissue. The results are also consistent with other experiments that find no apparent neuropathology or gross functional deficits. The functional shifts reported in these animals were not great enough to manifest a pathologic condition. The data invite investigation of two hypotheses, one that proposes altered synaptic function as a result of chronic stimulation of the peripheral sensory system and another that proposes a direct effect on the affected neurons. To date, there is evidence that strong peripheral fields can excite sensory neurons at the dorsal root of the spinal cord (Jaffe 1982), but there are no other data bearing on these models.

Retinal Cells in a Magnetic Field: Magnetophosphenes. Lovsund (1980); Lovsund, Nilsson, and Oberg (1980); and Lovsund, Oberg, and Nilsson (1979) investigated the magnetophospene effect in human subjects and in frog retina ganglion cells in vitro. During magnetic field exposure of the frog retina above the threshold of 20 mT at 20 Hz, the latency of response to a light stimulus was increased by 4 ms (5 percent). Observation of "on-cells" (that respond only as the light is turned on) during magnetic field exposure showed they were "off-cells" with respect to the magnetic stimulus and vice versa for "off-cells." The latency to response for the magnetic stimulus was very brief (5 ms) in contrast with the average of 85 ms for a light stimulus. Simultaneous blockade of light and magnetic field responses by sodium-aspartate or cobalt ions was evidence that the magnetic detection was at the photoreceptor or following cells and not at the ganglion cells. The studies supported the hypothesis that the phosphenes were due to induced electrical currents at the level of the retina, especially in the photoreceptor and bipolar cells, rather than in cortical tissue or in retinal tracts. However, it was not possible to conclusively determine whether currents in the head, eye globe, or over other paths were at the proper magnitude and direction to have the observed effects. A role for direct magnetic field effects (e.g., at photoreceptor molecules) was not explicitly ruled out, although the experiment clearly indicates that induced electric currents are adequate to account for the phenomena.

From Faraday's Law it follows that a 15-mV/m electric field is induced in tissue of a 0.012-m-radius eye globe subjected to a 20-Hz field at 20 mT. Lovsund (1980) estimates that the current density required to stimulate the cells of the retina upon the assumption of a magnetically induced current flowing over the eyeball is about 1 mA/m^2 at 20 Hz (the most sensitive frequency). This is about 3 to 4 orders of magnitude below the currents required to cause significant change in membrane polarization in the model referred to above (National Academy of Sciences 1977, Appendix D) and at least one order of magnitude more sensitive than the *Aplysia* pacemaker cells. The rms rate of change for a 20-Hz, 20-mT field is about 1.8 T/s.

Budinger (1979, 1981) cites the magnetophosphene literature to establish a threshold for faradaically induced current densities of about 20 mA/m^2 and a threshold for the time rate of change for the magnetic field at about 2 T/s. The order of magnitude difference between the Lovsund 1980 and Budinger (1979, 1981) estimates of threshold current densities (and electric fields) derives from the Budinger assumption that the appropriate loop is 0.1-m in radius, taken to model the head rather than the eye globe, as was appropriate for the isolated eye. In the Budinger assumption, the estimated current density is "only three times less" than the current density required for direct electrical stimulation of phosphenes, whereas in Lovsund's model, the discrepancy is about a factor of 30. In the Lovsund model, the current paths are tangential to the eye globe and would be likely to produce the phosphene effect over most of the retinal surface. However, currents in the retina would be organized more or less perpendicular to the axis of cellular organization, which is also parallel to the length of the photoreceptor cells. In contrast, Budinger appears to assume that current paths flowing through the head intersect the eye globe. These paths affect the retina with currents that vary in orientation with respect to the direction normal to the retina for different loci on the eyeball. If sensitivity to the current is strongly dependent on orientation, these currents would be less able to excite the retinal cells, so that their greater magnitude may not be the dominant factor for the in situ eye. Resolution of these issues is desirable, especially as it would help clarify the threshold current density in retinal tissues with greater precision.

Light Response in Turtle Retinas. The amplitude of the b-wave recorded from the turtle retina evoked potential was significantly reduced while under the influence of static magnetic fields of 1 mT or more (Raybourn 1983). This finding was strongly dependent on the daily light-dark cycle as shown by the fact that it could be observed only during a brief period following the onset of the dark phase. This and other evidence suggested a relation with the circadian cycle in melatonin synthesis. The dynamic range of response to the magnetic field showed a threshold at about 1 mT and saturation above about 10 mT. As is true for the magnetophosphene effects, it is difficult to establish a plausible cause for effects (1) that occur at field levels below those required for direct interactions with the magnetic moment of the rhodopsin molecule and (2) that occur at interaction energies reported to be at least one order of magnitude weaker than thermal energy ($kT=0.026$ eV at 25°C).

Isolated Heart Tissue. The heart rate of isolated frog heart was altered in a manner that depended linearly on field strength above a threshold of about 20 to 30 V/m (measured in the medium) and was also dependent on the frequency of the applied field (Kloss and Carstensen 1983). The greatest effectiveness was at frequencies near the natural beating rate of 0.5 Hz, but effects at 60 Hz were detectable in less than 50 percent of the preparations exposed to the maximum levels of about 50 V/m.

Plant Roots. Pea roots (*Pisum sativum*), grown in a low conductivity solution in which a 60-Hz electric field of 150 to 450 V/m was imposed, showed a field-strength-dependent change in growth rate at fields above 250 V/m for fields aligned parallel to the length of the root tip (Miller et al. 1979, 1980, 1984; Robertson, Miller, and Carstensen 1981; Robertson et al. 1981). The effects, reaching more than 80 percent attenuation in growth rate at the maximum field, are attributed to the changes in transmembrane potential produced by the field. Orientation-dependent sensitivity was also observed, in accord with the foregoing hypothesis. Mitotic index in cells from the exposed roots was found depressed in vertically oriented electric fields greater than 350 V/m. The estimated required transmembrane potential changes are 3 to 8 mV.

Marino, Hart, and Reichmanis (1983) reported a 5 percent decrease in the germination rate of sunflower seeds exposed to 60-Hz electric fields in air of 5 or 1 kV/m. Estimates of the electric field in the seed depend on water content and ranged from 30 V/m in the dry state to 7.5×10^{-4} V/m when water-loaded, as at germination. Previously, Coate et al. (1970) found a similar effect for seeds germinated in combined electric and magnetic fields (10 to 20 V/m, 1 to 2 x 10^{-4} T).

Studies with Cultured Cells

Slime Mold (*Physarum polycephalum*). An extensive series of studies with the slime mold *Physarum polycephalum* has shown field strength and frequency-dependent effects for separate and combined electric and magnetic field exposures. In these studies (Goodman, Greenebaum, and Marron 1976, 1979; Greenebaum, Goodman, and Marron 1979; Marron, Goodman, and Greenebaum 1975) both electric (0.035 to 0.7 V/m) and magnetic (0.01 to 0.3 mT) fields were applied at 45, 60, and 75 Hz with significant effects on mitotic rate (observed over a period of months or years), protoplasmic streaming, and cell respiration. Moreover, separate magnetic or electric fields of similar magnitudes and frequencies had effects that were somewhat less than those seen when combined fields were used (Goodman, Greenebaum, and Marron 1979). The latency period between start of exposure and observation of a shift in mitotic rate was highly variable. These studies were reviewed by the 1977 National Academy of Sciences' Committee. They emphasized that fields such as the 0.7-V/m electric field strength in the medium could not occur for organisms capacitively coupled to the weak ELF antenna fields in air. However, the magnetic fields used in this research include those with field strengths as low as 10 μT, which is similar to the 3-μT maximum field near the ELF Communications System antenna. Thus, these data may have direct relevance for some organisms in the immediate region of the antenna in addition to their value in indicating that the field effect can be elicited by both electric and magnetic fields and that the changes take many cell divisions to be evident.

The same organism was studied during a gametic stage. Haploid cells of Physarum were grown in orthogonal electric and magnetic 60-Hz fields (1.0 V/m, 0.1 mT) (Marron et al. 1983). Post-exposure studies of membrane surface affinity for the polymer poly-(ethylene glycol) showed slightly lowered affinity among the cells exposed for 2 weeks or longer. This change was evidence for a field-induced alteration in surface charge.

Genetic Studies. Perhaps because of the absence of effects in most previous research and because of the seeming implausibility of an effect on the genetic apparatus, only a few additional studies with electric fields have been conducted. Williams (1983) found no evidence for a direct effect of field exposure on replication or repair processes of DNA but did report increased production of lambda viral particles in E. coli that resulted from less than 30-min exposure to 70- to 130-V/m fields (measured in the medium). On the basis of a second experiment with synchronously induced cells, it appears that the field interaction occurs only when the virus is associated with the cell membrane, a stage in the reproductive process of this virus. A similar effect was not noticed in another viral/bacterial system not involving a membrane binding step.

Williams began a study of other DNA-related events, including the interesting question of synergy between mutagens and the applied electric field, but the preliminary results were inconclusive. Because of the recent data on developmental defects during embryogenesis and the general interest in effects on cancer promotion or other cellular changes that may be mediated by effects at the molecular level, it is desirable to continue study of these effects, even though the fields used clearly exceed those that might be expected in tissues of exposed animals or human beings.

Studies of sister chromatid exchange in bone marrow cells of rats exposed to 100 kV/m in vivo showed no field-related change in this or other chromosomal parameters (Williams 1983). There was no evidence for a field effect on sperm cells following 5-day exposures of mice to 100-kV/m, 60-Hz fields for 8 h/day. Neither numbers of abnormal sperm nor uptake of thymidine were altered (McClanahan 1981).

Magnetic Field Effect on DNA Transcription. Because transcription of the gene for beta-galactosidase is usually inhibited by a repressor protein bound to DNA, production of the enzyme provides evidence of an alteration in binding to repressor DNA or in availability of the repressor. Using a square wave magnetic field at 50 Hz, Aarholt, Flinn, and Smith (1982) observed a windowed increase in enzyme synthesis for magnetic fields between 0.5 and 0.6 mT, and an even narrower window for a decrease in synthesis at about 0.3 mT. The observed relative rates of synthesis were markedly altered by factors of up to two or four. An interaction between culture concentration and magnetic field effects was also seen, and although suggestive of some long-range interaction between cells, it is not readily interpretable.

DNA Synthesis in Fibroblasts. Incorporation of thymidine into human-derived foreskin fibroblasts was enhanced in a frequency-independent manner by sinusoidal magnetic fields of 15 Hz to 4 kHz (Liboff et al. 1984). Although synchronous cultures were not used, it was reported that the peak in thymidine uptake corresponded to mid-S phase of the cell cycle. The change in DNA synthesis is relatively small, but the most interesting outcome of the data is the implication that the interaction does not have the frequency-dependence expected from a mechanism involving faradaic induction. The threshold was estimated to be between 5 and 25 μT/s (a factor of 1 million less than estimated for neural system interactions illustrated by magnetophosphenes). Additional research is desirable, including studies through several generations, use of other magnetic field strengths, an electric field control, and the use of synchronous cultures.

Mitotic Activity in Fibroblasts. Human fibroblast cells were exposed in vitro to 50-Hz electric fields of 50 and 150 kV/m (in air) produced by a parallel plate capacitor (Dyshlovoi, Panchuk, and Kachura 1981). Mitotic index was significantly reduced after 24-h continuous exposure to the 50-kV/m field, and a recovery period of less than 6 h was noted. In striking contrast to the lowered mitotic index seen from 24 to 48 h of exposure, there was a significant increase after 96 h that was still observable at one week. The absence of detailed information on the exposure system does not allow comparison with the electric fields generated in the medium in the technique used by Lymangrover, Keku, and Seto (1983, see below) or by Liboff et al. (1984).

Division of Cells Exposed In Vivo. Measurements of mitotic activity in epithelial tissue of the cornea were reported by Strzhizhovskii, Galaktionova, and Chermynkh (1979) for mice exposed in vivo to static fields for 1 h. Above 0.3 to 0.8 T, the mitotic index was seen to fall to less than 50 percent of its initial value, reaching only about 20 percent at 12.7 T. When the magnetic field was turned off, there was an overshoot period of about 2 days, and then there was an eventual recovery to control levels of mitotic activity. No effect on the rate of chromosomal abnormalities was seen, and despite the effects on mitotic cycle, there was no evidence of changed cell counts.

Unicellular Organisms. Ramon et al. (1981) reported inhibition of growth in *E. coli* bacteria exposed to magnetic fields of 600 Hz at field strengths of 2 to 30 G for periods of 50 h or longer. (The magnitude of the induced electric field that would be found in the medium due to the alternating magnetic field is not indicated.) Experiments conducted at 60 Hz were negative, perhaps reflecting the much lower level of induced electric field at the lower frequency. The authors suggest that the field has a direct effect on the flagellar apparatus of the bacterium, but the biophysical details are not presented and do not appear obvious.

E. coli subjected to square wave magnetic fields at 50 or 16.66 Hz grew with a significantly reduced mean generation time that reduced the control value of 0.85 h by up to 5 percent, a value many times the standard error in these measurements (Aarholt, Flinn, and Smith 1981). A sharp threshold was observed at 0.48 mT at 50 Hz and at 0.8 mT at 16.66 Hz. Although significant changes persisted at higher field stengths, there was a windowed region in which effects were about 5 percent versus a reduction of about 2 percent at higher fields (above 8 and 1.5 mT at 60 Hz and 16.66 Hz, respectively). There was no evidence for an effect on cell viability. Aarholt, Flinn, and Smith suggested that this effect on cell division may reflect a quantal interaction with magnetic flux, and they noted that a single quantum of magnetic flux links a dividing cell at the 0.48-mT threshold level found for 50-Hz square wave fields. However, if correct, the explanation is incomplete insofar as the same flux linkage has no reported effect at 16.66 Hz. Square wave rise times were not given.

Other recent reports suggest that strong static magnetic fields can effect growth in Tetrahymena pyriformis. Tabrah et al. (1978) found greatly reduced growth rates, higher cell mortality, cytomorphologic changes, and altered oxygen uptake after a 49-h exposure to 60 G (or 100 G in the respiration study) at 60 Hz. These solenoidal fields had a spatial gradient of 0.02 T/m. Studies with DC magnetic gradient fields (0.15 T, 2 T/m) showed no effects of field exposure. (The magnitude of the induced electric field that would be found in the medium due to the alternating magnetic field was not indicated.)

Application to the protozoan Spirostomum ambiguum of a strong static magnetic field of up to 5.5 T led to the observation of reduced contractile frequency and significantly increased cell death rates (Ripamonti, Frankel, and Ettienne 1979; Ripamonti, Ettienne, and Frankel 1981). Survival times were inversely proportional to magnetic strengths in the range of 0.5 to 5.5 T.

Adrenal Gland Tissue. Additional evidence of an intensity window was seen in a study where cultured rat adrenal tissue was exposed to a 60-Hz field (Lymangrover, Keku, and Seto 1983). A threefold increase in the corticosterone response to stimulation by ACTH was seen at 0.17 mV/m (calculated value for the tissue); however, there was no significant response at either higher (1.7 or 17 mV/m) or lower (0.084 mV/m) fields. (The fields were produced by a capacitive plate system that exposed the medium and tissue to fields in the gap of from 5 to 1000 kV/m, and the field that affected the tissue was 10 kV/m.) The field effect on corticosterone production was found after 5 h of exposure but not at the beginning of exposure (samples collected from exposure minutes 15 to 105). Also, field exposure had no effect on basal steroid production.

Neuroblastoma Cells. Dixey and Rein (1982) exposed a clonal neuroblastoma cell culture to a pulsed magnetic field (0.16 to 0.85 mT) that produced electric fields of 38 or 19 mV/m in the medium. Release of the neurotransmitter noradrenaline following a 13-min exposure to the pulsed field was significantly elevated above the control levels. The field-related increase was abolished when 15 mM of magnesium was added to the medium, suggesting that the magnesium blocked transport of the extracellular calcium ions required for the stimulation of transmitter release. By inference, the primary step in the field-produced change in transmitter release is an effect on calcium binding, possibly related to the effects observed in studies of calcium efflux by Adey, Bawin, and Lawrence (1982); Bawin and Adey (1976); Bawin, Adey, and Sabbot (1978); Bawin, Kaczmarek, and Adey (1975); Bawin, Sheppard, and Adey (1978); Blackman et al. (1979, 1980, 1982a, 1982b, 1983, 1984); Dutta et al. 1984; and Lin-Liu and Adey (1982).

Human and Murine Tumor Cells. Cultured Burkitt lymphoma cells were exposed to static 1-T magnetic fields or 0.16-T, 60-Hz magnetic fields daily for 1- or 2-h intervals for 1 to 3 days (Chandra and Stefani 1979). Studies of growth and cell morphology showed no magnetic field effects.

Kronenberg and Tenforde (1979) exposed EMT6 mouse mammary tumor cells to a 1.65-mT rms, 60-Hz magnetic field in a test for possible effects on mitotic cycle length, cell growth, or morphology. Exposures lasting up to 100 h showed no differences between exposed and control cultures. The magnetic field was oriented so that the field was parallel to the culture surface, a situation allowing minimal eddy currents in the 1.2-cm medium depth.

Preliminary reports by Winters and Phillips (1984a) indicated an effect of

60-Hz electric and magnetic fields on growth of human cancer cells. Plating efficiency was reported to be affected following a 24-h exposure to either 300-mA/m^2 electric current density and/or 0.1-mT rms magnetic field with only slight evidence for a synergistic effect in combined exposures. An assay for tumor-associated antigens was reported to show effects that depended on the duration of exposure from 6 to 24 h (Winters and Phillips 1984b).

Cytotoxicity of Lymphocytes. Lyle et al. (1983) found significant effects on the cytolytic ability of CTLL-1 lymphocytes that were exposed to a modulated radio frequency field (15 W/m^2). Significant decrements in cytolytic capacity (up to 20 percent) were observed at the 60-Hz modulation frequency and to a lesser extent at other frequencies. By exposing the cells at different times before and after combination of the effector and target cells, it was concluded that the effect on cytolytic capacity was expressed during an early allogeneic recognition phase. Full recovery was observed 12.5 h after the end of field exposure. The authors suggested that the lymphotoxic process could be affected at several steps, either involving effector-target recognition or the membrane-related processes by which the toxic factors are delivered to the target cell. Lymphotoxic interactions are calcium-dependent, as is true for many membrane-related cell processes.

CHO cells. Frazier, Samuel, and Kaune (1982, 1983) and Frazier et al. (1981) reported on experiments with mammalian ovary tissue (CHO-K1) grown in the electric field induced within a toroidal chamber by a 60-Hz magnetic field. At fields to 10.9 V/m, no cytotoxic or mutagenic effects were observed, but 8-h exposures at 0.7 to 3.7 V/m for 24 h reduced cell survival due to an effect on cell plating efficiency. Presumably this effect is an expression of an alteration in the cell membrane surface.

In a similar experiment, the growth of CHO cells was unaffected by exposure to roughly equivalent peak electric fields of 1.5 to 300 mV/m (60 Hz) and corresponding current densities of 2.75 to 555 mA/m^2 (Tobey et al. 1981). Stevenson and Tobey (1982) reported on potassium ion flux across the

In a similar experiment, the growth of CHO cells was unaffected by exposure to roughly equivalent peak electric fields of 1.5 to 300 mV/m (60 Hz) and corresponding current densities of 2.75 to 555 mA/m^2 (Tobey et al. 1981).

Stevenson and Tobey (1982) reported on potassium ion flux across the membrane of CHO cells exposed to the much larger field of 2.85 V/m (60 Hz) using a magnetic induction technique. Exposures were continued over about six generations (96 h). The results show no difference between potassium influx for control and exposed cultures. However, when a similar study was conducted on the transport of amino-isobutyric acid, there was a significant field effect on cells previously treated by centrifugation, but no effect otherwise (Ley, Tobey, and Price 1982).

Other reports of effect on cultured cells are referenced in the report by Winters and Phillips (1985), which was prepared in conjunction with this document.

Field-Induced Migration of Membrane Macromolecules. Studies with static electric fields have demonstrated an "in-situ electrophoretic" motion of membrane-bound molecules. Moving slowly under the field influence an asymmetric distribution is produced and is observable by fluorescent staining of the macromolecules (McLaughlin and Poo 1981; Poo 1981; Poo, Poo, and Lam 1978; Poo et al. 1979). Lin-Liu, Adey, and Poo (1984) used the *Xenopus* myoblast cells first used by Poo, but used pulsed electric fields to characterize the effects of fields that, depending on pulse parameters, permit varying trade-offs between molecular motion and backwards diffusion toward a symmetric distribution. Rabinowitz (1982, 1983) has developed a model that suggests that even sinusoidal fields may perturb the macromolecular distribution. Generally, these effects require fields in the medium of 100 V/m or greater, and although of interest in defining the properties of membrane components, the basic phenomena of field interactions on cell surfaces, and possibly a local effect of synaptic activity in dendritic regions of the nervous system, electrophoretic-like fields could not occur in tissue exposed to environmental fields.

Chiabrera and co-workers have developed models based on a change in the free energy of the reaction between ligands and receptor molecules of the cell surface (Chiabrera et al. 1981) or on a change in receptor-ligand encounter lifetimes due to a microiontophoretic effect of the applied electric field (Chiabrera, Grattarola, and Viviani 1984). These models for cell surface dynamics take into account several calcium ion changes associated with fields or such events as lymphocyte activation.

Oviposition and Egg Development in *Drosophila*. Ramirez et al. (1983) exposed female *Drosophila* to square wave, sinusoidal, and static magnetic fields at 1.76 mT, 1.0 mT rms, and 45 mT, respectively. The flies showed a signficant avoidance of exposed regions when depositing eggs. Signficant effects also were found in egg mortality for all field exposures that occured only during a 48-h period that included egg stage and early larval stage of developement. Pupal mortality was affected only in those eggs exposed to the sinusoidal fields.

Fertilization Success in Fish. Ova and sperm obtained from rainbow trout were exposed in vitro to a 1-T static magnetic field for 1 h (Strand et al. 1983) with the finding that subsequent fertilization was more successful for the exposed ova and sperm. Effects were greater on the ova. Although effects of more than 1 percent were seen only for the first year, a statistical treatment showed significant effects over the 3-yr course of the study.

Effects on Bone Growth and Fracture Repair

Fundamental Electrical Phenomena in Bone. It has been hypothesized for over a century that bone growth in normal organisms is subject to the influence of electric fields, and that application of externally generated electrical fields might be therapeutically useful in the treatment of fractures or defects in bone growth (Hartshorne et al. 1840, cited in Dealler 1981). The modern era of research on this topic was initiated in 1957, with the report of Fukuda and Yasuda that samples of dead bone exhibited piezoelectric properties. This finding has been confirmed and extended to hydrated bone tissue by numerous workers (e.g., Bassett and Becker 1962; Cochran, Pawluk, and Bassett 1968; Friedenberg and Brighton 1966). Piezoelectric currents are apparently generated in bone during normal movement of the organism by stressing of the collagen matrix in bone. The mineral component of bone (hydroxyapatite) apparently contributes to the process mainly as an insulator that limits dispersion of charges generated in collagen fibers (Anderson and Eriksson 1970). The precise mechanism by which mechanical stress produces charge separation and current flow in bone is not known. There is, however, general agreement that the electric fields detectable in living bone originate not only from the piezoelectric properties of extracellular matrix but also from the electrical activities of living bone cells (Borgens 1984; Friedenberg et al. 1973), thus accounting for higher current levels detected in living bone as opposed to dead bone. Fracture of bone dramatically enhances the generation of charges and the flow of current in the area around the fracture site, especially during the first few minutes or hours after injury (Borgens 1984; Friedenberg and Brighton 1966). Both piezoelectric and cellular electrical processes are believed to contribute to these fracture currents.

Effects on Bone Growth and Remodeling. Locally generated electric fields in normal bone are believed to be important in remodeling and fracture healing, but the mechanism is unknown. Areas of bone having excess negative charge are subject to increased deposition of bone matrix, while areas of positive potential are subject to increased resorption of existing bone matrix (Dealler 1981). This hypothesis is based on observations that, during chronic flexure of living bone, the areas of bone undergoing compression are the sites of both increased bone formation ("Wolff's law," Wolff 1892) and increased negative charge (Bassett and Becker 1962; Fukuda and Yasuda 1957), while the areas undergoing tension are the sites of bone resorption and positive charge. Numerous experimental and clinical studies (e.g., Brighton, Friedenberg, and Black 1979) have confirmed that bone formation was increased in the immediate area of an implanted negative electrode and bone resorption was increased in the area of the positive electrode. A window or optimum range of currents within which these effects are observable is generally specified as 5 to 20 μA, with no effect observed at lower currents and cell death occurring at higher currents (Friedenberg et al. 1970). (Note that there is considerable controversy about the actual current and voltage levels experienced by individual bone cells, because the microscopic impedance of bone is complex and incompletely measured.)

Studies of Fracture Healing With DC Electrodes. In 1964, Bassett, Pawluk, and Becker reported stimulation of bone growth in vivo using implanted electrodes in unfractured dog bone. This led to a variety of studies with various apparati and with widely varying results (summarized in Hassler et al. 1977). The first clearly documented successful studies of fracture healing using implanted electrodes were those reported by Friedenberg et al. (1971), in which fibular fractures in rabbits healed significantly faster than sham-treated controls by application of 10 μA of direct current by a negative electrode implanted directly in the fracture site. Friedenberg, Harlow, and Brighton (1971) reported a single human case of a nonunion fracture that was healed by a similar apparatus. Subsequent case reports and large clinical studies (e.g., Brighton et al. 1981; Paterson, Lewis, and Cass 1980) documented improved healing of nonunion fractures (i.e., those not healing under classical therapy) and congenital bone defects (pseudoarthroses and failed arthrodeses) by means of direct currents and implanted electrodes. The effectiveness rate for procedures that use either fully implanted or percutaneous electrodes is generally cited as over 80 percent, with some variations at different clinical facilities.

Effects of Induced Pulsing Electromagnetic Fields (PEMF). Early studies of the electromagnetic properties of bone found that specific time-varying current pulses could be detected in bone undergoing stresses similar to those involved in locomotion (Bassett and Becker 1962). Pulsed current delivered by implanted electrodes appeared to decrease the amount of tissue damage due to electrolysis at the electrode surface (Levy and Rubin 1972). The group headed by Bassett at Columbia University set out to influence osteogenesis by reproducing these pulses of current using noninvasive means to avoid the complications encountered with invasively implanted electrodes. Early studies attempted to produce pulsing currents in bone by placing the subject between electrostatically charged plates in which the charge was altered rapidly; however, these studies were unsuccessful (Bassett and Hermann 1968). Subsequently, Bassett, Pawluk, and Pilla (1974a, 1974b) developed the strategy of using electromagnetic induction to produce intratissue current flows by means of Helmholtz-type induction coils placed adjacent to the tissue. The coils produced pulses of about 1 mV in the adjacent tissue, at current densities estimated to be about 10 $\mu A/cm^2$ at the tissue level. (Note that although the amplitude and general waveform of the pulses produced by this apparatus resembled those found in living bone, the pulse rise times were microseconds long as opposed to fractions of a second in normal locomotion (Bassett, Pilla, and Pawluk 1977). An initial series of clinical studies with this type of device, using a pulsed waveform with a single 300-μs positive voltage pulse repeated 72 times/s, indicated that at least 70 percent of resistant nonunion fractures and pseudoarthroses were healed by treatment with the device (Bassett, Pilla, and Pawluk 1977). Subsequent larger series of clinical cases have reported success rates for PEMF approaching 90 percent (Bassett, Mitchell, and Gaston 1982).

Subsequent developments in the induced pulsed electrical signal involved use of a burst of about twenty 200-μs pulses, repeated 15 times per second, rather than the earlier single pulse signal, with similar levels of success in fracture treatment (Bassett, Mitchell, and Gaston 1982). However, the single-pulse signal is apparently more effective in the treatment of osteonecrosis and disuse osteoporosis (Bassett 1982). A variety of other externally induced electromagnetic fields have been used in animal and human studies with varying degrees of success. (See McClanahan and Phillips (1983) for additional studies.) No side effects have been reported in the several thousand patients treated thus far (Compere 1982), even though Becker (1974, 1984) asserted that all possible risks of PEMF have not yet been assessed. There is very little support in the research community for this objection.

Effects of ELF on Normal Fracture Healing. Despite the strong evidence that healing of nonunion fractures and pseudoarthroses is accelerated by ELF, there is no convincing evidence from human studies that the treatments so far developed have any influence on healing of uncomplicated fractures. These fractures have not been widely treated with ELF procedures, however, simply because healing begins almost immediately in normal patients. Bassett (1982) implies that once the final repair phases of the healing process have been "triggered," whether by normal events or by ELF, treatment with the fields might only marginally accelerate the remaining events of fracture healing. On the other hand, there have been reports of ELF use to improve incorporation of bone grafts, to facilitate spinal fusions, and to improve certain types of osteoporosis (Bassett 1982; Friedenberg and Brighton 1981). Further research is appropriate on the possible use of ELF in the treatment of orthopedic disorders.

Marino et al. (1979) reported a decrease in fracture repair in rats exposed to 60-Hz electric fields following surgical osteotomies. McClanahan and Phillips (1983) observed a delay in bone repair among rats exposed to 60-Hz electric fields during a 16 to 26-day period that followed surgical osteotomy. Approximate current densities in the rat leg were about 9 $\mu A/cm^2$ for the effective field strength in air of about 65 kV/m. A parallel study of bone growth in rats showed no field effects on bone weight, growth rate, or anatomy.

Potential Mechanisms of ELF Effects. There are as yet no clearly established mechanistic bases for the effects of either DC or pulsed electromagnetic fields on bone healing. Most researchers would agree that regardless of the source of the current, the major locus of the effects is likely to be the active bone cells themselves, primarily osteoblasts. The osteoblast is responsible for synthesis, secretion, and calcification of bone extracellular matrix. Most evidence is persuasive that changes in osteoblast activities are the major functions responsible for bone responses to ELF (Bassett 1982; Dealler 1981; Friedenberg and Brighton 1981; Watson 1979). It is possible, although there is no clear agreement, that DC and PEMF may act on osteoblasts by different mechanisms. DC fields morphologically appear to stimulate osteogenesis mainly by stimulating the proliferation and differentiation of preosteogenic cells in the fibrocartilage matrix that fills the fracture gap in nonunion fractures (Friedenberg et al. 1974). These cells then go on to form new bone as if they had gone through an uninterrupted differentiation induced by the fracture process itself. Brighton and Friedenberg and others have suggested that lowered oxygen tension in the area of the cathode may play a significant role in triggering this differentiation (Brighton and Friedenberg 1974). Other possibilities are local changes in ionic concentrations and/or blood vessels (Becker 1974) or membrane effects on cells by the direct current (Cone 1971).

Bassett (1982), on the other hand, stresses the effects of PEMF on functions of already differentiated bone cells rather than on precursors, suggesting that PEMF is less effective on osteogenesis as a proliferative process per se than it is on stimulating the function of bone cells existing at or near the fracture site. Bassett (1982) classifies the demonstrated tissue effects of PEMF as (1) a major and primary effect of reducing bone destruction, possibly by decreasing the sensitivity of bone cells to parathyroid hormone; (2) increased vascularization of the fracture site; (3) increased rates of bone formation by osteoblasts; and (4) for some PEMF signals, decreased intracellular calcium concentrations in chondrocytes, promoting the replacement of chondrocytes by osteoblasts. A number of in vitro laboratory studies on isolated bone and bone cells, as well as on animal model systems in vivo, support these hypotheses (Bassett 1982).

Although the effects of ELF at the tissue level have been clarified somewhat by research over the past two decades, the primary biochemical and biophysical effects at the molecular or ionic level remain obscure. One clear likelihood for the effects of ELF on bone is that the plasma membrane of target cells is likely to be the initial site of action, leading to subsequent cellular mechanisms. The levels of current and voltage involved in these effects are much lower than those that might be required to overcome the resistance of the plasma membrane and induce intracellular effects directly (Adey 1983). Several laboratories have shown that ELF produces modifications in the activities of the plasma membrane of skeletal tissue cells. For example, Luben and others (e.g., Cain and Luben 1985; Luben and Cain 1984; Luben et al. 1982) have demonstrated that exposure of bone and bone cells in vitro to PEMF causes a membrane-mediated desensitization of the osteoblast to parathyroid hormone. Pilla and others (e.g., Colacicco and Pilla 1983a, 1983b) have examined both calcium transport and sodium transport processes in chick tibia exposed to PEMF, factors likely to be related to osteoblast function. Fitton-Jackson and others (e.g., Fitton-Jackson and Bassett 1980; Fitton-Jackson et al. 1981) have studied the influence of PEMF on chondrogenesis and osteogenesis. Rodan and others have examined the effects of mechanical and electric stimulation on the activity of adenylate cyclase in skeletal tissues (Norton, Rodan, and Bourret 1977; Rodan, Bourret, and Norton 1978). A number of other membrane effects of PEMF have been reported in a variety of systems (Adey 1983; Borgens 1984; Schmukler and Pilla 1982). The possible molecular mechanisms by which these various membrane activities may be influenced by charge flows at or around the membrane, however, remain obscure and will be the subject of future research activities.

Developmental Changes Related to Pulsed Magnetic Fields

Delgado et al. (1982) and Ubeda et al. (1983) reported severe disturbances in embryological development of chicks exposed for 2 days to magnetic fields with peak amplitudes from 0.12 to 12 μT pulsed at repetition rates of 10, 100, and 1000 Hz. Unlike the controls, where malformed embryos were observed about 10 percent of the time, the exposed eggs showed malformation rates greater than 50 percent. Effects depended on pulse repetition rate and magnetic field strength in a manner that suggests a windowed response with maximum effects at 100 Hz, 500-μs pulse duration, 42-μs rise time (later corrected to 1.7 μs (Microwave News 1984)), and an amplitude of 1.0 μT. In comparison with a criterion based on faradaically induced effects in the nervous system (see above) a corrected field has about one-third the temporal gradient (about 0.6 T/s). The effects on embryogenesis were also found sensitive to the orientation of the embryo with respect to the geomagnetic field and to the rise time or spectral composition of the magnetic field pulse.

Delgado et al. (1982) and Ubeda et al. (1983) proposed that developmental deficits can be attributed to an effect on the negatively charged glycosaminoglycans coat at the cell surface, and Ubeda also suggested an effect on membrane ionic transport similar to that proposed by Pilla (1974).

In summary of the work with pulsed magnetic fields, the induced electric fields have an indeterminate effective electric field strength and uncertain spectral distribution that includes the ELF range. Such fields can interact strongly with cell functions. Many cell functions are active at the plasma membrane, and generally, these biochemical processes involve calcium ions. Changes in cellular biochemistry, tissue morphology, and regenerative capacity, as well as effect on normal chick embryogenesis, have been reported. Although there are some data concerning the importance of the magnetic field per se in some experiments, in studies with pulsed magnetic fields, this has been discussed only in connection with the chick embryogenesis studies, where the authors believe induced electric currents may still be the most likely mode to directly affect cellular processes.

SUMMARY

Although desirable, it was not possible to have more detailed critical commentary for the studies described above. Isolated studies or those with especially striking and unexpected results must be examined skeptically as is usual in scientific debate. It is likely that several of the experiments will be subject to revisions in interpretation or in essential findings of fact. Nonetheless, the body of work is now large enough that the generalized conclusions that follow should not be greatly affected by such revisions.

A number of studies were reviewed. Table 1 lists representative examples in apparent order of threshold or characteristic electric field strength.

Table 1 indicates an extraordinary range of more than 8 orders of magnitude from the weakest reported effects to the strongest. There are a few effects, particularly involving excitable membranes, at the order of 0.1 to 1 V/m, but, including the results in frog heart, even the phenomena in this tissue class are spread over 2 orders of magnitude. The data on calcium efflux from chick brain in ELF fields easily involves the weakest fields in this listing. The table excludes all magnetic field effects. If some of these magnetic field effects were included, assuming the applicability of faradaic induction, they would be near the middle of the chart--at about 1 V/m. Note that in the case of the in vivo exposures listed, the estimates of electric field strength represent an upper limit for regions of greatest concentration of current density in the human body.* *Data prior to 1977 are omitted.*

It would be remarkable if one mechanism were to underlie effects over such a broad range. It is possible to discern that the tissues in which the various effects are reported are arranged more or less in a hierarchical fashion beginning with a basic chemical process (binding of the calcium ion to brain tissue) and progressing to responses in various excitable systems that range from synaptic regions to individual cells, muscle tissue, and plant cells. There are far too few data to assume from this observation that the tissues at greater levels of organization require correspondingly greater fields to show an observable effect. One can speculate that effects demonstrable at the lower levels of organization may not be easily observed in short-term studies of tissues functioning at higher levels as a result of the

*On the basis of a maximum current density of 5.5×10^{-3} A/m^2 in the necks of humans exposed to a 10-kV/m vertical 60-Hz field (Kaune and Phillips 1980), one can estimate that the induced currents at 76 Hz in a field of 100 V/m (found adjacent to the antenna) would be about 7×10^{-5} A/m^2, which for a resistivity of 1 ohm-m yields an electric field of 7×10^{-5} V/m, or 70 μV/m.

TABLE 1.

THRESHOLD OR CHARACTERISTIC LEVELS FOR SELECTED BIOLOGICAL EFFECTS OF EXTREMELY LOW FREQUENCY ELECTRIC FIELDS STUDIED IN VITRO

Effect and Comments	Tissue Electric Field Strength (est.) (V/m)	Note
Enhanced calcium efflux from chick brain exposed to 2- or 15-V/m rms	$< 10^{-6}$	1
Enhanced adrenal steroid response from cultures exposed to 10 kV/m	1.5×10^{-4}	2
Loss of diurnal melatonin rhythm (39 and 1.8 kV/m), 60 Hz, in vivo exposure	5×10^{-5} to 10^{-3}	3
Increased excitability on C-T test of synaptic function of rats exposed in vivo (65 kV/m, 60 Hz)	2×10^{-3}	4
Phosphenes	10^{-2} to 10^{-1}	5
Firing rate of invertebrate neurons exposed to about 1 Hz	10^{-1} to 1	6
Mitotic cycle in slime mold exposed to 76 Hz, 0.7 V/m	10^{-1} to 1	7
Various effects on brain tissue calcium, synaptic vesicles, lymphocytes toxicity, lymphocyte kinase activity, pancreatic beta cells, neuroblastoma cells with ELF amplitude-modulated radio frequencies	< 1	8
Excitability of brain tissue slice	1	9
Pulsed magnetic field effects on bone	1	10
Beating rate of frog heart	20 to 30	11
Altered viral production in a host *E. coli* bacterium	0.7 to 1.3×10^{2}	12
Surface migration of membrane macromolecules	$> 10^{2}$	13
Growth of plant roots	250	14

NOTES

1. Bawin and Adey 1976; Blackman et al. 1982a, 1982b, 1983.
2. Lymangrover, Keku, and Seto 1983.
3. Anderson 1984; Anderson et al. 1982; Wilson et al. 1981.
4. Jaffe et al. 1980.
5. Lovsund 1980; Lovsund, Nilsson, and Oberg 1980; Lovsund, Oberg, and Nilsson 1979.
6. Sheppard 1980; Terzuolo and Bullock 1956; Wachtel 1979.
7. Goodman, Greenebaum, and Marron 1976, 1979; Marron, Goodman, and Greenebaum 1975.
8. Bawin, Adey, and Sabbot 1978; Bawin, Kaczmarek, and Adey 1975; Bawin, Sheppard, and Adey 1978; Blackman et al. 1979, 1980; Byus et al. 1984; Dutta et al. 1984; Jolley et al. 1983; Lin-Liu and Adey 1982; Lyle et al. 1983; Merritt, Shelton, and Chamness 1982; Schwartz, Delorme, and Mealing 1983; Shelton and Merritt 1981; Sheppard, Bawin, and Adey 1979.
9. Abu-Assal et al. 1985; Bawin et al. 1984.
10. Bassett, Pilla, and Pawluk 1977; Fitton-Jackson, Farndale, and Jones 1980; Luben et al. 1982; Pilla 1980.
11. Kloss and Carstensen 1983.
12. Williams 1983.
13. Lin-Liu, Adey, and Poo 1984; McLaughlin and Poo 1981; Poo 1981; Poo, Poo, and Lam 1978; Poo et al. 1979.
14. Miller et al. 1979, 1980, 1984.

complex regulatory mechanisms, competing chemical reactions, or compensatory physiological mechanisms.

A number of studies with time-varying magnetic fields also may be considered on the basis of the estimated induced electric fields. These studies are presented in Table 2.

Table 2 exhibits the remarkably wide range over which effects have been reported. Categorization into strong and weak fields, with an approximate division at 10 μT and 10^{-2} T/s is possible. However, it is likely that this is merely an accident of the few papers and an arbitrary selection process by both experimenters and this reviewer.

It appears that the experiments involving the stronger magnetic fields can be interpreted on the basis of induced electric currents, whereas the weak field findings do not appear to be described in terms of the induced currents. One study, involving fibroblast cell growth, explicitly found evidence against such a basis.

Several factors make it difficult to understand the extent of the biological effects of environmental electric and magnetic fields, including the existence of credible data for phenomena of unknown significance for human health; the absence of an established field "signature"; few links between most of the biological systems in which effects have so far been seen; and inadequate theoretical understanding of the physical or biological basis for an interaction. The circumstantial evidence for effects on cellular genetic material or its expression is especially baffling in view of the robust nature of these biochemical processes and the absence of any direct means for the field to affect those processes. Where these effects are clearly related to fields, they are probably manifestations of intermediate biochemical alterations in the cell, although in at least one example at a high field strength, a membrane-bound virus may have been affected by a change in the cell membrane.

In this situation, it is possible to conclude that an agent such as the ELF electric or magnetic field, which at the strongest levels does not produce characteristic pathological changes, cannot be a practical problem. Or to the contrary, it is possible to conclude that, in general, the potential for undesirable or harmful effects cannot yet be evaluated if fundamental cellular processes are modified by extremely weak fields acting by unknown mechanisms.

TABLE 2.

THRESHOLD OR CHARACTERISTIC LEVELS FOR SELECTED BIOLOGICAL EFFECTS OF EXTREMELY LOW FREQUENCY MAGNETIC FIELDS STUDIED IN VITRO

(arranged in order of increasing induced electric field)

Effect	Magnetic Field Characteristics	Note
Fibroblast growth in sinusoidal fields, 15 Hz to 4 kHz	2.3 to 56 μT 5 to 25 μT/s	1
Defective chick embryogenesis	1.2 μT; 2.8×10^{-2} T/s	2
Slime mold exposed to 76 Hz	0.2 mT; 0.1 T/s	3
Magnetophosphenes (maximum sensitivity at 20 Hz)	20 mT; 2 T/s	4
Firing rate of invertebrate neurons sinusoidal fields at 60 Hz square wave fields	 11.5-mT rms; 4-T/s rms 16.2 mT; 23 T/s	5
Biochemical responses in cultured bone tissue	2 mT; 10^2 T/s	6
Stimulated bone repair	2 mT; 10^2 T/s	7

NOTES

1. Liboff et al. 1984.
2. Delgado et al. 1982; Ubeda et al. 1983.
3. Goodman, Greenebaum, and Marron 1976; Greenebaum, Goodman, and Marron 1979; Marron, Goodman, and Greenebaum 1975.
4. Budinger 1981; Lovsund 1980; Lovsund, Nilsson, and Oberg 1980; Lovsund, Oberg, and Nilsson 1979.
5. Sheppard, Burton, and Adey 1983 (3-mm fluid depth).
6. Luben et al. 1982.
7. Bassett, Pawluk, and Pilla 1974a, 1974b.

Lack of information about the phenomena and mechanisms is such that only this latter conclusion is scientifically sound.

It would be wrong, however, to adopt this view and, further, determine the inability to comprehend that the phenomena presumes that harmful effects are likely. Although several effects on basic biological systems have been identified in vitro, in only one case has a biological system been altered to the extent that it is abnormal or ineffective. This exception is the strong suppression of melatonin synthesis for in vivo exposed rats. There is not yet a link established between the altered melatonin and related physiological processes (e.g., reproductive function, circadian rhythmicity) that might be coupled to melatonin.

In vitro studies indicate that frequency and field strength windowing of the response are important considerations, but their significance should not be overstated. The final evidence for the physiological significance of windowing must be obtained from studies in whole organisms for which many factors may smooth or eliminate the sharp responses seen in vitro. However, until the window effects are better understood, experiments that try to account for possible response windows must be designed.

The in vitro data strongly suggest that electric field interactions do not follow the models developed for established environmental agents (i.e., toxic chemicals, ionizing radiation, nonionizing radiation, physical factors, or infectious agents) insofar as the "dose response" relations (as they exist) are not simple, nor are they described by a model. Unlike studies with toxicologic agents, the effects at high levels in the laboratory may not scale to the effects that occur in an entire population exposed at lower levels due to either threshold, saturation, or windowing of effects.

A meaningful comparison can be made between the ELF Communications System's fields and the 60-Hz fields found in the environment due to the prevalent use of 60-Hz electric power. In comparison with the ELF Communications System's fields at 76 Hz, which are never more than 120 V/m at points beneath the antenna wire and are attenuated to less than 10 V/m at points more than 35 m from the antenna, electric fields in the home near appliances are often in the range 1 to 100 V/m, and household fields appear to fall in the range of to 1 to 20 V/m (Caola, Deno, and Dymek 1983).

The ELF Communications System's antenna produces a 76-Hz magnetic field that exceeds the typical household field of about 0.1 μT (Appendix A; Caola, Deno, and Dymek 1983) for a distance of 300 m from the antenna line and never exceeds 3 μT anywhere at ground level. At 76 Hz, the maximum temporal gradient of the magnetic field is 0.23 mT/s, and at 300 m, it is 47 μT/s. This should be compared with 2 T/s for induction of effects in the nervous system, or 0.28 mT/s reported effective in inducing defective chick development, or 5 to 25 μT/s reported effective in some cell culture studies. Thus, of the effects from time-varying magnetic fields, the effects on chick embryogenesis and the slight alteration in cell growth rate observed in fibroblasts were observed at flux rates of change similar to values in the antenna environment out to 300 m. At field strengths found beyond 300 m, no in vitro experiment indicates any biological effects. Note that the fibroblast data explicitly rule out an explanation on the basis of a time rate of change in field, and thus, consideration of those data on the basis of the time variation of the field is illogical.

CONCLUSIONS

The following conclusions can be drawn from in vitro studies of cellular systems:

- A review of the experimental data shows that electric and magnetic fields of various strengths, frequencies, and waveforms can alter biochemical and physiological functions in cellular systems. It is difficult to be precise in the extrapolation from in vitro exposure conditions to in vivo. However, it is clear that in many cases the in vitro exposure conditions could not occur for any environmental exposure, and in other cases the tissue-level field strengths are at the level of some exceptional environmental exposures that could not be achieved by the ELF Communications System. Generally, the System's electric and magnetic fields are so weak that very few studies examined fields at that level.

- The quality of the research conducted with ELF fields varies considerably. A few findings have been replicated or studied intensively enough to be accepted as without obvious artifact or experimental error. Much of the research is at a preliminary level and requires further intensive study before results can be accepted without serious question.

- With the exception of studies on magnetophosphenes and bone growth, the functional or biochemical changes seen in vitro have not been closely linked to in vivo conditions, nor has the expression of the laboratory observations in a whole organism been established.

- At the very low field strengths typical of the ELF Communications System antenna environment, only the calcium efflux studies appear to involve similar strength electric fields. Only the studies of slime mold mitotic cycle, fibroblast growth, and chick embryogenesis involve magnetic fields like those of the System, and these occur only close to the antenna wire.
- None of the in vitro studies or other studies of cellular systems indicates that significant functional changes might occur in organisms subjected to the electric and magnetic fields in air near the ELF Communications System's antenna.
- On the basis of an analysis of the literature on biological effects of ELF electric and magnetic fields on cellular systems, and despite the considerable uncertainties on issues of biological interest and importance, there is essentially no probability of deleterious biological effects on organisms exposed to the ELF Communications System's fields in air.

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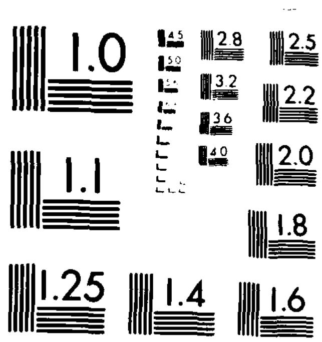

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CHAPTER 6

INTERACTION OF ELF ELECTRIC AND MAGNETIC FIELDS WITH NEURAL AND NEUROENDOCRINE SYSTEMS

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INTRODUCTION

Many of the biological effects observed in animals exposed to extremely low frequency (ELF) electric fields appear to be directly or indirectly associated with the nervous system. This apparent relationship is not altogether unexpected because the nervous system is fundamentally involved in the interaction of animals with their environment. The major segments of that interaction (transmittal of sensory input from external stimuli, central processing of such information, and subsequent efferent innervation of tissues or organs) may provide both the mechanisms and the explanations for possible links between ELF exposure and observed biological consequences. Additionally, it should be noted that influences of the nervous system on other biological systems are often mediated indirectly through neuroendocrine or endocrine responses.

In early experimental studies, nervous system parameters were measured only occasionally, although many of the observed effects, especially those involving behavior, were related to nervous system function. Reports from the the Soviet Union in the late 1960s and early 1970s claimed a variety of exposure-related neurological symptoms, including headaches and increased excitability in switchyard workers (Asanova and Rakov 1966; Korobkova et al. 1972). Although it was not possible to conclude that these reported functional, somewhat subjective changes were the result of exposure to electromagnetic fields, the findings led to increased research in the USSR and throughout the rest of the world. Numerous studies were initiated to assess the potential biological consequences of exposure to ELF electromagnetic radiation. Results of these initial studies are summarized in several outstanding reviews: National Academy of Sciences (1977), Phillips and Kaune (1977), and Sheppard and Eisenbud (1977).

Prior to 1977, studies on ELF exposure that related to nervous system function could generally be classified into three categories: (1) assessments of activity or startle-response behavior; (2) evaluations of stress-related hormones (e.g., corticosteroids); and (3) general measurements of central nervous system responses (e.g., electroencephalograms (EEG) and inter-response times). The results were often contradictory, resulting in claims of both effects and noneffects due to ELF exposure. Because of the apparent sensitivity of the nervous system to ELF fields, studies were subsequently expanded to include a wider range of neurological assessments. Concomitant with this increased emphasis, investigators began to use specific nervous system responses as biological end points. This effort was mounted to determine the extent and nature of ELF-tissue interaction and to attempt to understand the mechanisms underlying the observed biological effects.

This review will focus on research conducted since 1977 that examines the effects of 1- to 300-Hz ELF exposure on the neural and neuroendocrine systems. Some of the experimental results reviewed here may overlap those reviewed in other chapters (e.g., magnetic fields effects, cellular, and human studies). By far the largest body of data comes from experimental work conducted at power-frequency fields of 50 to 60 Hz. Fewer investigations, including some cellular and in vitro studies, have been conducted at lower frequencies (15 to 35 Hz); essentially no studies have been performed at frequencies between 75 and 300 Hz.

An overview of the available literature suggests that ELF electric-field exposure is an environmental agent or influence of relatively low potential toxicity to biological systems. There are no well-supported examples of ELF-related neuropathological conditions. Generally, many of the biological effects reported are quite subtle, and differences between exposed and unexposed subjects may be masked by normal biological variations. Careful examination of the data, however, emphasizes the limited understanding of biological interactions with electromagnetic fields, and the questions concerning the potential health implications of ELF electric-field exposure have yet to be clarified.

HUMAN STUDIES

Principal sources of information on the effects of ELF fields on man are surveys of utility workers and people living in the vicinity of high-voltage lines, as well as a few laboratory and clinical investigations and several epidemiological studies. The value of most of the human studies to date has been compromised by one or more of three serious problems: (1) small sample sizes, with extremely limited statistical power; (2) failure to obtain quantitative data on levels and durations of exposure; and (3) failure to include an appropriate control group. Although these difficulties do not necessarily invalidate the results of such studies, it is important to recognize these potential biases and problems when evaluating the results.

Laboratory Studies

With the exception of some behavioral parameters, few human studies have addressed the effects of ELF exposure on the nervous or neuroendocrine systems. Probably the most extensive and important laboratory experiments using human subjects were conducted by Hauf and coworkers in Germany (Hauf 1974, 1976a, 1976b). Beginning in 1974, the comprehensive clinical work evaluated over 100 volunteer subjects exposed for relatively brief periods (two 45-min sessions for three consecutive days) to 1-, 15-, or 20-kV/m, 50-Hz fields. Of the many parameters tested, no field-related effects were observed in EEG patterns; however, a slight reduction in reaction time was seen in exposed subjects. These data, along with data from a small epidemiological medical evaluation study involving 32 subjects exposed in a 380-kV facility (Bauchinger et al. 1981), are summarized in a semicritical review paper by Hauf (1982). Again, no changes in behavior or EEG patterns were seen. In exposed subjects, a slight elevation was observed in levels of norepinephrine, which, the authors proposed, might reflect a minor stress situation. In a further attempt to accurately define the cause of the slight variations indicated, Hauf conducted a study on the effects of injected currents (200 μA) in humans. These currents, calculated to equal the displacement currents expected from previous electric-field exposures, caused no alterations in either reaction times or EEG. These results led Hauf to conclude that the slight effects previously observed in exposed subjects were probably due to "unspecified stimulation" effects (Hauf 1976b).

A more recent study involving laboratory exposure of human subjects has been conducted by Cabanes and Gary (1981) in France. In this study, no specific neural parameters were measured; rather, the object of the experiment was to determine the threshold for perception of a 50-Hz electric field. Seventy-five subjects were exposed to varying electric fields in three body positions. Thresholds for perception ranged from 0.35 kV/m in 4 percent of the subjects to greater than 27 kV/m. Forty percent of the subjects did not detect 27 kV/m with their arms against the body. Data that support these results were obtained by Deno and Zaffanella (1982), who conducted comparable experiments using 60-Hz fields. They reported similar results: 5 percent of the exposed subjects were able to detect a 1-kV/m field; the median for perception was 7 kV/m. If this large perceptual threshold variation applies to other species, it may provide some explanation for the great variability in biological data obtained to date.

Epidemiological Studies

Two epidemiological studies containing some neurological data analyses have been reported during the past 6 yr. Stoops and Janischewskyj (1979) and Knave et al. (1979) have described carefully conducted health surveys in electrical workers. These exceptionally thorough studies examined, over a period of 5 to 10 yr, a wide range of biological variables. Neither study reported significant effects on nervous system function. The Stoops and Janischewskyj study is one of the few epidemiological studies in which field characteristics and length of exposures are defined. Results, in both cases, agree with the few other human studies examining neurological parameters in showing no significant effects. Unfortunately, both studies are based on small numbers of subjects (30 and 53 men, respectively).

Magnetic Field Studies

ELF magnetic fields of moderate intensity (100 G or more) produce a visual phenomenon, know as "phosphenes," in man (Lövsund, Öberg, and Nilsson 1979). This phenomena appears to arise from the induction of electric currents in the retina and is highly frequency-dependent, with maximum effects at approximately 20 Hz (see Chapter 4 for more detailed discussion). Other magnetic field effects on neural tissue or neurochemistry in man are relatively unexplored, and to date, no effects have been found (Sheppard 1978, 1983). Based on a review of all the available literature concerning neural effects in humans exposed to low intensity electric fields, the conclusions of the National Academy of Sciences (1977) still stand: no behavioral, neurophysiological, or neurochemical effects would be predicted from the available data.

ANIMAL STUDIES

Although the interaction of humans with electric fields is of prime concern, many areas of biological investigation are more efficiently and appropriately conducted using various other animal species. Experiments have been performed primarily using rodents (mice and rats), but a wide variety of other subjects have also been used, including insects, birds, dogs, swine, and nonhuman primates. Exposures have varied from a few volts per meter to more than 100 kV/m, and as in the human studies, most of the experimental work has been conducted at powerline frequencies of 50 to 60 Hz. Because of the large number of studies conducted on animals, this review will address only those studies that examine neurochemical, neuroanatomical, neurophysiological and neuroendocrinological functions. In addition, nervous-system related areas of behavior and circadian effects will be briefly reviewed particularly as they pertain to specific chemical or physiological impacts of ELF exposure on the nervous system.

Neurochemistry

The relationship between the neurotransmitters (norepinephrine/epinephrine) and the physiological responses of stress and arousal is well established. As researchers investigated the potential biological effects of ELF electric fields, measurement of these neurotransmitters was one assessment used to examine the state of the nervous system. This was, in part, because these chemicals are easily measured in blood, urine, or brain tissue. Another reason was that ELF fields were reported to act as mild stressors (Dumansky, Popovich, and Prokhvatilo 1976; Marino et al. 1977). Unfortunately, some of the potential methodological problems that raised questions as to the validity of these early reports (Michaelson 1979) have also been evident in subsequent studies.

Groza, Carmacia, and Bubuiann (1978) measured catecholamines in both urine and blood following exposure of rats to 100-kV/m, 60-Hz fields. They reported significant increases in epinephrine levels in both blood and urine following acute (6-h to-3 day) exposures, but no changes in norepinephrine or epinephrine with longer term (12-day) exposures. The presentation of their methods is somewhat difficult to follow, and the data show a lack of reliability, possibly because of the assay methods chosen.

Increased norepinephrine levels in the blood of rats exposed to 50-Hz fields (50 V/m and 5.3 kV/m) were reported by Mose (1978). A companion paper by Fisher, Udermann, and Knapp (1978) examined norepinephrine content in the brain tissue of rats exposed to 5.3 kV/m for 21 days. After 15 min of exposure, the levels increased rapidly; however, after 10 days of exposure, levels were significantly decreased when compared to those of a control group.

Examining another neurochemical parameter, Kozyarin (1981) and Babovich and Kozyarin (1979) have measured acetylcholinesterase (AChE) enzyme in rats exposed to 50-Hz electric fields. They reported that blood AChE activity was higher than normal, by approximately 25 percent, in both young and old animals exposed to 15 kV/m for 60 days, 30 min/day. Brain levels of AChE were lower than normal in exposed animals, although not by such large percentages. All values had returned to normal one month following cessation of exposure. The authors concluded that electric fields can cause changes in the functional condition of the central nervous system, although the changes appeared not to be permanent. The earlier paper (Babovich and Kozyarin 1979) suffers from the same major weaknesses that have reduced the value of much of the Soviet work (e.g., no animal numbers are provided and only the briefest mention of any statistical evaluation of the data are given). No methods or sampling information were published, and only a few references were given. This study did have a control group, but no information is presented on the exposure system or conditions. The later paper (Kozyarin 1981) includes the number of animals per group (10) and presents a statistical analysis. However, general deficiencies in reporting methods and results make it extremely difficult to evaluate the significance of these studies.

A number of studies have examined the role of Ca^{++} in tissue response to ELF exposure. This research has been conducted primarily with in vitro preparations and is extensively reviewed in Chapter 5 of this report.

In general, neurochemical data provide only weak evidence that exposure to electric fields in the power-frequency range causes slight changes in nervous system function. The number of experiments is small, and there are significant questions about the validity of several of the studies. Nevertheless, the findings are quite consistent across studies and agree with the hypothesis that ELF exposure may result in increased arousal in the animal.

Neuroanatomy

Several laboratories have examined the morphology of brain tissue from animals exposed to ELF electric fields. Carter and Graves (1975) and Bankoske, McKee, and Graves (1976) exposed chicks to 40 kV/m and observed no effects on central nervous system morphology. This finding was supported by the findings of Phillips et al. (1978), who examined rats exposed to 100 kV/m for 30 days. Again, no morphological evidence of an electric field effect was observed. However, results from a recent study in Sweden (Hansson 1981a, 1981b) suggest dramatic changes in the cell structure in the cerebellum of rabbits exposed to 14 kV/m. Exposed animals showed disintegration of Nissl bodies and the three-dimensional endoplasmic reticulum structure, as well as the abnormal presence of many lamallar bodies, particularly in the Purkinje cells of the cerebellum. Reduced numbers of mitochondria, reduced arborization of the dendritic branches, and an absence of hypolemmal cisterns was also evident in these cells. These changes, which are in conflict with the above mentioned earlier reports in a different species, would, if substantiated, represent major alterations in cellular structure for which serious dysfunctional changes in cells would be expected. Therefore, this work represents either a very important observation or an impressive artifact. However, two questions arise concerning the interpretation of these results: (1) the health of the exposed animals was clearly compromised, although a companion study apparently did not show the same health problems in the exposed rabbits, and (2) it is unclear whether the evaluation of exposed and control animal tissues by electron microscopy was performed "blind." Additionally, methods used for preparing tissue for electron microscopy were not clearly described, leading to potentially equivocal results because of artifacts.

These questions concerning neuroanatomical changes have yet to be resolved. However, the lack of obvious significant central nervous system functional deficits in the thousands of animals exposed to date suggests that the dramatic morphological alterations reported in rabbits may result from something other than electric field exposure.

Neurophysiology

Possibly because the nervous system is by nature an electrically sensitive system, it has been assumed that it would be particularly influenced by external electric fields. To some degree, this assumption has been borne out by experimental results, although in the area of neurophysiology, there is a confusing array of studies claiming both effects and noneffects of ELF field exposure. Several examples are described below.

In an early study by Blanchi et al. (1973), significant changes in EEG activity were seen when guinea pigs were exposed for a half hour to a 100-kV/m, 50-Hz field. Beischer and Knepton (1966) discovered a large effect on EEG amplitudes and power spectra when squirrel monkeys were exposed to very high magnetic fields (2 to 9 T). Takashima, Onaral, and Schwan (1979) examined the EEGs of rabbits, exposed at 1 to 10 MHz and modulated at 15 Hz, that had silver-electrode implants for recording the EEG. After 2 to 3 weeks of exposure, the EEGs were abnormal. However, if the electrodes were removed during actual exposure, the EEG returned to normal. The investigators thus concluded that the effect on the EEG was due to the local fields created by the presence of the electrodes in the cranial cavity. In a similar but somewhat more refined assessment, Jaffe et al. (1983) performed assessments of the visual evoked response in 114 rats exposed in utero through 20 days postpartum to a 65-kV/m, 60-Hz electric field. No consistent, statistically significant effects of exposure were observed.

Two other excellent neurophysiological studies have provided clear, replicable results. In the first, Jaffe et al. (1980) demonstrated an enhanced neuronal excitability in synaptic junctions from exposed rats (60 Hz, 100 kV/m, for 30 days). An effect was evident in the conditioning-test response, but many other parameters tested showed no changes in exposed animals. The second experiment (Jaffe, Laszewski, and Carr 1981) examined a wide range of physiological parameters of the peripheral nervous system and the neuromuscular junction. The only effect to be observed was a slightly faster recovery from fatigue after chronic stimulation in one class of muscle (the soleus, slow-twitch muscle).

There is some confusion regarding the EEG response to electric field exposure. However, in an assessment of a more specific electrical "fingerprint" of the brain, the visual-evoked response, no effects due to exposure were observed either in the adult or developing rat. The evidence from these two well-designed studies indicates a general lack of effects on the peripheral nervous system and a possible enhancement of neuronal excitability in the autonomic nervous system.

Neuroendocrinology

The studies that have examined possible effects of ELF electric field exposure on neuroendocrine function can be divided into two classes: the work on the pineal gland, and its associated hormone products, and studies related to corticosteroids of the adrenal gland. Data in the first area are limited but straightforward; the latter effort is addressed in many studies, often with conflicting results.

Concentrations of neuroendocrine substances in pineal glands were significantly changed when rats were exposed for 30 days to either 65 kV/m or 1.9 kV/m (Wilson et al. 1981). Both melatonin and an associated biosynthetic enzyme, serotonin-n-acetyl transferase (SNAT) showed a dark phase decrease in exposed animals; levels of 5-methoxytryptophol, another neuroendocrine product of the gland, was increased at night. Tests at intervals of from 1 h to 4 weeks after the start of exposure showed that at least 3 weeks of exposure was required for the effect to reach significance (Anderson et al. 1982). The position of the pineal gland as a "neuroendocrine transducer" and its integral tie with the circadian cycle make this effect particularly interesting. Several other indications that electric field effects relate to circadian cycling seem to tie these results together and emphasize the possibility of electric field influences on such rhythms (Russell and Ehret 1982; Sulzman 1985). Although they did not use AC fields, three recent studies have reported decreases in nocturnal pineal components in mice and rats exposed to rotated magnetic fields (Kavaliers, Ossenkopp, and Hirst 1984; Semm 1983; Welker et al. 1983).

Measurements of corticosteroids in animals exposed to electric fields have resulted in a somewhat confusing picture, perhaps due to the rapid response to stimulus of these adrenal steroids (Michaelson 1979). Studies at The Pennsylvania State University examined the hypothesis that 60-Hz electric fields act as a biological stressor (Hackman and Graves 1981). Corticosterone levels in plasma in that study showed an acute, transient increase in mice exposed to 25 or 50 kV/m; levels of steroid return to normal within a short time. Earlier studies conducted in the USSR (Dumansky, Popovich, and Prokhvatilo 1976) also showed an increase in corticosteroids in rats exposed for 1, 3, or 4 months to 5 kV/m.

A study conducted by Marino et al. (1977) showed a decrease in serum corticosteroid in animals exposed for 30 days to 15 kV/m; however, pooled group samples of serum were used in this study. It also had several other potential problems, e.g., in four of the experiments, exposed rats were individually housed, whereas control rats were group-housed.

Studies in which rats were exposed to 100 kV/m for 30 or 120 days provided negative results that contradict the Marino et al. (1977) and Dumansky, Popovich, and Prokhvatilo (1976) data (Free et al. 1981). Gann (1976) provided additional support for these data showing no effect on adrenal secretion in dogs exposed to 15 kV/m.

Behavior

There is extensive literature on the behavioral effects of electric fields. Field intensities in these studies range from less than 1 V/m to above 100 kV/m. Several species of animals have served as subjects, and the studies have examined both short-term and chronic exposure conditions.

Nonhuman primates provide an excellent model for generalizing the experimental findings of ELF electric field exposure to man. Several such studies were conducted in the early 1970s and were reviewed in the 1977 National Academy of Sciences' document. Experiments conducted since that review are few, including behavioral studies in the baboon and a recently initiated study using the pigtailed macaque. Results are not yet available from the latter investigation; however, preliminary results in the former study suggest that baboons exhibit sensitivity to a 60-Hz field at 30 kV/m (Feldstone et al. 1981). Exposed animals show increased startle and arousal responses that quickly disappear with continued exposure. The authors conclude that none of the behavioral effects seen in baboons were permanent or harmful.

The majority of investigations on ELF effects on behavior have been conducted using rodents as experimental subjects exposed to a wide range of field intensities. In these studies, many of which present somewhat contradictory results, motor activity is the most commonly measured behavioral end point. Smith, D'Andrea, and Gandhi (1979) examined exploratory activity in rats exposed to a 60-Hz, 25-kV/m field and found no effect of exposure. Babovich and Kozyarin (1979), however, observed changes in unconditioned reflexes produced by daily exposure to 50-Hz, 7-kV/m fields. These effects had disappeared by one month of exposure. Hilmer and Tembrock (1970) reported increased activity at night in rats exposed to 50 Hz, 50 to 70 kV/m. These results are in contrast to those of Bawin et al. (1979), who reported decreased motor activity at night in rats exposed to 1 kV/m.

Some of these activity changes may be produced by some type of peripheral stimulation in the animals during exposure to the field, particularly during the initial exposures. Behavioral evidence, in this regard, supports the neuroendocrinological data. Rosenberg, Duffy, and Sacher (1981) reported that the general activity level in mice increased during the inactive phase of their circadian cycle when initially exposed to a 60-Hz, 100-kV/m field. This arousal response, however, was quickly extinguished with repeated exposures. It was further demonstrated that field strengths lower than 50 kV/m seldom produced reliable arousal responses (Rosenberg et al. 1983).

Differential responses to a gradient of voltage levels has been demonstrated by other investigations in rats. Hjeresen et al. (1980) observed avoidance behavior to 60-Hz fields greater than 75 kV/m. In 24 h tests, a field aversion at 75 kV/m and higher and a preference for fields of 25 and 50 kV/m were shown. Exposed rats were also more active during the first hour of exposure, concurring with the results of Rosenberg, Duffy, and Sacher (1981). A similar study with swine (Hjeresen et al. 1982) showed that pigs also spent most of their time out of the field at 30 kV/m. The basis for these preference and aversion behaviors has not been identified.

Rats probably can detect the presence of electric fields at levels as low as 1 kV/m, although the average threshold for preception appears to be between 4 and 10 kV/m (Stern et al. 1983). Graves et al. (1978) observed that pigeons detect 60-Hz electric fields at 32 kV/m, and Kaune et al. (1978) report detection limits of fields in pigs to be approximately 30 to 35 kV/m.

Evidence for a direct effect on the nervous system as revealed in behavior is not available. For example, the possibility of an effect on the developing nervous sytem was investigated in two experiments using a visually evoked response (Jaffe et al. 1983). These investigations could find no effects on the visual evoked response when rat pups were exposed to a 60-Hz, 65-kV/m field for 20 h/day from conception to 11 or 20 days after birth.

In conclusion, evidence for detrimental effects on behavior from exposure to electric fields at transmission line frequencies and intensities is sparse and contradictory. The preponderance of research shows that when behavioral effects do occur they are minimal and probably relate to an animal's ability to perceive the electric field. In those cases, the field seems to function as do other low-level novel stimuli, and adaptation occurs quickly with no cumulative effects. No harmful or even stressful effects seem to be present at intensities in the range of those proposed in the ELF Communications System.

SUMMARY AND CONCLUSIONS

Numerous studies have been initiated to determine to what extent an electrical environment containing electric or magnetic fields of 1 to 300 Hz poses a health hazard to living organisms (particularly to humans). The biological effects reported in many of the experiments have not yet confirmed any pathological effects, even after prolonged exposures to high-strength (100-kV/m) fields or high-intensity magnetic (10-mT) fields. Areas in which effects have been demonstrated appear to be primarily associated with the nervous system, including altered neuronal excitability, altered circadian levels of pineal hormones, and indications of transient arousal responses. In addition, in several instances where unconfirmed or controversial data exist, observed effects may or may not be real (e.g., changes in serum catecholamines or corticosteroids, morphology of brain tissue, and changes in electroencephalographic wave forms). It is not yet known whether these and other putative effects are due to a direct interaction of the electric field with tissue or to an indirect interaction, e.g., a physiological response due to detection or sensory stimulation by the field. The nature of the physical mechanisms involved in field-induced effects is obscure, and such knowledge is one of the urgent goals of current research.

Results to date have demonstrated various neurological effects in specific species exposed in the laboratory to a wide range of field strengths. The extrapolation of specific effects that occurred under controlled laboratory conditions to a general assessment of the health risk for a human population exposed to electric or magnetic fields is very tenuous. At least four considerations are critical to implement such an extrapolation with validity: (1) the relationship of specific laboratory conditions to the real-world environment; (2) the relevance of effects in laboratory animals to other species, particularly humans; (3) dosimetric considerations, including scaling between species; and (4) an evaluation of the biological consequences of observed effects.

Many of the experiments reviewed in this report were designed to study the effects of electric fields under laboratory conditions and a few were designed to study magnetic fields under those conditions. Because most experiments were performed at frequencies of 50 to 60 Hz, field strengths and intensities usually corresponded to those characteristic of power lines; however, factors other than the electric field may have affected experimental results. Such factors (e.g., ozone, ions, spark discharge, audible noise) can produce biological effects and must be recognized and controlled to determine whether the electric or magnetic field is actually the agent responsible for the observed effects.

Any extrapolation of effects from one species to another depends on the mechanism by which the field exerts its influence on the biological system. This requires a knowledge of the biological structures and functions involved, as well as dosimetric scaling of exposure from the test animal to another species. It is hoped that the rapidly expanding knowledge of interactions between electric fields and neural tissue and systems will hasten this understanding.

Perhaps most difficult is the question of when the occurrence of a "biological effect" constitutes a health hazard. Specific answers may be forthcoming; however, experimental results to date show no clear implications of health risks to humans exposed to a range of from 1- to 300-Hz electric fields. The amount of data on comparable magnetic fields is still too minimal to make such an assessment.

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CHAPTER 7

HEMATOLOGIC AND IMMUNOLOGIC EFFECTS OF EXTREMELY LOW FREQUENCY ELECTROMAGNETIC FIELDS*

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INTRODUCTION

Over the past several years, a substantial research effort has been mounted in an attempt to determine what effects, if any, extremely low frequency (ELF) fields have on biological systems. For the most part, this research has been motivated by a growing concern, within the scientific community and consequently the public sector, for potential health and environmental effects associated with ELF exposure. This concern was originally fostered by reports from the Soviet Union literature dealing with ELF-induced biological effects. More recently, as public awareness of this research area has increased, concern has mounted because of the proliferation of ELF-emitting devices that have accompanied technological advancements in this country. In addition to concern for 60-Hz high-voltage generating, storage, and transmission systems, one of the major underlying motivations for increased concern about potential ELF biological effects stems from the U. S. Navy's interest in developing and deploying a submarine communication system with the potential for large scale environmental exposure to ELF.

A literature survey indicates that a substantial effort has been made in response to this exposure concern. Several reviews have indicated a link between ELF and behavioral, neurological, and physiological alterations, as

*This report has been reviewed by the Health Effects Research Laboratory, U. S. Environmental Protection Agency, and approved for publication. Approval does not signify that the contents necessarily reflect the views and policies of the Agency, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

well as cellular and molecular interactions (Anderson and Phillips 1984; Bridges and Preache 1981; Marino and Becker 1977; Sheppard 1983; Tenforde 1984; Waskaas 1981). Unfortunately, much of the earlier (i.e., pre-1977) and some of the current research on ELF biological effects have resulted in inconclusive data with inappropriate interpretation of the results (Bridges and Preache 1981). Consequently, a review of the ELF literature requires careful attention to the experimental design of the reported studies, the ELF exposure system design and exposure regimen, and the statistical analysis of the data in order to avoid arriving at spurious conclusions (Anderson and Phillips 1984).

This chapter critically reviews the reported effects of ELF fields on the hematologic and immunologic systems of laboratory animals. Reports dating from 1978 to the present were evaluated for ELF-induced effects on the cellular and humoral components of these systems during or following in vivo or in vitro exposure. Reference to earlier reports are made as appropriate. On the whole, direct comparisons between many of these studies are difficult to make because of the differences in species, in exposure parameters, and in the biological end points examined. Furthermore, the reported alterations, if present, are generally inconsistent and highly variable, with no apparent trends. Nevertheless, from this review, the following generalizations may be formulated:

- Exposure of animals to ELF fields may lead to a variety of changes in the hematologic or immune systems;
- Such changes are generally transient and reversible with time;
- Some of the earlier (i.e., pre-1978) reported effects of ELF fields on the hematologic and immune systems were probably due to secondary electric field effects (e.g., shocks, noise, vibration, and ozone), which resulted in stress;
- In vitro studies of the reversible alteration of lymphocyte function during amplitude-modulated radiofrequency (RF) radiation are very interesting but require corroborative evidence from both in vitro and in vivo studies; and
- There is currently no convincing evidence from in vivo or in vitro experiments for adverse alterations in the hematopoietic or immune systems following ELF field exposures.

For convenience, this chapter is presented in two general topics: hematologic effects and immunologic effects of ELF fields. The latter topic is further subdivided into reviews of studies in which cellular components of the immune system have been exposed in vitro and studies dealing with in vivo exposure to ELF fields.

HEMATOLOGY

Hematology is the study of the anatomy, physiology, and pathology of the blood and blood-forming tissues. The hematopoietic system is composed of a variety of cells and cell products. In fetal life, the production of blood cells occurs in the liver, spleen, and bone marrow. After birth, this function is limited largely to the bone marrow, which produces red cells (erythrocytes), white cells (neutrophilic, eosinophilic, and basophilic granulocytes; lymphocytes; and monocytes), and platelets. Each of these cell types performs specific functions that are essential to life. For example, mature erythrocytes transport O_2 and CO_2 to tissues, granulocytes and monocytes phagocytize invading microorganisms, and lymphocytes are involved in immune responses. These functional cells are all descendants of progenitors (stem cells) that reside within the bone marrow. Blood-cell formation consists of two essential processes: proliferation and differentiation. Bone marrow progenitor cells proliferate and differentiate into red and white cells. As the process of differentiation progresses, the capacity for cellular proliferation decreases. Impairment of either of these processes may lead to dysfunctions in the hematologic system.

Most reports of ELF-induced changes in the hematopoietic system have focused on the overall distribution and number of the cellular components in peripheral blood. In a review of the pre-1978 literature, Bridges and Preache (1981) indicated that one of the most frequently affected hematological variables in animals exposed to ELF fields was the distribution of leukocytes in peripheral blood. However until recently, little attention has been paid to the underlying causes or potential functional changes associated with these observations. It is important to emphasize that the hematopoietic and, for that matter, the immune system function as multicomponent systems in which no one component functions mutually exclusive of the others. Furthermore, the hematopoietic and immune systems are affected by other physiological systems that can exert their influence either directly or indirectly.

Table 1 summarizes the post-1977 literature on the hematologic effects of ELF fields in experimental animals. Although changes in leukocyte and erythrocyte numbers and distribution have been reported, there is no general trend or consistency within or across studies.

Ragan et al. (1979), in a well-designed group of studies, were unable to identify any unequivocal hematologic effects in rats and mice exposed to 60-Hz ELF fields at unperturbed field strengths of 100 kV/m (rats) and 0.15 to 0.25 kV/m (mice) for 21 h/day for 15, 30, 60, or 120 consecutive days. Although statistically significant differences between exposed and sham-exposed rats and mice were observed in initial studies, these investigators failed to replicate those effects in subsequent experiments. For example, following a 60-day exposure, a significant decrease was observed in circulating neutrophils and lymphocytes from exposed mice. However, in a replicate experiment, just the opposite effect was observed--that is, an increase in neutrophil and lymphocyte counts. When these replicate experiments were combined, no significant differences were observed between exposed and sham-exposed mice. Similarly, in two replicate experiments in which rats were exposed for 15 days to ELF fields at 100 kV/m, leukocyte levels were reduced in one study, but in a subsequent study no reduction was observed.

Application of rigorous statistical evaluations of hematologic data from a series of experiments in which rats were exposed to 60-Hz ELF fields at 100 kV/m for up to 120 days failed to detect any consistent effects (Ragan et al. 1983). These data are presumably those presented above (Ragan et al. 1979). These investigators reported that within any individual study it was not unusual to detect significant differences between exposed and sham-exposed animals for certain variables. They, therefore, emphasized the need to design studies in which replicate experiments are used to ensure corroboration of subtle biological effects due to chemical or physical insults of low toxicity and to use appropriate multivariate analyses (Ragan et al. 1983).

Fam (1980) exposed male and female mice to a 60-Hz field at an unperturbed field strength of 240 kV/m, 22 h/day, 7 days/week for up to 204 days. No differences were observed between exposed and sham-exposed males for the hematologic parameters examined. However, exposed female mice had

TABLE 1

Summary of Studies of Hematologic Effects of ELF Fields

Effects	Species	Exposure Conditions: Fields	Frequency	Field Strength	Duration (day x h)	Reference
No consistent, statistically significant, or reproducible differences in hematologic parameters except an increase in platelet concentration in rats after 60 days	Rats Mice	Electric Electric	60 Hz 60 Hz	100 kV/m 0.15–0.25 kV/m	15, 30, 60, or 120 x 21	Ragan et al. (1979)
No consistent, statistically significant, or reproducible differences in hematologic parameters examined	Rats	Electric	60 Hz	100 kV/m	15, 30, 60, or 120 x 21	Ragan et al. (1983)
Decrease in leukocyte counts and hemoglobin and increase in juvenile neutrophils in females but not males	Mice	Electric	60 Hz	240 kV/m	240 x 22	Fam (1980)
Decrease in erythrocyte count and hematocrit	Mice	Electric	60 Hz	5 kV/m	2 x 24	Marino et al. (1980)
No differences in hematologic parameters	Rats	Electric	45 Hz	2,10,20,50, or 100 V/m	28 x 24	Mathewson et al. (1979)
Increases in neutrophil and lymphocyte counts	Rats	Electric	50 Hz	100 kV/m	56 x 0.5; 14, 35, or 49 x 8	Cerretelli et al. (1979)
Increases in reticulocyte counts and decrease in hemoglobin concentration	Dogs	Electric	50 Hz	25 kV/m	14, 28, or 42 x 8	Cerretelli et al. (1979)
No differences in hematologic parameters	Mice	Magnetic (Alternating)	60 Hz	0.11T	23 x 7	Fam (1981)
No differences in hematologic parameters	Rats	Magnetic (Rotating)	0.5 Hz	10^{-3}, 10^{-4}, or 5×10^{-6}T	5 x 24 (Prenatal and/ or Postnatal)	Persinger et al. (1978)

significantly lower leukocyte counts and lower hemoglobin concentrations compared with sham-exposed females. The decreased hemoglobin concentrations in exposed females was not accompanied by a concomitant decrease in erythrocyte counts nor a decrease in hematocrit, which calls into question the physiological significance of this decrease in hemoglobin. A significant increase in the relative percentage of band neutrophils was observed in exposed females; however, no other shift in leukocyte populations was observed. The increase in juvenile neutrophils and the lack of any shift in the other leukocytes from exposed female mice is not consistent with the observed decrease in total leukocyte count. These results are therefore of questionable value because they are physiologically inconsistent. Ragan et al. (1983) pointed out that Fam (1980) used a univariate t-test to evaluate each hematologic end point rather than a more appropriate multivariate analysis. Furthermore, no replication of this study was performed to corroborate the finds in exposed female mice.

Male and female mice were exposed to a 60-Hz, 5-kV/m electric field for 2 days by Marino et al. (1980). Mice were either sham exposed for 2 days followed by a 2-day ELF exposure or vice versa. Two blood samples were obtained from the orbital sinus from each mouse, one after the first 2-day period and the other after the second 2-day period. A consistent significant decrease in erythrocyte concentration was observed in both male and female mice following the second 2-day period regardless of whether the field exposure preceded or followed the nonexposure. A decrease in hematocrit accompanied the decrease in erythrocyte counts in three of four experiments, but hemoglobin concentrations were decreased in only two experiments. No other consistent changes were observed in the erythrocyte parameters examined. Marino et al. (1980) attributed their findings to the ability of the mice to respond physiologically to a change in their electrical environment rather than as a result of the electric field itself. They indicated that the observed changes were consistent with the electric stress hypothesis (Marino et al. 1976). However, Ragan et al. (1983) questioned this conclusion because "corticosteroids have a stimulatory, not depressive, effect on erythropoiesis." Another criticism of this work by Ragan et al. (1983) deals with the fact that Marino et al. (1980) "treated these highly interdependent parameters as independent variables" in their statistical analysis of the data. In any event, although the measured erythrocyte parameters are somewhat internally consistent, the physiological significance of these findings (Marino et al. 1980) is questionable, particularly because these hematologic values are within normal limits (Mitruka and Rawnsley 1977).

Mathewson et al. (1979) found no consistently reproducible differences between male rats exposed for 28 days (24 h/day) to 45-Hz vertical electric fields at field intensities of 2, 10, 20, 50, or 100 V/m compared with sham-exposed rats in three replicate experiments. In a fourth experiment, in which rats were exposed to 20 V/m for 28 days, no significant differences were observed when exposed rats were compared with controls. The following hematologic parameters were examined: erythrocyte count, hematocrit, hemoglobin concentration, and total and differential leukocyte counts. Furthermore, necropsy and histopathological examination of tissue from 16 organs, including spleen and adrenal gland, revealed no changes that could be attributed to the ELF electric fields.

Cerretelli et al. (1979) exposed rats for periods ranging from 30 min to 8 h per day for up to a total of 2 months to 50-Hz fields at an intensity of 100 kV/m. These investigators found a significant increase in the percentage of neutrophils and a decrease in lymphocytes in peripheral blood under all exposure conditions. These alterations were reported to persist for up to 7 weeks following the ELF exposure. No difference, however, in the total leukocyte count between exposed and control rats was observed under any of the exposure conditions. The significance of these findings is difficult to determine because the actual data were not presented (changes were indicated by +, -, or 0). Furthermore, the statistical analyses used to arrive at the indication of increased (+) or decreased (-) cell counts were not provided.

In the same report, Cerretelli et al. (1979) presented results from experiments in which dogs were exposed for 2 to 7 weeks to 50-Hz fields at intensities of 10 or 25 kV/m. No differences in the hematologic parameters examined were observed in dogs exposed to the 10-kV/m fields compared with controls. A significant increase in reticulocyte counts and a decrease in hemoglobin concentration were observed in dogs exposed for 2 or 4 weeks to 25-kV/m fields. No changes in erythrocyte counts or hematocrits accompanied the reported changes in hemoglobin concentration and reticulocyte counts at these higher field strengths, thereby suggesting that these results are not physiologically consistent. Again, the authors do not present the actual data nor do they indicate the analyses performed. Consequently, the results presented by Cerretelli et al. (1979) are of questionable value for providing a reliable data base upon which conclusions about the hematologic effects of ELF fields can be made.

Fam (1981) examined the hematologic effects of exposure of male mice to alternating magnetic fields. Mice were exposed for 23 h/day for 1 week to 60-Hz, 0.11-T, alternating magnetic fields. No differences in erythrocyte or leukocyte parameters were observed between exposed and control mice. It is interesting to note that the leukocyte counts for the control mice in this study were 43 percent higher than the leukocyte counts from control male mice in the electric field study reported by Fam (1980) (i.e., $9.63 \times 10^3/mm^3$ and $5.51 \times 10^3/mm^3$, respectively). This comparison of data underscores the care that should be taken in evaluating these data. The highly variable nature of these hematologic parameters is obvious despite the fact that mice of the same sex and strain (i.e., SW-ICR) were used.

Using low intensity magnetic fields, Persinger et al. (1978) found no significant differences in differential leukocyte counts between exposed and nonexposed rats. Rats were exposed from 2.5 days before birth to 2.5 days after birth to either 0.5-Hz rotating magnetic fields (RFM) at field intensities of 10^{-3}, 10^{-4}, or 5×10^{-6}T or to sham fields. These rats were then reexposed as adults to one of three 0.5-Hz, rotating magnetic fields of 10^{-6}, 10^{-7}, or 10^{-8}T or to sham fields or room control conditions. Although no differences were observed in leukocyte counts from peripheral blood, a 17 percent decrease in thymus weights was observed in rats that had been exposed perinatally to the magnetic fields compared with sham-exposed rats. These authors indicated that "despite the small absolute differences between ... thymus weights between perinatal RMF-exposed and sham field-exposed rats, the effects were comparable in magnitude to the differences between types of postweaning caging, a condition sufficient to also significantly alter body weights, consumptive behaviors, and several blood measures." In light of these findings, the physiologic significance of the observed decrease in thymus weight in RMF-exposed rats is highly questionable.

In summary, a variety of changes in hematologic parameters has been reported to result from exposure of experimental animals to electric or magnetic ELF fields. Questions about the internal consistency between the blood parameters measured, the physiological significance of the reported changes, and the appropriateness of the statistical analyses used have been raised in those studies in which alterations have been reported. Because of the inherent biological variability of these measured parameters, the determination of a "statistically significant" difference between exposed and sham-exposed animals is not sufficient evidence upon which to conclude that ELF fields alter the hematopoietic system. This fact is underscored by the work of Ragan et al. (1979, 1983) and Mathewson et al. (1979) in which purported significant differences in blood parameters in one experiment were not corroborated in subsequent experiments. Based on the studies described, no strong case has been made for any physiologically significant alteration in the hematopoietic system of experimental animals exposed to ELF fields under the conditions used.

IMMUNOLOGY

The immune system is composed of myriad mechanical, cellular, and humoral components that act as the body's defense against various pathogenic microorganisms, viruses, and neoplasias. The immune system is broadly divided into the soluble elements (i.e., antibodies (humoral immunity), complement, interferon, and lymphokines), and the cellular elements, which are composed of the lymphoid and phagocytic cells. The phagocytic cells responsible for engulfing and digesting certain microorganisms are the neutrophils or polymorphonuclear leukocytes (PMNs) and the monocytes or macrophages. In the presence of antibodies and complement, neutrophils are aided in engulfing and digesting invading organisms. The monocyte is also a phagocytic cell. Monocytes move into an area in which an infection has begun and then differentiate into macrophages. Macrophages can be "activated" to kill certain microorganisms (e.g., intracellular, facultative bacteria such as Mycobacteria tuberculosis and Listeria monocytogenes, viruses, and fungi) through the interaction of certain subpopulations of lymphocytes, such as the T lymphocytes (Friedman 1978).

The other cellular components of the immune system are the lymphocytes. These cells are broadly presented in two groups: the B lymphocytes and T lymphocytes. Although these cells are similar morphologically, they are different functionally: B and T lymphocytes can be distinguished by the presence of unique antigens or receptors on their membrane surfaces. Both T and B lymphocytes are believed to originate in the bone marrow and then to proceed through various stages of development and differentiation, maturing into functional cells of the immune system (Benacerraf and Unanue 1979).

The B lymphocyte, or bursa-equivalent lymphocyte, is responsible for humoral immune responses. The B lymphocytes, after appropriate stimulation by antigens, proliferate and undergo morphological changes and develop into plasma cells that actively synthesize and secrete antibodies (Glick, Chang, and Jaap 1956).

The T lymphocyte, or thymus lymphocyte, is processed through the thymus after leaving the bone marrow. Classically, cell-mediated or T lymphocyte responses include protection against viruses, fungi, and several bacteria. T lymphocytes are also involved in reactions such as delayed hypersensitivity or contact hypersensitivity and rejection of tumors and foreign tissues such as transplants (allografts). Cell-mediated reactions are so named because these reactions, which operate by specifically sensitized T lymphocytes, can be transferred by these cells to normal animals. B lymphocyte-mediated humoral responses, in contrast, are transferable by serum (Miller 1964).

The recent availability of monoclonal antibodies has made the typing of lymphocyte subpopulations possible on a routine basis. Various functional categories of T cells can be recognized: "helper" (inducer/amplifier) T cells, "suppressor" T cells, and "cytotoxic" T cells. Immature thymocytes may be identified by surface antigens distinct from mature peripheral T cells. Cellular interactions between the various T cell subtypes and other cells of the immune system are vital to the modulation of the immune response. Because of their pivotal role in enhancing antigen-mediated immune responses, disorders involving T-cell subsets may result in immunodeficiency syndromes involving either cell-mediated or humoral immunity (Bellanti and Rocklin 1979).

Each element of the immune system plays a cooperative role in defending the host against infection and disease. At the same time, a delicate balance that prevents the immune system from reacting to the host tissues is maintained, thus preventing autoimmune reactions. The alteration or dysfunction of any of these elements may lessen the host's ability to combat infection or may lead to autoimmune disease. However, because of adaptability and redundancy in the immune system, the host can generally survive subtle perturbations. Consequently, although subtle effects on the immune system may be generated by physical or chemical agents, all such effects may not lead to clinically significant immune dysfunctions.

In addition to being internally regulated, the immune system is responsive to other physiological systems of the host. The endocrine system has a major influence on the distribution and function of immune cells (Ahlquist 1981). A number of studies have shown that changes in circulating glucocorticosteroid levels, due to various types of stress, cause major shifts in distribution of different cell populations of the immune system as well as changes in function (Claman 1972; Dougherty and Frank 1953; Fauci 1975; Riley 1981; Schultz et al. 1979). Similarly, it is now apparent that the nervous system imposes some control over the immune system (Ader 1981). Exposure of animals to stress, such as intermittent foot shock, causes the the release of opioid peptides from central and peripheral sites (Shevit et al. 1984). These peptides have been shown to alter the distribution and function of several immune cells including T cells, NK cells (natural killer), and granulocytes (Gilman et al. 1982; Mathews et al. 1983; Wybran et al. 1979).

Thus, any consideration of the immunological bioeffects of external stress such as ELF must deal with potential indirect effects such as those mediated by glucocorticosteroids and opiod peptides as well as direct effects on components of the immune system itself.

<u>In vivo Studies</u>

Table 2 summarizes the immunologic effects of exposure of experimental animals to ELF fields. Cerretelli et al. (1979) summarize the effect of electric fields on resistance to infection in mice as reported by Margonato, Viola, and Cantone (1978) at the Congress of the Italian Physiological Society. Male and female mice were exposed for 8 h/day for 42 days to 50-Hz electric fields at a field strength of 25 kV/m. The mice were injected intraperitoneally with graded concentration of <u>Staphylococcus</u> <u>pyogenes</u> (<u>aureus</u> Smith var.) following exposure. Resistance to infection was checked against identically injected control mice. The $LD_{50(72)}$ was found to be the same in exposed and control mice. Unfortunately, these results are impossible to evaluate because the actual data are not presented by Cerretelli et al. (1979). In earlier work, Krueger and Reid (1975) failed to observe any change in the resistance of mice exposed to influenza virus following exposure for 21 days to 75-Hz ELF at 100 V/m.

In two well designed and executed studies, Morris and Ragan (1979) and Morris and Phillips (1982) were unable to detect any differences between mice exposed to 60-Hz electric fields and sham-exposed mice for a variety of immunological end points. Male or female mice exposed for 21 h/day for 30 or 60 days to 60-Hz unperturbed electric fields at a field strength of 0.15 to 0.25 kV/m showed no consistent change compared with sham-exposed mice in the following areas: (1) IgM, IgG, or complement levels; (2) numbers of splenic T and B lymphocytes; (3) primary antibody response to keyhole limpet hemocyanin (KLH); or (4) leukocyte or lymphocyte counts in peripheral blood (Morris and Ragan 1979). In another study, Morris and Phillips (1982) exposed male mice to 60-Hz electric fields at field strengths of 0.15 to 0.25 kV/m for 20 h/day for 30 to 150 days. No significant differences were observed in primary antibody responses to KLH between exposed (30 or 60 days) and control mice. Furthermore, no significant changes in the mitogen-stimulated responses of T and B lymphocytes were observed between mice similarly exposed for 90 or 150 days compared with sham-exposed animals.

The above two studies provide strong evidence for the lack of any biologically relevant and consistent, statistically significant effects of ELF fields on the humoral or cellular components of the immune system of mice. Furthermore, these studies indicate that the functional integrity of the components of the immune system examined is not affected under the described conditions of ELF exposure.

Persinger and Coderre (1978) reported that adult rats that had been perinatally exposed to rotating magnetic fields (0.5 Hz, 10^{-3} to 10^{-6}T) displayed a "marginally significant" elevation in thymic mast cell number (20 to 35 percent) relative to sham-exposed controls. However, rats exposed only as adults did not show significant changes in the number of mast cells in the thymus. These investigators indicate that the increase in thymic mast cells in perinatally exposed rats correlated with the reduction in thymus weight reported in rats similarly exposed (Persinger et al. 1978). They suggested that these changes in thymic mass and cellularity might be attributed to the

TABLE 2

Summary of Studies of Immunologic Effects (in vivo) of ELF Fields

Effects	Species	Exposure Conditions: Fields	Frequency	Field Strength	Duration (day x h)	Reference
No change in resistance to infection with <u>S. pyrogenes</u>	Mice	Electric	50 Hz	25 kV/m	42 x 8	Cerretelli et al. (1979)
No differences in IgM, IgG, or complement; no differences in T and B lymphocytes numbers; and no differences in antibody response to KLH	Mice	Electric	60 Hz	0.15–0.25 kV/m	30 or 60 x 21	Morris and Ragan (1979)
No differences in antibody response to KLH and mitogen-stimulated responses of T and B lymphocytes	Mice	Electric	60 Hz	0.15–0.25 kV/m	30–150 x 20	Morris and Phillips (1982)
Elevation in mast cells in thymus	Rats	Magnetic (Rotating)	0.5 Hz	10^{-3}, 10^{-4}, or 5×10^{-6}T	5 x 24 (Perinatal)	Persinger and Coderre (1978)
Decrease in thymus weight	Rats	Magnetic (Rotating)	0.5 Hz	10^{-3}, 10^{-4}, or 5×10^{-6}T	5 x 24 (Perinatal)	Persinger et al. (1978)
Partial restoration of suppressed antibody response to sheep red blood cells in mice held in a Faraday cage	Mice	Electric	50 Hz	15 kV/m	540 x 24	Fischer et al. (1981)

release of glucocorticoid, ostensibly due to a stress reaction, because glucocorticoids induce thymic mastocytopoesis in the rat (Persinger and Coderre 1978). They believe that the most "impressive feature" of their findings was the "apparent long-term expression of the change." The significance of these results is highly questionable from both a physiological and a statistical standpoint. The thymic mast cells were elevated in 200-day-old rats despite the fact that the postweaning treatments varied. Furthermore, the investigators admitted to a "large statistical overlap with sham-field controls" and stated that the purported change in mast cell members was only "marginally significant" (Persinger and Coderre 1978).

Fischer et al. (1981) reported that mice placed in a Faraday cage over an 18-month period had significantly reduced primary antibody responses to sheep red blood cells as measured by the hemolytic plaque assay. When mice housed in a Faraday cage were exposed to a 15-kV/m, 50-Hz AC field, a slight increase was observed in the antibody response compared with Faraday-caged mice. Decreased and increased hemagglutination titers accompanied the decreased and increased plaque numbers for Faraday-caged mice and mice exposed to 50-Hz fields, respectively. These results were obtained in two replicate experiments. These investigators offered no conclusions about the possible consequences of the observed effects, except that screening ambient atmospheric electric fields appears to suppress the immune response and that the screening or "Faraday effect" can be compensated for by introducing ELF fields. Although these are intriguing results, much more work is required to corroborate these findings that suggest that 50-Hz fields are beneficial to the immune response of mice.

In summary, the above in vivo studies fail to provide substantial convincing evidence for physiologically significant and reproducible effects of ELF fields on the immune system of experimental animals under the conditions described.

<u>In vitro Studies</u>

Table 3 summarizes the immunologic effects of in vitro exposure to ELF fields. Conti et al. (1983) exposed human peripheral blood lymphocytes to square-wave magnetic fields at 1, 3, 50, and 200 Hz at field strengths of 23 to 65 G in the presence or absence of mitogens. Lymphocyte cultures were

TABLE 3

Summary of Studies of Immunologic Effects (in vitro) of ELF Fields

Effects	Cells	Exposure Conditions: Fields	Frequency	Field Strength	Duration	Reference
Decrease in PHA, Con A, and PWM stimulated ^{3}H-thymidine incorporation	Human lymphocytes	Electro-magnetic	1, 3, 50 or 200 Hz	(23-65 G)	12 or 72 h	Conti et al. (1983)
Decrease in lymphocyte viability with increasing pulse discharge time or increasing field strengths	Human lymphocytes	High voltage pulses (transient currents)	50 Hz	>2.6 kV/m	>1 μs	Mild et al. (1982)
Decreased T-lymphocyte cytotoxicity	Mouse CTLL-1 cell line	AM/RF	16, 40, 60, 80, or 100 Hz; 450 MHz	RF=1.5mW/cm^2	4 h	Lyle et al. (1983)
Decreased protein kinase activity	Human lymphocytes	AM/RF	16, 40, or 60 Hz; 450 MHz	RF=1 mW/cm^2	0.25-0.5 h	Byus et al. (1984)
No change in capping of B lymphocytes in absence of temperature increase	Mouse lymphocytes	AM/RF	9, 16, or 60 Hz; 147MHz	RF=0.1-48 mW/cm^2	0.5 h	Sultan et al. (1983)

exposed to ELF fields either throughout the 72 h incubation period or for intermittent periods during the 72 h culture period. The three mitogens used were concanavalin A (Con A) and phytohemagglutinin (PHA), both T cell mitogens, and pokeweed mitogen (PWM), which stimulates B cells as well as T cells. These investigators reported that ELF exposure of cultures for 72 h resulted in a significant ($p < 0.01$) reduction in PHA-stimulated lymphoproliferation at each of the four frequencies. Con A-stimulated lymphoproliferation was reduced at 3 and 50 Hz, and PWM responses were affected only at 3 Hz. Unfortunately, the authors' word must be accepted for these "significant differences," because there are no indications in the table as to which of the many data sets of ELF-exposed versus nonexposed cultures are different. At 3 Hz, where significant reductions in PHA, Con A, and PWM responses were observed, lymphocytes cultured in the absence of any mitogen and exposed to the magnetic fields had consistently reduced ^{3}H-thymidine incorporation compared with matched control cultures. Because the authors do not indicate in their table of data if any of these "no mitogen," ELF-exposed lymphocytes are significantly different from controls, it is difficult to determine whether these reductions might contribute to the reductions in mitogen responses at 3 Hz.

In other experiments in this report, Conti et al. (1983) indicated that exposure of lymphocytes with 3-Hz ELF fields only during the first 12 h of culture resulted in significant reductions in ^{3}H-thymidine incorporation in the presence of PHA and Con A but not PWM. When lymphocytes were exposed at 3 Hz for the last 48 h of culture, excluding the last 6 hours, PHA and Con A but not PWM responses were also reduced. The data from these experiments are presented in a figure, which, like the data for the 72-h ELF field exposures, does not indicate which data sets are "significantly different." Furthermore, it appears from this table that one "no field" control for each mitogen was used for the field exposure during the first 12, last 48, and last 6 h of culture. The interpretation of these results is difficult not only because of problems in the design of the experiments but also because inappropriate statistical analyses were performed on the data.

Conti et al. (1983) indicate that at the end of the 72-h culture period, "the cell viability was evaluated by trypan blue exclusion and it was always over 90% both field off and field on"; however, these very important data are not presented. Even if the viability data indicated no difference between "field-off" and "field-on" conditions, this does not preclude the possibility that there may have been fewer cells in the "field-on" cultures compared with the "field-off" cultures. If there were fewer cells in the "field-on" cultures, this could account for the observed reduction in mitogen responses. Until evidence that eliminates this possibility is presented, it is premature to make any conclusions about these data. Although these results are interesting and suggest that ELF fields may affect lymphocyte responsiveness to mitogens, more thoroughly designed and analyzed experiments are needed in order to corroborate the current data.

Mild et al. (1982) exposed human peripheral blood lymphocytes in vitro to electric pulse discharges at pulse lengths of 0.2, 1, and 3 μs field strengths of 2.6 kV/cm. At fields strengths above 2.6 kV/m, pulse discharge times of 1 and 3 μs increased the number of trypan blue stained (i.e., nonviable) cells. For a shorter pulse (i.e., 0.2 μs), a field strength of about 5 kV/cm was required to cause a decrease in lymphocyte viability. These investigators concluded that cell membrane damage occurs at a critical peak E-field in the sample of about 2.6 kV/m. If one assumes σ = 0.6 μs/m, then the current density at this field strength is about 16 A/cm^2. This current density is less than that which would be expected if, for example, a spark discharge enters the body of a person at the index finger. These investigators state that it is "therefore reasonable to assume that a spark discharge ... may cause cell damage to the leukocytes also in vivo." Whether the damage caused in vitro would occur in vivo is uncertain because of the rapid spreading of the current in the body during the discharge.

There are two recent reports on alterations in lymphocytes exposed in vitro with RF radiation sinusoidal amplitude modulation (AM) at ELF frequencies. Although these studies did not use ELF electric or magnetic fields, they are worthy of mention in this review because of their potential importance in electromagnetic radiation biologic effects research.

Lyle et al. (1983) reported a significant inhibition of allogeneic cytotoxicity of mouse lymphoma MPC-11 target cells by the murine CTLL-1 T lymphocyte effector cell line during a 4-h cytotoxicity assay conducted in the presence of a 450-MHz RF field amplitude-modulated at 60 Hz. Exposure of the effector cells to the field prior to addition to target cells also resulted in inhibition of cytotoxicity. This inhibition was found to be affected by exposure to the fields for the first 2 h of the 4-h culture period; however, only partial inhibition was observed when the cultures were exposed during the last 2-h of the culture period. Kinetic studies revealed that the field-induced inhibition of cytotoxicity at 450-MHz AM persisted for only 9 h. Inhibition of cytotoxicity was observed in a series of experiments at AM frequencies of 16, 40, 80, and 100 Hz. Inhibition of cytotoxic T cells at these frequencies was not as dramatic as that produced under 60-Hz exposure. No increases were reported in culture temperatures in exposed verses control cultures. The incident power density was 1.5 mW/cm^2 during exposures. Cell viabilities were reported to be "99% or greater ... after a 4-h field exposure," although these data were not presented. No reduction in allogeneic cytotoxicity was observed in the absence of an unmodulated 450-MHz field. This suggests that the amplitude modulation was responsible for the observed effect. It would be interesting to determine what effect, if any, 60-Hz electric and magnetic fields might have on this system.

The results of Lyle et al. (1983) suggest that nonthermogenic RF radiation amplitude-modulated fields affect T lymphocyte cytotoxic activity in vitro. This work must be corroborated and in vivo studies undertaken before any claims about the physiological significance of these findings can be made.

In other work from this laboratory, Byus et al. (1984) reported that a decrease in protein kinase activity in human tonsil lymphocytes occurred during 15- and 30-minute exposures to a 450-MHz RF field sinusoidally amplitude-modulated at 16 or 60 Hz. This reduction in non-cAMP-dependent protein kinase returned to control or preexposure levels by 45 and 60 min. It is interesting to note that the "specific identity of this kinase is unknown." (Byus et al. 1984). Consequently, the biological role played by this kinase and the physiological significance of its reduction during RF field exposures are unknown. No change in kinase activity was observed when only 450-MHz continuous wave fields were used. No differences were observed in viability or culture temperatures between exposed and sham-exposed lymphocyte cultures. These findings are similar to those reported by Lyle et al. (1983) in that they purport to show a "windowing effect with respect to modulation frequency and exposure duration" (Byus et al. 1984). However, because both phenomena are reversible, their in vivo physiological significance is questionable.

Sultan, Cain, and Tompkins (1983) failed to demonstrate any change in the ability of mouse B lymphocytes to "cap" antigen-antibody complexes on their cell surface during exposure to nonthermogenic levels of 147-MHz RF fields amplitude-modulated by 9-, 16-, or 60-Hz sine waves when cultured at 37°C. When lymphocytes were cultured at 42°C, however, capping was equally inhibited in both control and irradiated cells. No significant differences in capping were observed between exposed and control cells at any modulation frequencies and power densities provided that both preparations were maintained at the same temperature.

The different results reported by Byus et al. (1984), Lyle et al. (1983), and Sultan, Cain, and Tompkins (1983), are difficult to reconcile. In each case, the studies appear to have been well designed and executed with appropriate statistical analyses applied. Byus et al. (1984) and Lyle et al. (1983) reported alterations in lymphocyte function or biochemistry especially at an AM frequency of 60 Hz; however, Sultan, Cain, and Tompkins (1983) failed to observe any effects. In each of these three studies, the only common thread is the amplitude modulation frequency of 60 Hz. The cells used and the end point studied in each of these three reports were totally different, and one might argue that this is the underlying reason why Sultan, Cain, and Tompkins (1983) failed to observe any effects. However, Byus et al. (1984) and Lyle et al. (1983) used two totally different cell types (T lymphocyte cell line and human tonsil lymphocytes, which are composed of 50% T and 50% B lymphocytes, respectively), and yet, a 60-Hz window was observed in both of those studies. Furthermore, a 60-Hz window was observed by Byus et al. (1984) and Lyle et al. (1983) for two totally different end points (i.e., cytotoxicity and protein kinase activity, respectively). Unfortunately, these are the kinds of conflicting reports that have plagued nonionizing electromagnetic radiation research for years. Before any informed conclusions about the physiological significance of these findings can be made, independent, replicate experiments must be performed to corroborate the finds.

CONCLUSIONS

Many of the studies reviewed here are flawed because of poor experimental design and statistical analysis of the data. In those studies that appear to be well designed and adequately analyzed, no clear, consistently reproducible, and physiologically significant effects of ELF fields on the hematologic or immunologic systems or on their cellular elements have been demonstrated. The reported alterations caused by ELF fields have, for the most part, been found to be transient and mild in nature. The fact that no consistent effects have been observed even when similar exposure conditions and experimental parameters have been used indicates that low-level ELF-field-induced effects are very subtle and consequently may be of little or no physiological significance as regards the hematopoietic and immunologic systems.

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CHAPTER 8

REPRODUCTIVE AND DEVELOPMENTAL EFFECTS IN MAMMALIAN AND AVIAN SPECIES FROM EXPOSURE TO ELF FIELDS*

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INTRODUCTION

The normal development, growth, and maturation of an organism is brought about by a complex series of interrelated genetic, biochemical, and morphological events occurring in a precise temporal sequence. It has been long established that substantive interference with any of the key events involved in development may have serious results: embryonic or fetal death, the occurrence of birth defects, failure to thrive postnatally (or posthatching), or failure to reproduce. A diverse series of agents including disease, drugs, environmental chemicals, and physical agents (such as X-irradiation) are known to have produced serious effects in humans (Wilson 1973). Because of this known sensitivity, the scientific community has been called on to devise and conduct studies in laboratory species that will indicate any special sensitivity in the developmental processes to specific external influences.

A number of studies designed to evaluate the potential developmental toxicity of extremely low frequency (ELF) electric or magnetic radiation have been reported from 1976 to the present. The following review centers on those studies in which mammalian or avian species were exposed to ELF electric and magnetic radiation and their subsequent effects on growth and/or development

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monitored. The review is divided into those studies that used electric fields with frequencies of 50 or 60 Hz at intensities simulating those found in the vicinity of power lines and those studies that used low intensity magnetic fields.

STUDIES WITH 50- OR 60-HZ ELECTRIC FIELDS

Avian Species

Graves (1984) reported on a series of experiments in which chicken eggs and hatched chicks were exposed to 60-Hz electric fields ranging from 0.1 to 100 kV/m. Eggs were checked for embryotoxic effects including teratogenicity on days 7 or 14 of incubation. Other groups were exposed during the first 19 days in ovo and allowed to hatch (generally on day 20 or 21); the emerging chicks were monitored for changes in growth, viability, or behavioral alterations during a 6-week period after hatching. There were no significant dose-related effects found in any parameters studied; the statistically significant effects that were noted appeared to be random. The author's conclusion that these studies produced "no consistent direct effect of 60-Hz electric fields on processes associated with growth, development, and overall health and well-being of avian embryos" is an accurate interpretation of the data.

In another series of experiments, Graves et al. (1978) exposed chicks postnatally to either 30-minute or 3-week exposures of 60-Hz fields (40 or 80 kV/m) and monitored growth and livability. No effects were noted with short-term exposure. Long-term exposure resulted in a slight enhancement of growth in male birds through day 16 of posthatching. This effect was not seen in female birds. The authors also recorded the EEGs and ECGs of chicks immediately after removal from the field and found no differences.

Mammalian Species

A variety of species have been used in experiments to evaluate the potential effects of electromagnetic fields in growth or development. Such species have included the rat, mouse, guinea pig, and swine. Andrienko (1977) studied the effects of 50-Hz fields at 5 kV/m on rats of unknown strain before, during, and after embryo/fetal development. Male and female rats were exposed for 1.5, 3.5, and 4.5 months and examined. An additional group was allowed to recover for 1 month and then was examined. The author reports numerous effects of the fields on the offspring of both exposed males and females. Close examination of the data raises questions that are impossible to resolve, however. The author presents the postnatal death data as % $\pm\sigma$ which are difficult to understand because the standard deviations are extremely low for this type of presentation (i.e., 4.3 $\pm$ 0.008 or 14.8 $\pm$ 0.2). Data presented as percents invariably have larger standard deviations than those presented by Andrienko. It is difficult to interpret some of the data biologically: e.g., after 1.5 months of exposure, there are no differences in breeding efficiency; at 3.5 months, treated females were affected; and at 4.5 months, only treated males were affected. In general, however, the weight of the newborn pups and their viability at 21 days were reduced in litters of both treated males and females. The author does not offer any biological explanation for the male-mediated effect that resulted in such relatively slight effects. Male-mediated effects usually result in embryonic lethality, but in these studies there was no reduction in litter size in any of the treated groups. The author also reports that reproductive function was adversely affected in both treated females (an altered cyclicity and ovarian histopathology) and males (a decrease in sperm number and in testicular histopathology).

Cerretelli et al. (1979) studied a variety of biological phenomena in diverse species exposed to 50-Hz electric fields at 10, 25, and 100 kV/m. The experiments that focused on the developmental effects in rats are somewhat difficult to interpret. The growth rates were reported to be decreased in the 25- and 100-kV/m groups, but the ages of the rats were not specified. Although the authors reported food intake values, they did not provide information on water intake. Male reproductive function was measured, but some of the parameters were again difficult to interpret. There is no explanation as to how the number of copulations may be derived by the methodologies used. No description is given of the microscopic alterations found after examination of testes tissue. No indication is given as to how the "vitality" of sperm was measured. The authors concluded that fertility was not affected and the treatment was not teratogenic, although they did see a reduction in fetal weight (data not given).

Free et al. (1981) examined the effects of 60-Hz electric fields at

64 kV/m (effective field strength) on endocrine profiles of Sprague-Dawley rats exposed for 7 weeks starting at 20 days of age. Testosterone, FSH, LH, corticosterone, prolactin, TSH, GS, and thyroxine were monitored in addition to the body and organ weights. The experiments were repeated in the same month for three consecutive years. Data were not consistent from year to year with the exception of testosterone levels, which were reduced when compared to the controls in all three years. A key difficulty in such work is pointed out by the authors--examining cyclical hormone levels at specific time points--and they suggest that some of the changes noted may have been due to alterations in the hormone cycles.

Margonato and Viola (1982) studied the offspring of male rats exposed at 50 Hz, 100 kV/m either for short periods (30 minutes per day) or longer periods (8 hours per day) for up to 48 days. No consistent effects in fertility, sperm viability, or sperm morphology were noted in any of the exposed groups. There were no treatment-related effects in the number of implantations, percent of live fetuses, or incidence of malformations. The authors concluded that there were no significant treatment-related effects on male reproductive parameters.

A series of studies were performed by Sikov et al. (1984) in which the effects of 60-Hz electric fields (65 kV/m effective) on prenatal and postnatal development in Sprague-Dawley rats were investigated. Experiments were designed to test reproductive performance and prenatal development, postnatal secondary results of exposure throughout gestation and the first week postpartum, and postnatal effects of late gestation and 25 days postnatal exposure. There were no consistent treatment-related effects noted in any of the parameters studied. Fetal development was unaffected as was postnatal growth, viability, and the development of reflexes.

Seto et al. (1981) reported that the chronic exposure of rats to 60-Hz, 20-kV/m electric fields for four generations did not affect organ weights or histological parameters of selected organs. Burack, Dunlap, and Seto (1981) reported the effects of 60-Hz, 80-kV/m electric fields on the offspring of rats exposed from days 14 through 21 of gestation. Group sizes were small (seven animals per group), and no significant changes were detected in litter size or viability. The authors state that exposed offspring were generally of lighter body weight and had delayed ear flap and eye opening.

The mouse has also been used by a number of investigators to study the effects of electric fields on development. Marino, Becker, and Ullrich (1976) reported studies in which ICR mice were exposed for three generations at 60 Hz with a 15-kV/m vertical or 10-kV/m horizontal electric field. The vertical field reduced litter weights in all generations, and the horizontal field had a similar effect on the first two generations. These studies were compromised by the potential presence of substantial grounding microcurrents that would affect the eating and drinking behavior of the exposed animals. This same group repeated these studies in an improved apparatus designed so that grounding microcurrents would not be present (Marino et al. 1980). Animals were exposed to 60-Hz electric fields with either horizontal or vertical strengths of 3.5 kV/m. The results were variable, and in some cases (e.g., growth) the results were opposite of that seen in the first experiment. The authors stated that increased preweanling or postweanling mortality occurred in some generations. They attribute the variablity inconsistencies to generalized stress caused by the exposures.

Fam (1980) exposed male and female ICR-SW mice to 240-kV/m, 60-Hz electric fields throughout the entire developmental period. Animals were bred and the resultant litters were monitored for growth, histology and biochemical parameters of the blood, and histology of critical organs. Drinking water consumption of the parental animals was depressed and the growth (between 53 and 123 days of age) of the females was significantly reduced during the exposure period. No changes were noted in the number, growth, or survival of the offspring.

Two studies using swine have been reported. Mahmoud and Zimmerman (1982) reported on the growth of pigs (average age at the initiation of the experiment was 79 days) housed under a 60-Hz, 345-kV power line. No significant differences were noted between the growth of the animals exposed to 3.5- to 4.2-kV/m intensity and those housed 0.5 mile from the line. A multigeneration study was done with Hanford Miniature Swine continuously exposed to a vertical electric field (60 Hz, 30 kV/m) (Sikov et al. 1985). Animals were exposed for four months and then bred, some being sacrificied to allow for fetal evaluation and others allowed to go term. After 10 months, the remaining dams were again bred, and their fetuses examined. The young that had been born to the parent generation were, in turn, bred at 18 months, allowed to litter normally, and then rebred 10 months later, sacrificed, and their fetuses evaluated. There was, thus, a total of three teratology series and two groups of live births. The data generated in these studies were highly variable across generations, and although there was a significant increase in malformations in the exposed litters of the second breeding of the F_0 generation, malformations were not seen in either of the first breedings of the F_0 generation. Malformations were also seen in the first litters of the F_1 generation. It should be noted that there was a wide spectrum in the types of defects seen, and there was no apparent specific morphological pattern that occurred throughout these studies. These studies fail, therefore, to present clear evidence of a treatment-related effect, although such a possibility cannot be ruled out.

Sasser, Kaune, and Phillips (1984) studied the effects of electric field exposure on the prenatal development of the guinea pig (Duncan-Hartley strain). Experimental animals (females) were exposed to 60-Hz electric fields (100 kV/m) for 40 days, bred, and allowed to litter. The parental animals were bred a second time. However, this portion of the experiment was terminated prematurely due to physical plant problems; therefore the results are difficult to intepret. Results of the first breeding indicate no statistically significant adverse effects in terms of pregnancy rate, percent dams that aborted or resorbed, or number of litters with stillborns. There were also no differences noted in the pups at birth in terms of average litter size or birth weight. No significant incidences of birth defects were noted in these groups.

STUDIES WITH MAGNETIC FIELDS

Avian Species

Immediately after hatching Delgado et al. (1982) exposed chicken eggs for 48 hours to pulsed magnetic fields (10, 100, or 1000 Hz at repetition frequencies of 0.12, 1.2, or 12 μT). There were 9-dose groups (42 eggs in all) plus a control group (26 eggs). The embryos were harvested after the exposure period, preserved, and examined for morphological and histological anomalies. The criteria for normality used by the authors was embryological development to Stages 11 to 12 of Hamburger and Hamilton (1951). The embryos exposed to 10 Hz were almost all normal. At 100 and 1000 Hz, however, exposed embryos were significantly retarded (equivalent to Stage 6 of Hamburger and Hamilton) at all intensities tested. Histological analyses confirmed the results noted after gross examination. The numbers of embryos used in the study were small, ranging from three to nine per group, and, although the authors refer to statistical significances, no p-Values or methodologies are given. It would appear, however, that growth retardation did occur in the exposed eggs.

The same group of workers reported on additional studies with chicken eggs in which four different pulse types were used at different intensities (Ubeda et al. 1983). The results are extremely difficult to interpret. Using pulses with rise and fall times of 100 μs, an increase in abnormalities was seen at 1.0 μT but not at 0.4, 10.4, 13.9, or 104.0 μT. There were six replicates in which embryos were exposed to 1.0 μT, and, although there was a constant trend toward a greater effect in exposed eggs, it was also apparent that both control and exposed eggs varied widely in the percentages of abnormalities noted from replicate to replicate (56% abnormalities in replicate 1 controls versus 0% ties in replicate 3). Furthermore, it is apparent that the percentage of abnormalities followed the same overall replicate pattern in both controls and exposed eggs. The authors considered positive effects to be associated with specific pulse shapes because they found effects with pulse B that had fast rise and fall times of 2 μs (at 0.4 μT) and with pulse D that had rise and fall times of 42 μs and were without ripple during the on period (1.0 μT). But they found no effects with pulse C which was identical to pulse D except for a ripple during the on period (1.0 μT). Embryos exposed to pulse B were more advanced than concurrent controls. This is an extremely unusual finding because embryonic toxicity almost always is manifested as growth retardation. The authors did note that in the pulse D experiments there was a retardation of development in exposed embryos compared to controls. To adequately interpret these data, information on the temperatures in the incubation chambers must be given because such differences may affect the relative rates of development.

Mammalian Studies

Fam (1981) exposed male SW-ICR mice to a 60-Hz, 0.11-T alternating magnetic field for one week. Exposed animals tended to lose weight, although their water consumption was increased relative to controls. No significant differences between treated and untreated animals were noted in blood counts, blood proteins, or critical organ histology. A reproductive study was performed on one control and one exposed mouse, but data derived from n's of this size cannot be interpreted.

Persinger et al. (1978) exposed pregnant Wister rats to one of three treatments (0.5 Hz rotating magnetic field at 5, 100, or 1000 μT) from day 19 of gestation to 3 days postpartum. Group sizes were small (three animals per group). Pups were sacrificed after weaning, and approximately 20 blood serum parameters measured. The differences noted appeared to be random, having as much to do with the type of housing (plastic versus metal caging) as with the exposure conditions.

Grissett (1979) exposed rhesus monkeys (ages unspecified) to a magnetic field of 0.2 mT and simultaneously to an electric field of 20 V/m. These fields were alternating at approximately 76 Hz. The animals were monitored for growth rate and blood chemistry and (in the third year) for spermatogenesis. The only difference seen was an increased growth rate in male animals during the first year of exposure. Sham and exposed animals were matched for weight rather than for age so that it is possible that the differences noted were due to an inadvertent difference in the growth rate of exposed and sham animals at the beginning of the experiments (a point the author himself raises). Using the same exposure regimen, Grissett, Prettyman, and Griner (1981) reported a similar experiment using younger animals. In this study, no differences in growth and development were noted in animals exposed from 4 to 67 weeks of age, indicating that the fields did not cause a general enhanced growth rate.

SUMMARY

The adequate evaluation of studies investigating potential developmental toxicology requires three critical components. The first is a demonstrable compound-related effect. Studies must use enough experimental animals to ensure a maximum probability of finding a real effect. Concurrent controls must be run under conditions that ensure that the only variable being tested is the agent of concern. Rigorous and appropriate statistical analyses must be performed. This latter is especially critical for studies in which a large number of agents or end points are being investigated because such analyses help identify differences due to normal random biological variation.

The second critical component for adequate evaluation is the presence of a dose-response relationship. If a given chemical has a reported effect at x mg/kg, it might be expected that x + y mg/kg will produce either a similar effect (if the system is saturated) or a greater effect (either quantitatively or qualitatively). Most toxicity bioassays are, therefore, run with multiple dose levels, and the presence of a real dose-response relationship is one of the strongest evidences of the validity of the reported effect. Finally, a key component of any evaluation of an agent is the replicability of the effect. Experimental parameters must be defined with sufficient rigor so as to allow other scientists to produce similar results in replicate experiments. It is impossible to draw definitive conclusions from a study that cannot be replicated until the reason for this inability is fully documented.

Given the criteria for adequate evaluation, it is impossible to draw any definitive conclusions concerning the effects of ELF fields on reproduction or development in either avian or mammalian studies. Although a number of studies have reported possible agent-related findings, few of these studies have dealt with dose-response phenomena, and none have been clearly replicated by different research groups. Studies on the possible effects of 50- or 60-Hz electric fields on mammals range from the positive effects of Andrienko (1977) with rats and Marino et al. (1981) with mice, to the negative findings by Margonato and Viola (1982) and Sikov et al. (1984) with rats and Fam (1980) with mice. Studies with swine have internal variabilities that prevent drawing firm conclusions, but the data certainly do not indicate definitive adverse effects due to ELF exposure. The studies with guinea pigs (Sasser, Kaune, amd Phillips 1984) appear to be negative as do those studies using avian species (Graves 1984).

The exposure of mammalian species to magnetic fields indicate a possible increased growth rate (Grissett 1979), but the experimental design does not allow for definitive conclusions on this point. In avian species, studies have indicated that such fields produce adverse effects (Delgado et al. 1982; Ubeda et al. 1983), but the nature of the internal variability and lack of dose-response data in these studies again do not allow for definitive conclusions.

In summary, therefore, ELF fields have not been demonstrated to produce adverse reproductive or developmental effects in either mammalian or avian species. There are a small number of studies (especially with magnetic fields) that suggest some agent-related effects, but these studies must be replicated before any definitive statements can be made.

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CHAPTER 9

HUMAN STUDIES OF CARCINOGENIC, REPRODUCTIVE, AND GENERAL HEALTH EFFECTS OF ELF FIELDS

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INTRODUCTION

This chapter reviews human studies of potential adverse effects of extremely low frequency (ELF) fields, including studies directed at carcinogenicity, adverse reproductive outcomes, suicide, psychological function, and cardiovascular effects. The emphasis is on studies of carcinogenesis, not because this is inherently the most likely health outcome of ELF field exposure, but rather because it has received the most attention and concern. The major studies in each area are reviewed and evaluated, followed by general comments on the major methodological issues. Each section closes with conclusions summarizing the current state of evidence regarding the impact of ELF fields on that particular set of health end points. Cancer will be considered first, then reproductive outcomes, and finally the other general health outcomes.

CARCINOGENIC EFFECTS OF ELF FIELDS

Overview

In the past 5 years, there has been an increasing concern with the possibility that exposure to electric or magnetic fields might increase human cancer risk. The plausibility of this hypothesis must be judged in light of experimental in vitro and in vivo investigations reviewed in several other sections of this report. Although a biological rationale for carcinogenic effects of such exposures exists (Becker and Esper 1981; Easterly 1981; Winters and Phillips 1984), there is substantial empirical evidence against

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such effects (Bauchinger et al. 1981; Noda et al. 1984). The hypothesis regarding cancer-promoting effects of magnetic fields is predicated primarily on interference with the immune surveillance system allowing otherwise suppressed cancers to develop. Smialowicz (Chapter 7) comprehensively reviewed the literature on immunological effects of ELF fields and concluded that

> no clear, consistently reproducible, and physiologically significant effects of ELF fields on the hematologic or immunologic systems or on their cellular elements have been demonstrated. The reported alterations caused by ELF fields have, for the most part, been found to be transient and mild in nature. The fact that no consistent effects have been observed even when similar exposure conditions and experimental parameters have been used indicates that low-level ELF-field-induced effects are very subtle and consequently may be of little or no physiological significance as regards the hematopoietic and immunologic systems.

Thus, although the experimental literature does not suggest specific or strong effects of ELF fields on immune function, the possibility remains that exposure to a prolonged mild stressor could affect the probability of cancer development.

In spite of the limited support for a carcinogenic effect of ELF fields from experimental research, observational epidemiologic studies in humans still merit consideration. There are serious limitations in the ability to extrapolate from animal studies to human risk, inherently limiting the certainty of laboratory results for characterizing risks to humans. Furthermore, experimental studies of cancer induction in humans are ethically and logistically unfeasible. Given these constraints, observational studies in humans will continue to provide an important source of information for assessing risks of exposure to ELF fields.

Because epidemiologic studies have taken on such a critical role in assessing risks of ELF field exposure, the characteristics of these studies that pertain to assessing causal relationships must be considered. In spite of the inherent limitations in an observational rather than experimental method, sufficient evidence can be assembled from epidemiologic studies to establish a causal relationship, as has occurred for cigarette smoking and lung cancer, for example. Rothman (1982) recently reviewed some of the criteria by which causality (a biological inference), rather than simple association (a statistical pattern), can be inferred. In general, a causal relationship is supported by a strong association between exposure and disease, with a large relative risk or odds ratio. Consistency in demonstrating the same association across different populations, for example different occupational groups or different regions of the country, supports a true causal relationship. Exposure temporally preceding effect is absolutely necessary for the association to be interpreted as causal. A dose-response gradient in which risk increases with increasing levels of exposure supports an inference of causality. Finally, biological plausibility based on experimental laboratory evidence in humans or experimental animals is essential for establishing a causal relationship. These criteria are directly applicable to assessing the strength of evidence that human exposure to ELF fields cause cancer. For example, an isolated finding of an association between ELF fields and cancer cannot stand alone as demonstrating a causal relationship.

The literature is conveniently divided into studies of persons exposed to ELF fields in their residences and those exposed through their occupations. The goal of this chapter is to critically review the existing literature and attempt to determine the extent to which the human studies indicate a causal association between exposure to ELF fields and adverse health effects. To accomplish this, the studies are reviewed individually for the strengths and weaknesses of the methods used and the credibility of the results. Consideration is given to contradictory findings and critiques of these papers. Finally, the conclusions that can be drawn from these studies in the aggregate are provided.

Residential Exposure

Review of Major Studies. There are only four studies to date addressing residential ELF fields and human cancer risk. The methodological details and results of those four studies are summarized in Table 1 and discussed individually below.

Wertheimer and Leeper (1979) compared 491 residences of children who died of cancer between 1950 and 1973 with residences of 472 controls selected from birth certificates. The exposure to ELF fields was characterized by the outdoor transmission-line configurations, with the assumption that typical current flow past the home could be inferred from the wiring and that this

TABLE 1

Methodological Characteristics of Epidemiologic Studies of Cancer and Magnetic Field Exposure

	Wertheimer and Leeper (1979)	Fulton et al. (1980)	Tomenius, Hellström, & Enander (1982)	Wertheimer and Leeper (1982)
CASE GROUP:				
Geographic Source	Colorado	Rhode Island	Stockholm County	Colorado
Time Period	Deceased 1950-1973	Onset 1964-1978	Registered 1958-1973	Deceased 1967-1975, 1977; Survivors diagnosed before 1974
Diseases	All cancers: leukemia, lymphoma, nervous systems, other	Leukemia, subtypes	All tumors, including benign	All cancers (sample of lung cancer); subtypes
Age range	0-18	0-20	0-18	19 +
Size	344 (491 dwellings)	119 (209 dwellings)	716 (1,172 dwellings)	1,179
Other Eligibility Criteria	Colorado birth certificates; residence in Denver area, 1946-73; subsets based on residence information	Identified at Rhode Island Hospital; in-state for 8 years prior to onset	Not stated	Known residence for 4+ years
CONTROL SERIES:				
Description	Birth Certificates	Birth Certificates	Birth Certificates	Non-cancer deaths, random sample, or neighborhood controls.
Matching	Some by county, month of birth; others by broad time spans	Year of birth	Some by church districts; others by county	Sex; age; year of death; socio-economic level
Size	344 (472 dwellings)	240 (240 dwellings)	n.a. (1,015 dwellings)	1,179
Exclusions	Subset formed based on residence information	Only birth addresses considered	Not stated	--

TABLE 1

Methodological Characteristics of Epidemiologic Studies of Cancer and Magnetic Field Exposure

	Wertheimer and Leeper (1979)	Fulton et al. (1980)	Tomenius, Hellström, & Enander (1982)	Wertheimer and Leeper (1982)
EXPOSURE: Definition	High-current configurations (Wire gauge, type, number, proxmity to home and to transformer)	Exposure estimated from measurements in Colorado, divided into quartiles	Wiring configurations electrified railways, subways; measured 50-HzAC magnetic fields visible; electrical constructions within 150 m	Five classes of wire configurations, case-control pairs coded as higher/lower.
Range	.001 to .035 G[1]		0.004-19.000 m G	0.005-.006 G (median)
POTENTIAL CONFOUNDERS ADDRESSES:	Age of onset; sex; urban-suburban residence; socio-economic class; maternal age; birth order; traffic density	Year of birth; father's socio-economic level; age of onset		Vital status; sex; age; urban; city; socio-economic level
RESULTS:	Positive association between high-current configurations and cancer, with dose-response gradient; observed for all cancer types	No evidence of association between exposure level and leukemia	More visible electrical constructions within 150 m; more case residences and ≥3 m G than control residences	Positive association between higher current configurations and cancer

1. These measurements were taken directly under wires and were not taken at the homes considered in the case-control analysis.

correlated with magnetic field exposures in the home. The only other variables potentially related to cancer risk that were available for consideration were those derived from the birth certificate (maternal education, birth order) and those that could be inferred from the residence (urban–suburban residence, traffic flow past the home). The investigators found that high current configurations were significantly more common for case homes compared to control homes. This occurred for essentially all case subgroups (males and females, different cancer types, different ages).

Several aspects of the design of the Wertheimer and Leeper (1979) study limit the strength of its conclusions. These aspects include the study of only deceased cases; residential mobility restrictions; lack of validation of the exposure measure; and failure to consider possible confounding variables, each of which is described in detail below. First, the case group included only deceased children with cancer rather than all incident cancer cases. If some factor affected survival rather than incidence, it would spuriously appear to be a risk factor. Second, the restrictions imposed on residential mobility and birthplace of cases and controls may have introduced biases that could affect the pattern of wiring configurations. Limited knowledge about the attributes of persons who live in low and high current configuration homes makes it difficult to speculate on the importance of this consideration.

Third, the exposure measure itself (wiring configuration) is unsubstantiated as being a valid indicator of ELF field exposures. Furthermore, the investigators assigned the exposure status to the homes without being blinded to whether the residence was occupied by a case or control. Even such objective measures as pulmonary function tests are subject to biased interpretation, so it is quite plausible that assignment of exposure status contained subtle biases to produce their positive results. The consistency of their findings across all cancer subtypes, all ages, and both sexes would be consistent with such a subtle measurement bias. Finally, any attribute correlated with living in a high current configuration home that relates to childhood cancer risk (e.g., property value, occupation, nutritional status) could have caused the observed pattern. This is referred to as confounding the ELF field or cancer association by mixing the effects of the extraneous variable and ELF fields. Because so little is known about the causes of childhood cancer and about the correlates of wiring configurations, it is impossible to be specific and argue convincingly that confounding occurred. Nonetheless, data were not gathered to refute this possibility, and the strength of epidemiologic study findings is a function of how well the study can isolate the exposure of interest by refuting the role of such potential confounders.

In spite of the limitations in Wertheimer and Leeper's (1979) study, it was an extremely important preliminary investigation and continues to serve as the prototypical study to which others are compared. Given the absence of human studies of cancer in relation to ELF fields prior to that time, this study raised questions that would not otherwise have been asked, but as a preliminary study it could not provide conclusive results.

Fulton et al. (1980) attempted to replicate these findings in a study of 119 Rhode Island children with leukemia who were compared to 240 controls. Most of the aspects of their study were identical to Wertheimer and Leeper (1979) (see Table 1), except for the inclusion of incident (rather than deceased) leukemia cases (rather than all childhood cancer cases). Their exposure indicator was derived from Wertheimer and Leeper's (1979) measurements of magnetic fields. Their results failed to corroborate the earlier findings, with no suggestion of an excess of high current configuration homes among their cases compared to their controls.

Many of the criticisms directed to the Wertheimer and Leeper (1979) study are equally applicable to the Fulton et al. (1980) study. There was limited information on potential confounding factors, and the uncertainty regarding the legitimacy of the indicator of magnetic field exposure remains. The small study group size introduces an additional concern with the statistical power to detect any effect, although their estimated relative risks were very close to the null value of 1.0. Despite the fact that the Fulton et al. (1980) study represents a failure to replicate Wertheimer and Leeper's (1979) findings, it is not a sufficiently high quality study to provide convincing evidence that domestic ELF field exposures are unrelated to cancer risk. This point is in accord with concerns raised by Wertheimer and Leeper in a 1980 "Letter to the Editor."

Tomenius, Hellström, and Enander (1982) conducted a study of childhood cancer and ELF exposure in Sweden. Although details of their study have not been published, the available information indicates that their case-control study included all 716 incident childhood cancer cases in Stockholm County compared to control children randomly selected from birth certificates in that same population. Their exposure variable consisted of a measurement of the magnetic field level present near the front door of the residence in addition to observation of a variety of electrical constructions. A modest but statistically significant excess of case homes had fields above 3 mG, interpreted as supportive of Wertheimer and Leeper's (1979) findings.

A major problem with the Tomenius, Hellström, and Enander (1982) study is the unavailability of detailed methodology, because since only an abstract has been published. The measurement is certainly open to criticism as an adequate reflection of long-term levels of ELF fields within the home, which would be the time frame of relevance to cancer development. Without methodological details, one cannot determine how time-of-day and day-of-week effects were controlled because field strengths are partly a function of the time and even the season of measurement. The decision to dichotomize their exposures at 3 mG does not appear to have been determined prior to collecting data and may reflect the cutoff that best discriminates between cases and controls. Such exploration would negate the value of their statistical significance testing due to multiple comparisons. The role of potential confounding variables remains unexplored in the Tomenius, Hellström, and Enander (1982) study, as in the studies by Werthiemer and Leeper (1979) and Fulton et al. (1980).

Wertheimer and Leeper (1982) conducted the other major published study of carcinogenic effects of residential ELF fields. Adult cancer cases (1,179) in the Denver area were compared to controls derived from death certificates and a telephone survey. A revised wiring configuration protocol was used that produced five levels of estimated exposure rather than a dichotomy of high and low. Remarkably similar findings of modest but statistically significant excesses of higher configuration homes were noted among cases compared to controls. Wertheimer and Leeper (n.d.) examined the pattern of risk for subtypes of adult and childhood cancers as an extension of their 1979 and 1982 papers. People with a younger median age of cancer occurrence tended to show stronger associations with wiring configurations, with positive results for nervous system, lymphatic system, and reproductive system cancers. In general, cases under the age of 70 and controls showed slightly more pronounced effects than subjects older than 70, although exceptions to this were present. Overall, there was relatively little difference in the strength of association between wiring configuration and cancer risk across cancer site, age, sex, and residence area. In fact, the results can be interpreted as providing evidence that the association with wiring configurations is homogeneous across these variables.

The same concerns with the validity of the exposure classification rationale and its objective implementation pertain to the study of adult cancers and the study of cancer subtypes. The failure to consider such well-established risk factors as tobacco use, reproductive history, and occupational chemical exposures can be pointed to more specifically as potential confounders of the apparent association between adult cancer and imputed ELF field exposures. If such attributes are related to wiring configurations (an untestable suggestion), then there would be a spurious association with cancer risk. The lack of specificity as to which cancers are affected argues against the observed association being causal, because few known carcinogens have such universal effects.

A recent paper reported a cluster of endodermal sinus tumors, a rare tumor of children, among five Black girls ages 1.5 to 18 in Jacksonville, Florida (Aldrich, Glorieux, and Castro 1984). Among speculations regarding the cause of this cluster, high tension (69-kV) power lines were noted in the area. Estimated exposures to case homes ranged from 0.04 to 1.69 G, notably higher than observed values in the studies reviewed above. Because such cluster reports are only intended to generate etiologic hypotheses, this suggestion must await further study.

Methodological Issues. Selection of a control series is a key concern in all four of the major studies of residential ELF fields and cancer, because any systematic bias in the exposure level of controls will manifest itself as a biased effect measure (e.g., odds ratio or relative risk) in the analysis. The goal is to select controls that represent the general population in their exposure characteristics, so that differences from the cases can be interpreted as excess exposure to cases rather than reduced exposure to controls. Although one can speculate at great length about notions of "representativeness" or "bias" in control groups, the absence of empirical data on correlates of exposure make it impossible to specify how the constitution of control groups might artificially reduce the levels of electric and magnetic field exposures among controls to produce a spuriously elevated exposure level among cases. Although the failure of all of these studies to measure and adjust for such possible confounding factors does not negate the results, the absence of reassurance that confounding did not occur leaves the results open to question.

Exposure characterization is one of the most problematic issues in this literature. The primary exposure measure was the presumed magnetic field strength based on wiring configurations in Wertheimer and Leeper (1979, 1982) and Fulton et al. (1980). There is the unresolved possibility that (1) wiring is not strongly predictive of fields, (2) wiring has some other correlates related to cancer risk, or (3) wiring configurations were classified in a biased manner. Wertheimer and Leeper (1982) provided data that addressed these three contentions and attempted to refute each of them. They could not, however, offer conclusive evidence to refute any of the possibilities. Only by measuring the fields in conjunction with wiring configurations in a large number of homes can the validity of the wiring configuration coding as a surrogate for magnetic field exposure be demonstrated. The concern with other correlates of cancer risk must also be addressed with empirical data on those other cancer risks, generally derived from interviews. The issue of biased coding can only be resolved by coding residences without knowledge of the health of the occupants. Anecdotal data addressing these points diminishes but does not eliminate the concerns.

The absence of information on potential confounding factors is another important issue, mentioned earlier in the context of control group selection. Because epidemiological studies are observational and subjects are not randomized to exposure groups, it is essential to consider what factors might be related to both cancer risk and to ELF field exposures. By measuring and adjusting for such factors, the influence of ELF fields can be isolated from other possible cancer determinants. None of the studies were able to measure and remove the influence of such factors to examine the independent role of ELF fields.

The statistical methods used and reported in both of the studies by Tomenius, Hellström, and Enander (1982) and Wertheimer and Leeper (1979, 1982) are difficult to interpret. They are not necessarily technically invalid, but the actual magnitude of association in the form of odds ratios was not reported. This constitutes an important weakness. When chi-square tests or other inferential statistics are provided without deriving a parameter reflecting the magnitude of association (Tomenius, Hellström, and Enander 1982; Wertheimer and Leeper, 1979, 1982), the reader cannot separate the issues of statistical significance and estimated degree of association. A nonsignificant association may be very large but imprecise and, thus, nonsignificant due to sampling variation. Alternatively, a statistically significant association may reflect a very precise measure of a very small relationship. Without presenting both a relative risk estimate and confidence limits or some other statistical test, the reader cannot distinguish among these possibilities.

Summary. Referring back to the criteria for establishing causality, these studies of residential ELF field exposures are inadequate to demonstrate such a relationship. When positive associations were observed, they were not very strong in magnitude, with estimated relative risks of 1.5 to 3.0. There is inconsistency in the findings, with Fulton et al. (1980) directly contradicting Wertheimer and Leeper's (1979) findings, without a satisfactory explanation of the discrepancy. The exposure based on wiring configurations or measured magnetic fields is likely to precede the cancer in the reported studies. None of the studies clearly demonstrated a positive dose-response gradient with higher levels of ELF fields (measured or imputed) associated with a higher cancer risk. Finally, there is little biological support for fields of the level observed in homes increasing cancer risk. None of these issues have been conclusively resolved in the sense that high quality research would be capable of exonerating as well as implicating ELF field exposures in cancer causation. The series of imperfect studies leaves the issue unresolved, but offers no convincing evidence that residential ELF fields increase cancer risk in humans.

Occupational Exposures

Review of Major Studies. A series of "Letters to the Editor" have been published in The New England Journal of Medicine and The Lancet from 1982 to 1984 concerning men occupationally exposed to electric and magnetic fields.

These surveys generally used available data from vital statistics or cancer registry sources in an effort to determine whether leukemias were overrepresented among employees of occupations assumed to entail high levels of electromagnetic field exposures. The opportunity to inexpensively explore these existing data bases is appealing, especially because of the large populations surveyed with consequently high statistical power. Unfortunately, the ability of such tabulations to address carcinogenic effects of ELF fields is severely limited.

The first two reports (Milham 1982; Wright, Peters, and Mack 1982) analyzed proportionate mortality and incidence from leukemia in Washington State and Los Angeles, respectively. They produced similar findings of an approximate 30 percent excess of total leukemia, and a 60 to 70 percent increase in acute leukemia, with Wright, Peters, and Mack (1982) noting a twofold excess specifically for acute myelogenous leukemia. MacDowall (1983) reported results of a similar analysis of mortality rates by occupation in England and Wales. For all "electrical occupations," leukemia (total, acute lymphoid, or acute myeloid) was not excessive, although a subgroup of occupations manifested a higher risk. An additional case-control analysis contrasting acute myeloid leukemia deaths with other causes of death suggested a twofold excess among "all electrical occupations." Leukemia incidence data for southeast England were tabulated by Coleman, Bell, and Skeet (1983), and proportional incidence was examined. A small (17 percent) excess of leukemia was noted among designated "electrical occupations." Somewhat more pronounced excesses were observed for acute lymphoid (46 percent), chronic lymphoid (29 percent), and acute myeloid (23 percent) leukemias.

All of these reports were based on the proportion of deaths (Milham 1982) or cancers (Wright, Peters, and Mack 1982) due to leukemia rather than the absolute risk of leukemia. Protection from other major causes of death (as is commonly observed among working populations) or other types of cancer would manifest itself as a proportionate excess of leukemia. Furthermore, such surveys are at best capable of providing evidence of large differences in risk due to the crudeness of the methods of assigning exposure (based exclusively on death certificate occupational title). Given the generally accepted notion that ELF fields are weakly related to cancer risk, if they are related at all, it could be argued that such surveys are inherently uninformative. If negative results are obtained, it merely indicates that a substantial excess of cancer is not present in the group, in this case a foregone conclusion. If positive results are observed in such a survey, the impact of ELF fields in isolation from other occupational exposures and other possible confounding factors cannot be assessed.

Occupational mortality data were cited by Wertheimer and Leeper (1979) as supportive of increased cancer among persons presumed to be exposed to magnetic fields, with a 15 percent excess of cancers. Sagan (n.d.) noted that the excess was accounted for in large part by lung cancer (known to be caused primarily by cigarette smoking) and that leukemia deaths were not substantially more frequent than expected (60 observed versus 53.1 expected).

A study of eye cancer (primarily melanoma) mortality in England and Wales (Swerdlow 1983) produced limited evidence of a proportionate excess among males employed as "electrical and electronics workers." An excess was observed from 1968 through 1975 based on the 27 cases reported to the cancer registry during that period, obviously a very small number of cases to establish a temporal pattern. The social class distribution of such workers (middle to lower) failed to explain the excess. Again, there are no data on exposure, but the pattern is legitimately interpreted as a suggestion to be pursued in more detailed studies.

Lin, Dischinger, and Farrell (1984) recently presented data on brain tumor mortality in relation to estimated occupational exposures to electromagnetic fields. Occupational histories of 951 brain tumor decedents in Maryland (1969-1982) were contrasted with the work histories of controls who died of causes other than cancer. Jobs in which electromagnetic field exposures were likely to occur were noted more frequently among victims of primary brain tumors (gliomas and astrocytomas) compared to controls. Unlike all of the preceding studies, this preliminary finding was followed by an effort to more accurately characterize exposure, but use of job titles rather than measured field strengths still constituted the indicator of exposure.

Potential job exposure to electromagnetic fields was categorized as definite, probable, possible, or no exposure based on expert opinion from an industrial hygienist, occupational physician, and radiation physicist. In the case-control analysis, definite exposure was 2.15 times as common among cases, probable exposure was 1.95 times as common, and possible exposure was

1.44 times as common.

The results of Lin, Dischinger, and Farrell (1984) provide a stronger suggestion of an association between at least some aspect of occupation and cancer than any of the preceding reports. The increased strength of association for primary brain tumors as opposed to those that could not be classified supports the existence of a nonartifactual relationship. Furthermore, the risk gradient based on their presumed exposure classification suggests more directly that the electromagnetic field exposures may have a critical role in their findings. The data are limited to presumed (rather than measured) exposures, and in spite of an intensive effort to accurately characterize occupations by the likely ELF field exposures, job titles alone are simply inadequate. Also, confounding factors were limited to those on the death certificate. Nonetheless, in spite of these real limitations, their study was of sufficient quality to encourage continued study of brain tumors and electrical occupations.

A recent study of cancer in the electronics industry in Sweden (Vagerö and Olin 1983) is probably more pertinent to chemical than electromagnetic hazards. Among male workers in this industry, small excesses were noted in pharyngeal and respiratory cancers. No evidence for excess leukemia incidence was provided. Similarly, Cammarano et al. (1984) reported on cancer risk among power plant workers, with an interest in chemical rather than physical hazards. An elevation in risk for total cancers was observed, but no specific cancer site accounted for the excess. This finding was attributed to exposure to known chemical carcinogens.

Methodological Issues. Some methodologic issues merit comment in interpreting the results of all of the occupational studies discussed above. First, the quality of exposure information (duration, intensity, field frequency) that can be derived from occupational titles is generally not characterized in these reports. Although precise methods for defining ELF exposures for occupationally exposed groups remain elusive, sufficient experience has accumulated to be confident that industry of employment or job title alone is simply inadequate (De Vizio, Duquette, and Trinh 1978; Kavet n.d.; Knave et al. 1979; Utidjian 1979). The choices of what groups to include as exposed was made arbitrarily and differed with the individual investigator. The heterogeneous groups contained persons essentially unexposed to electric or magnetic fields, persons exposed to different field intensities, and persons with different temporal courses of exposure. To identify a homogeneous exposure group based on occupational titles or industry of employment seems to be futile based on the available empirical data on exposure (Kavet n.d.; Knave et al. 1979).

Second, occupational exposures never occur in isolation. For example, Wright, Peters, and Mack (1982) noted that in addition to electric and magnetic fields, workers were potentially exposed to "metal fumes, solvents (including benzene), fluxes, chlorinated biphenyls, synthetic waxes, epoxy resins, and chlorinated naphthalenes." This same issue can, however, be viewed in the reverse in the case of brain cancer. Presumed chemical exposures in brain cancer etiology were reinterpreted by Lin, Dischinger, and Farrell (1984) as having a potential electromagnetic field explanation. The problem is that no occupational title unambiguously defines workers who are exposed only to ELF fields.

Third, other known cancer determinants such as ionizing radiation from medical treatment were not examined. Even readily available information on social class was not considered as a possible confounder. If "electrical occupations" contain a substantial proportion of technically trained, relatively well-paid workers and leukemia risk is somewhat elevated among the higher social classes, then the observed findings may be attributable to social class differences.

Finally, as letters to the editor or meeting abstracts, most of these reports were not thoroughly reviewed for technical merit. Though some appeared in prestigious publications, they should not be accepted with the same confidence as peer-reviewed manuscripts in those journals. Although the reports provide interesting suggestions, as should be expected from letters to the editor, they do not contain even the more thorough speculation required in a published article.

Summary. In summary, several letters suggest a rather modest increase in leukemia among workers presumed to have exposure to ELF fields, with some contradictory data also provided. Although there is some consistency across populations, the conclusiveness is limited by the critical and unproven assumption that such workers actually receive ELF field exposures (Bonnell 1982). Furthermore, these letters generally considered proportionate (rather than absolute) leukemia mortality or morbidity. Finally, there was a complete failure to consider other occupational exposures or other leukemia risk factors. Crude occupational surveys of the type reported in these letters to the editor are useful only in producing preliminary suggestions about possible risks, and their value in that regard is limited to dramatically increased risks. Their value in supporting or refuting the postulated small elevations in cancer in relation to ELF fields is minimal. The Lin, Dischinger, and Farrell (1984) brain tumor study merits more attention and attempts at a replication. One well-done occupational study with adequate documentation of exposure would carry more weight than the combined strength of all the reports that were reviewed.

Conclusions

The studies of residential exposures, in balance, contain preliminary suggestions of an elevated risk of cancer that have not yet been thoroughly refuted or confirmed. The studies of Wertheimer and Leeper (1979, 1982) and Tomenius, Hellström, and Enander (1982) are sufficiently credible to raise the interest that has ensued but are inadequate in demonstrating that ELF fields cause cancer in humans. In spite of a lack of support from laboratory studies, the possibility that ELF magnetic fields act as cancer-promoting agents remains a hypothesis worthy of further study. Alternate (noncausal) explanations of the data remain speculative as well (i.e., unmeasured confounders and biased coding of exposure). Until the conflicting explanations of the association between wiring configurations and cancer risk are tested, there is no firm empirical basis for assessing the risks.

The studies of cancer among occupationally exposed groups contain more reports of lower quality and even fewer details. The letters to the editor provide suggestions of some modest increase in leukemia occurrence among workers in "electrical occupations," but are inherently weak due to a reliance on broad occupational titles. These studies constitute very limited evidence to address the question of whether ELF fields are related to cancer risk. Until the exposure patterns of appropriate workers are assessed in relation to subsequent cancer risk, the presence or absence of an association cannot be resolved with any certainty.

The available literature on human cancer risk related to electric and magnetic field exposures does not support the presence of a causal association. Rather than a literature of methodologically sound but contradictory studies, a more accurate characterization of this literature is a predominance of methodologically flawed and inconclusive positive reports. The studies reviewed here are so inconclusive that they cannot distinguish between (1) an increased cancer risk due to ELF field exposures which are obscured by imprecise exposure data and the failure to adjust for confounding factors and (2) the absence of any real association with positive results attributable to extraneous cancer determinants or study biases. A Lancet (1983) editorial expressed this perception as well.

These conclusions are generally consistent with Roth's (1984) critique of part of this literature and Tenforde's (Chapter 4) comment that "it is not possible at this point in time to conclude that a definite association exists between the exposure of individuals to ELF magnetic (or electric) fields and their relative risk of contracting leukemia or other forms of cancer." Detailed analysis of the existing literature cannot effectively resolve this issue due to methodological limitations in past studies. Research that improves the exposure characterization and measurement of other cancer determinants offers the only method for resolving this issue.

REPRODUCTIVE EFFECTS OF ELF FIELDS

Few studies have directly addressed the possibility of human adverse reproductive effects from exposure to ELF fields (Knave et al. 1979; Nordström, Birke, and Gustavsson 1983; Wertheimer and Leeper 1984), although ancillary evidence is available from Buiatti et al. (1984) and Wertheimer, Fulton, and Leeper (n.d.). The sources of exposure were quite different, with Knave et al. (1979) and Nordström, Birke, and Gustavsson (1983) assessing reproductive function in males occupationally exposed to such fields and Wertheimer, Fulton, and Leeper (n.d.) concerned with electric blanket and heated waterbed exposures to the fetus.

Review of Major Studies

Knave et al. (1979) compared reproductive experiences of 53 power company workers exposed to electric fields from 400-kV substations to 53 matched power company workers without such exposures. The only questions pertinent to reproduction concerned fertility and sex of offspring. Overall, there was a deficit of children among exposed workers, which began prior to the time of employment and continued through the period of employment. Specifically, exposed workers fathered fewer male children. Because the pattern began prior to exposure, electrical or magnetic fields in the work environment are unlikely to have caused the pattern. The overall deficit of children may have been due to socioeconomic factors, though the deficit of males in particular remains unexplained.

The lack of precise exposure characterization limits the ability of the Knave et al. (1979) study to evaluate the effect of ELF fields. At best, differences in reproduction among occupational groups were addressed. The extremely small size of the study groups provides for [illegible]ed statistical power to detect effects, and self-reporting of reproductive experience is known to be a fallible source of data especially for male respondents.

The only other data directly pertinent to a possible effect of ELF fields on infertility comes from a recently reported case–control study by Buiatti et al. (1984). In this exploratory investigation, one of the few paternal job categories associated with infertility was "radioelectric workers" who were 5.9 times as likely to appear among infertile cases as among controls. Small numbers of subjects, ambiguity in the exposure definition, and severe flaws in the study design preclude conclusions, but the consistency with the Knave et al. (1979) suspicions is of interest.

Nordström, Birke, and Gustavsson (1983) surveyed 542 Swedish power company employees regarding reproductive experience and potential environmental reproductive hazards. Three groups of workers were defined based on work in 400-kV substations (331 men), work with 380- or 220-kV transmission lines (145 men), and work with less than 130-kV lines (66 men). These groups were assumed to define an exposure gradient, from high to low. In addition, exposure groups were defined by work task (high voltage switchyard, construction or repair of switchyard and lines, or other) and by electric field exposures of <70 kV, 130 to 200 kV, or 400 kV. The pregnancies occurring among these workers' spouses were classified as spontaneous abortions, perinatal deaths, livebirths with congenital malformation, or normal livebirths. Each pregnancy was classified by the father's occupation at the time.

The frequency of normal pregnancy outcome did not vary in relation to the voltage level, but switchyard workers were marginally less likely to have a normal pregnancy outcome (81 percent of conceptions versus 92 percent for construction/repair workers, 89 percent for other workers, and 87 percent for the reference group). Risks of spontaneous abortion and perinatal death were not notably elevated for switchyard workers compared to the others, but congenital malformations were elevated: 8 percent of the children were reported to have congenital malformations among switchyard workers versus 1 to 3 percent in the other groups. Adjustment for maternal and paternal risk factors (age, smoking, etc.) did not alter this pattern.

The value of this finding must be tempered because congenital malformations were not chosen in advance as the outcome of interest and, in spite of statistical significance testing, may well have occurred by chance alone. Furthermore, congenital malformations are quite heterogeneous, and one would not expect a single exposure to increase all types of malformations. If a subset of malformation types were affected by the exposures, a dramatic increase in such types would be indicated by the data. The exposure groups were defined in multiple ways with little corroboration that the classifications were valid indicators of ELF field exposures. Exploring several exposure indices in relation to several reproductive outcomes might suggest that their findings were due to chance alone because a large number of associations were explored. Although strong evidence that ELF field exposures to males cause reproductive problems is lacking in this report, subsequent studies should address this possibility to determine whether the same reproductive end points emerge as important.

Wertheimer and Leeper (1984) surveyed published birth records and surveyed use of electric blankets and heated waterbeds in relation to fetal losses. They found that winter conceptions to parents using such devices resulted in prolonged gestations. More congenital defects were also observed in exposed winter conceptions. In addition, a trend towards a higher rate of fetal losses preceding the live births were observed, again more pronounced for winter conceptions.

Wertheimer, Fulton, and Leeper (n.d.) were concerned with effects of magnetic fields on fetal development. Several types of evidence were called on to support the hypothesis that human fetal development can be adversely affected by ELF magnetic fields. First, a deficit of childhood cancer cases (especially males) in homes with the highest presumed magnetic field levels at the time of birth was interpreted as suggesting abortion of the fetuses who were most susceptible to cancer development. Second, a survey of wiring configurations at 285 homes in which pregnancies ended with stillbirth, perinatal death, or congenital defect compared to normal births showed an excess of high current configuration homes among the cases. Third, the greater susceptibility among males to such fields led to a search of U. S. birth records that indicated a deficit of males for November through April conceptions (months in which electric blankets or heated waterbeds would be used). The emerging pattern over the period 1940 to 1970 was consistent with the increased usage of such devices.

Neither of the above reports have been subjected to peer review, and there are several factors challenging their validity. Much of the evidence cited by Wertheimer, Fulton, and Leeper (n.d.) and Wertheimer and Leeper (1984) is highly circumstantial in that ELF field exposures are blamed when other explanations are equally plausible. For example, the deficit in male births from winter conceptions could be explained by any factor that varies by season including infectious diseases or temperature stress. The survey of electric blanket and heated waterbed use is limited by a poorly designed sampling frame in that birth announcements are not provided for all births. Furthermore, gestational age was established based on birth certificate records, which is known to be a fallible method. None of the numerous attributes known to be related to reproductive outcome (social class, nutrition, tobacco use, maternal diabetes, etc.) were considered as potential confounding factors, which is especially troublesome because it might be inferred that the exposure to electric blankets and especially waterbeds could be related to these same characteristics. Once again, data are not available to confirm or refute the role of such risk factors in accounting for the findings.

The ability of these studies to directly address effects of ELF fields on reproduction is very limited.

Summary

In summary, these studies claim a possible effect of ELF fields on five different reproductive end points: infertility and sex ratio (Knave et al. 1979), congenital malformations (Nordström, Birke, and Gustavsson 1983; Wertheimer, Fulton, and Leeper n.d.), and prolonged gestation and fetal loss (Wertheimer and Leeper 1984; Wertheimer, Fulton, and Leeper n.d.). None of the individual findings are convincing that ELF field exposures actually caused the observed reproductive problems. Exposures were notably different between the Swedish studies and the American study (power company occupational exposure versus electric blanket and heated waterbed), and even the sex of the exposed person (father versus mother) varied. There are no corroborations of any of the positive findings across studies. The conclusion from this literature is that evidence of adverse effects of ELF fields on human reproduction is lacking. Future studies of human reproductive effects, however, now have a context and should address the suggestions of Nordström, Birke, and Gustavsson (1983) and Wertheimer, Fulton, and Leeper (n.d.).

The biological basis for concern with reproduction and development is well-founded in the special sensitivity of these processes to environmental influences. To date, however,

> There have been no studies which clearly demonstrate deleterious effects of ELF electromagnetic field exposures during either prenatal or postnatal development of any mammalian species. Nevertheless, it seems that findings suggestive of such effects appear with a frequency that perhaps is greater than should be attributed to chance, although it should also be noted that an interplay of various biases may be involved. (Sikov 1985).

The experimental literature lends relatively little support to the human study findings. In fact, very similar conclusions to Sikov's (1985) might be drawn from the human literature. In combination, the experimental literature and human literature provide only tenuous support for the possibility that adverse reproductive effects ensue from exposures to ELF fields.

GENERAL HEALTH EFFECTS OF ELF FIELDS

Several surveys have been conducted to address possible adverse human health effects of chronic exposure to low-level ELF fields. This section discusses effects other than cancer or reproductive hazards and considers neurological, psychological, cardiovascular, hematological, and other health end points. Only studies of AC fields were included, which eliminated the recent study by Haupt and Nolfi (1984) of a population exposed to a DC transmission line.

Review of Major Studies

A substantial proportion of the early surveys were conducted in the Soviet Union as reviewed by Bonnell (1982), Cabanes (1980), and Knave et al. (1979). These studies suggest an excess of a variety of complaints such as headache, nausea, fatigue, and loss of libido. As concluded by the reviewers mentioned, the nature of the symptoms (very common, nonspecific, and amenable to reporting biases) and the quality of the study designs (no comparison groups, no verification of self-reported complaints, no documentation of exposure) leave the issue unresolved. Although there are frequent reports of dubious quality from the Eastern European literature concerning adverse psychological effects of occupational environments, the surveys did, in large measure, encourage more thorough evaluations of the possibility of general health effects of ELF fields.

Reichmanis et al. (1979) were concerned with the proximity of power lines to residences of suicide cases. They determined the residence locations of 651 suicide victims from 1969 to 1976 in selected areas of central England. The investigators also determined the locations of all overhead high-voltage (>33 kV) transmission lines. The estimated electric and magnetic fields associated with each case address and with a randomly selected set of control addresses were derived based on transmission line geometry, voltage, and current. Results suggested that suicide cases more often lived in residence with greater presumed electric and magnetic field exposures.

A more detailed report on suicide was provided by Perry et al. (1981) who conducted measurements of magnetic fields at the residences of the 598 suicide victims who resided in their homes 14 days or longer compared to controls randomly selected from voter registration lists. The measurements were taken at the front entrances of the homes, with the distribution of season and time of day balanced between cases and controls. The measured field strengths at case homes exceeded control homes by 0.158 mG on average, which is significant according to sign tests based on whether the case or control home was higher, overall distribution of exposures, or comparison of means of cases and controls. Consideration of other aspects of the home and neighborhood did not distinguish cases from controls, suggesting that nonspecific factors in the choice of residence did not act as confounding influences.

These results are limited in several respects. Suicide is a poor choice as a subject of investigation because it is the result of a number of different unspecified biological or psychological pathways. There is often some underlying psychological or physical problem and some precipitating factor that leads to the event. To address the effects of magnetic fields on either the underlying phenomenon or precipitating event requires more knowledge than could be obtained from the death certificate. Without the ability to analyze subgroups of suicide victims, the coherence and plausibility of their findings cannot be considered. This criticism would be equally applicable to positive or negative findings.

The exposure measurement consisted of a one-time outside assessment, which is undoubtedly an incomplete indicator. Although a few indicators of residence choice were examined, the broad array of potential confounders (suicide determinants) were ignored, including marital status (possibly related to housing characteristics), socioeconomic status, history of alcohol or drug abuse, etc., as possible explanatory factors, all of which are more plausible than a general effect of ELF fields. The findings are thus very weak in that the case group was poorly specified, exposure data were limited, and none of the established risk factors for suicide were considered (Bonnell et al. 1983).

A series of medical evaluations of 11 power company workers was conducted by Singewald, Langworthy, and Kouwenhoven (1973). A detailed medical history, physical examination, psychiatric evaluation, and laboratory survey were conducted on each of the men seven times between 1962 and 1972. No abnormalities were detected in any of the characteristics that were evaluated. Given the small number of men studied and the absence of any comparison group, only highly frequent adverse effects could possibly have been detected. The sensitivity of such a survey in identifying subtle effects on a small proportion of workers is inadequate.

Strumza (1970) analyzed medical care use patterns among two groups from the general population: exposed persons who resided within 25 m of high voltage AC power lines and unexposed persons residing and working more than [illegible] from such lines. French Social Security records provided data to determine the rate of medical consultations; house calls; visits to medical specialists; and pharmaceutical expenditures for men, women, and children residing in the exposed and unexposed groups. No excess of illness was found among exposed residents (men, women, or children). The only suggestive findings were opposite to the hypothesized direction, with an excess among the unexposed. Although the size of the population (525 individuals) is reasonably large, the categories of health outcome were so highly aggregated that many genuine excesses of health problems could have easily been overlooked. Each category represents such a broad aggregation of health complaints that adverse effects on all but the most common medical conditions would be missed.

Knave et al. (1979) surveyed an occupationally exposed group of Swedish power workers, with the 53 exposed workers defined based on their having experienced 5 or more years in 400-kV substations. The unexposed comparison group consisted of 53 workers for the same companies matched on age, geographic location, and duration of employment. The actual exposures experienced by the workers were found to be highly variable over the course of the day, with substantially higher electric field exposures on average among the workers classified as exposed. A rather thorough evaluation of the nervous, cardiovascular, and hematologic systems was conducted, including neuropsychological testing. No exposure-related differences were detected. Although some of the neuropsychological measures favored the exposed group, this was thought to be due to a slightly higher educational level compared to the unexposed group. No differences in other psychological tests, neurasthenia (nonspecific neurological complaints), electroencephalogram patterns, cardiovascular symptoms, electrocardiogram findings, or blood analyses were reported. Although confidence in the results is limited by the size of the study groups, these results provide the strongest evidence that routine, chronic exposures to ELF fields do not produce any obvious adverse health effects. Schuy and Waibel (1979) provide data on experimental human exposures that corroborate the absence of such general adverse physiological effects.

A specific area of concern regarding health effects of ELF field exposures concerns the potentially susceptible subgroup of individuals with heart conduction defects requiring use of pacemakers. A thorough review of theoretical and empirical considerations in adverse effects of ELF fields on pacemaker function (Griffin 1985) led to the following conclusions: "Clinically documented interference problems are extremely rare with the exception of the body's own endogenous myoelectric interference. ... Even if the pacemaker is affected, the patient still may not be placed at risk." These conclusions of minimal risk were, however, tempered by the paucity of empirical studies on the wide range of currently used pacemaker devices. Butrous et al. (1983) recently offered some empirical documentation that substation workers were subject to induced reversion of the pacemaker to the interference mode, a clinically nonsignificant effect, but confirming some of the theoretical concerns raised by Griffin (1985).

Summary

The quantity and quality of research addressing nonspecific adverse health effects of ELF fields is so limited that the only conclusion is that an overwhelmingly frequent and obvious adverse effect can be ruled out. The thorough review by Mehn (1979) generally supports this conclusion. The experimental literature has developed to the point where some rationale for human investigations should precede the studies. Further examination of suicide in the aggregate, for example, is unlikely to be informative. The possibility of important effects among a subset of highly exposed workers or a substantially increased risk of a relatively rare health event has not been addressed effectively. Nonetheless, these preliminary findings lend little support to justify a thorough evaluation of the general health of ELF-field exposed workers. Focused investigations or epidemiological research seem to be more likely to be productive than broad and generally insensitive surveys of health in either occupational or general population groups.

OVERALL CONCLUSIONS

The literature on the human health effects of ELF fields does not provide any convincing indication of a threat based on studies of cancer, reproductive outcomes, or general health. In each of the areas one or more studies offer suggestions based on isolated positive findings. The fallibility of any given study requires replication before accepting the conclusion that ELF fields are causally associated with health effects.

The methodological weaknesses are primarily related to exposure assessment and failure to address potential confounding variables. These are both potentially remediable, and the results of methodologically superior studies will directly affect the credibility of the earlier studies. In the areas of cancer and reproductive hazards, the inconclusive positive studies are balanced with inconclusive negative studies, leaving unresolved the scientific question of whether ELF fields pose a health risk. Continued examination of this issue is needed, which should culminate in more credible, conclusive results than have yet been produced.

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CHAPTER 10

POTENTIAL EFFECTS ON NATURAL BIOTA IN OPERATING AN EXTREMELY LOW FREQUENCY COMMUNICATIONS SYSTEM

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INTRODUCTION

This chapter evaluates current literature pertaining to effects that might be produced in native flora and fauna as a consequence of operating the USN Extremely Low Frequency Communications System in Michigan and Wisconsin. The evaluation was conducted as one aspect of a public policy process to decide whether or not the benefits of constructing and operating an ELF communications system out weigh the risks. Therefore, it was necessary to differentiate between facts meeting the scientific criteria of reproducibility and independent verification by different investigators and the unverified observations and speculations representing the early stages of scientific inquiry. The latter category of information may be accurate and should not be ignored. Conversely, it may remain suspect and be misleading. Unfortunately, much of literature pertinent to potential ecological effects fall into the latter category (Carstensen 1985).

Extrapolation of these uncertainties to potential ecological effects in the setting of the ELF Communications System is particularly difficult because (as the previous chapters attest) effects produced by ELF fields in the laboratory do not appear to be specific to ELF exposure; there are no agreed upon hypotheses to explain the mechanism of action; and there is little evidence for a predictable dose-response relationship. However, the question of whether or not ELF fields affect natural ecosystems is not trivial and should be answered. The physiochemical and electrochemical nature of critical life processes are well established. The probability that environmental electromagnetic fields superimposed on living systems will produce some

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detrimental effect would appear to be high, but evidence validating the concern is equivocal. In spite of the uncertainties, it is reasonable to attempt to establish a degree of risk to the ecosystem based on the body of scientific literature in hand.

ASSESSMENT METHOD

The effort to establish a degree of risk was limited to an assessment of literature published since release of the National Academy of Sciences evaluation in 1977 (NAS 1977). The literature was reviewed by specialists in different fields who prepared the critiques published as a separate document (Assessments and Opinions of the Biological and Human Health Effects of Extremely Low Frequency Electromagnetic Fields. Compilation of Commissioned Papers for the ELF Literature Review Project). These critiques were the primary data base from which the following chapter was derived.

Although the focus of this analysis is ecology, there are few published research reports on native species that bear directly on the effects of the ELF Communications System. Thus, projections of effect must be derived largely from experiments conducted in the vicinity of 60-Hz power transmission lines that frequently produced electromagnetic fields which are orders of magnitude greater than those anticipated to be produced by the ELF Communications System (Lee et al. 1982), or from laboratory findings that are difficult to extrapolate to species in the wild.

A second category of data is laboratory and field studies done in conjunction with the testing and development phase of the ELF Communications System (Projects Sanguine/Seafarer). These studies are best described as pilot experiments to help identify potential problems and to lay the groundwork for more sophisticated ecological studies to be conducted in parallel with operation of the fully developed communication system.

A third body of data deals with the ability of a few species to detect, and possibly use, naturally occurring electrical and magnetic fields for navigation or location of food. Although this ability is not typical of most species, the phenomenon is intriguing because, for these special cases, the intensity of the sensed natural earth fields approaches the intensities that may be produced by the ELF Communications System. Thus, operation of the System might alter behavior by producing confusing signals.

The critiques of laboratory experiments have been read with the expectation that if an effect was demonstrated in the laboratory it might occur as well in the wild. However, there are important caveats:

- It is difficult to extrapolate the effect observed in vitro or in one kind of organism in the laboratory to the vast array of species occurring in an ecosystem. For example, studies of circadian rhythms suggest that there are significant interspecies differences between laboratory and wild strains of rodents in the ability to detect high strength (kV/m), 60-Hz electric fields (Ehret et al. 1980).

- Detection of an ELF field does not necessarily imply an adverse effect. In the example above, detection of the 60-Hz field resulted in a phase-shift in the circadian rhythm of arousal. The effect, however, was transitory, with no residual effect. The animals rapidly habituated and failed to respond to continued treatment.

- A response may only be demonstrated under special controlled conditions. An example is the reported ability of electromagnetic fields to entrain circadian rhythms (Sulzman 1985). Although this may be true under some conditions, entrainment is not likely to occur if the experiment is conducted in a normal light-dark cycle. Photoperiod is clearly the dominant agent for native species and overrides other cyclic environmental stimuli.

- Subtle responses observed under controlled laboratory conditions may be overridden in the wild by other responses as the organism copes with day to day environmental stresses.

- It has been shown that there are narrow bands, or windows, of frequencies or intensities to which some organisms appear to be most sensitive (honeybees: Martin and Lindauer 1977; birds: Papi and Wallraff 1982; fish: Kalmijin 1966). Thus, lack of a response to a high intensity electromagnetic field in the laboratory does not mean that there will be no response to a low intensity electromagnetic field in the wild.

- A population in the wild is usually heterogenous compared to highly inbred laboratory strains and, consequently, is likely to show a wide range of individual susceptibilities to a given treatment--particularly if the treatment approaches threshold levels of detection. The response of only a few individuals may have no detectable effect at the population level.

- The response may be undetectable at the ecosystem level. A National Academy of Sciences evaluation (NAS 1977) identified ecosystem effects as particularly important because, in theory, they should represent an integration of all changes. However,

> the NAS also recognized that the observed changes could be caused by "most anything." The accepted implication, with which we agree, is that the reported effects of ELF radiation are subtle, not catastrophic, and typically are not effects specific to exposure to ELF. The same kind of responses might be anticipated from a variety of enviromental stressors. The ecosystem is a complex of biological species and physical factors that paradoxically is always in a state of flux while demonstrating a resiliency to environmental stressors. Such a system may indeed mask or buffer subtle changes introduced by ELF transmission leading to a false conclusion that no effect had occurred.

These caveats present a compelling case for conducting ecological research in conjunction with the operation of the ELF Communications System.

Although care must be taken in extrapolating laboratory findings to field conditions, laboratory experimentation is essential to a full assessment of ecological risks. It is in the laboratory that cause and effect and mechanisms of action are most clearly elucidated. Conversely, studies on species in the wild can identify new phenomena and point to new directions for laboratory research. Evidence from both arenas must be integrated to assess the ecological consequences of human actions.

ASSESSMENT

This chapter assesses information regarding the potential effects of natural biota in operating an ELF communications system. The information published since the 1977 NAS evaluation was evaluated in light of two questions: (1) Would the redesign of the ELF Communications System change the anticipated electromagnetic fields enough to invalidate the 1977 evaluation by NAS ? and (2) Does the literature published since 1977 contain new evidence that ELF communications are likely to alter the ability of a species to carry out their normal function in an ecosystem ?

The answer to the first question is no. The redesign has reduced intensities of ELF fields and increased confidence in the NAS prediction of negligible risk if the activity were to proceed accompanied by a program of ecological research.

The answer to the second question is also no. Although there is some evidence of improved standardization of exposure fields, the studies published since 1977 continue to be equivocal in experimental methods and in the interpretation of data.

Changes in ELF Communications System Design

The characteristics of redesigned communication systems are summarized in Appendix A. They include: redesign of ground terminals to reduce step potentials, single above-ground antennas mounted on 35-ft. poles (rather than the buried antennae of earlier concepts), changes in the antennae configuration from a grid to single north-south and east-west installations in Wisconsin and an F configuration in Michigan, and operation of the Michigan facility with an antennae current of 150 A rather than the 300 A characteristic of the Wisconsin installation (Zapotosky and Ambromavage 1983).

Redesign of the ground terminals, although effectively reducing step potentials, subjects a much larger area of the installation to low level underground ELF fields. It is not clear whether or not this represents an increased risk (compared to the original design) to organisms closely coupled to the soil (i.e., microorganisms, plant root systems, fossorial animals). With the exception of this uncertainty, it would be expected that the ELF fields produced by the redesigned system would be no more than those produced by a commercial 60-Hz power line installed over the same distance to service a local community (IITRI 1984; Lee et al. 1982) and less than the field intensities assumed in the 1977 NAS report.

New Literature on Biological Effects of ELF Fields

Ecological Perspective

Biology is traditionally organized according to increasing levels of complexity: organic molecules, cells, tissues, organs, organisms, populations, communities, ecosystems, and biomes. Ecology is concerned primarily with levels of organization between the organism and the biome and with the interaction of living things and the environment in which they occur. Each level of organization has its particular parameters of study.

Ecology is so complex that all the components of an ecosystem can never be studied simultaneously; however, individual research results can be assembled in models, sometimes descriptive, sometimes quantitative, but nevertheless representative of working ecosystems. The models may be conceptually correct, useful in accounting for observations and in guiding future research, but they are rarely of predictive value for site-specific problems. Lacking ecosystem models of the proposed ELF Communications System sites, and with limited data specific to species occurring at the sites, assessment of potential ecological effects of operating the Communications System is reduced to extrapolations of imperfect data constrained by the caveats presented.

Experiments in the Vicinity of Power Lines

The principal source of data taken under "natural" conditions was obtained in the vicinity of high voltage, 60-Hz power transmission lines with vertical field strengths in air on the order of 2 to 20 kV/m (Lee et al. 1982; Rogers and Lee 1985). Magnetic field strengths in the vicinity of power lines can range from 0.3 to 0.6 G compared to the earth's natural magnetic field strength of 0.6 G (Dodge 1984). In comparison, the anticipated vertical field strengths in air for the operating ELF Communications System is 150 V/m near the ground. Horizontal electric fields in the ground are anticipated to be about 1.5 V/m near the ground terminals and 0.14 V/m, and 0.07 V/m, respectively, under the antennas of the Wisconsin and Michigan communication systems, with magnetic field strengths on the order of 0.03 G (Zapotosky and Ambromavage 1983).

It is clear that studies in the vicinity of high voltage power lines were conducted with field strengths 1 to 2 orders of magnitude greater than that anticipated for the ELF Communications System and with negligible horizontal ground currents characteristic of an operating ELF antenna system. Nevertheless, the findings are pertinent to this assessment.

Effects on Plants. From an ecological perspective, the most dramatic change in an ecosystem would occur if plants were adversely affected by ELF fields. This is because only plants are capable of converting the radient energy of the sun into a form useful to drive biological processes. Most recent studies designed to investigate the possible effects of electromagnetic fields on plants have been concerned with electric power transmission lines. Pilot experiments in the vicinity of 765-kV power lines measured seed germination, chlorophyll content, seedling height and dry weights, and cell division and showed that electric fields from near background to about 20 kV/m had no effect on growth or productivity of crop plants (Greene 1979, 1981; Hodges and Mitchell 1979; Lee et al. 1982). Similar studies in the vicinity of other power lines also reported no adverse effects on crop plants or native vegetation (Endo et al. 1979; Rogers et al. 1980). Several studies have

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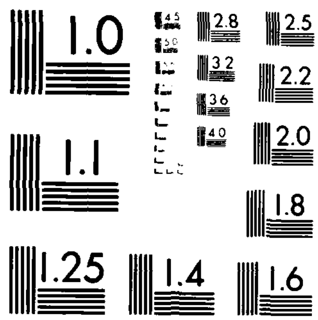

MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS 1963 A

reported damage to the leaf tips of trees exposed to coronal discharges greater than 20 kV/m. Normally, trees growing close enough to a commercial power line to be damaged by electric fields would be removed as part of construction and right-of-way maintenance activities (Rogers and Lee 1985).

Although studies in the vicinity of high voltage lines did not show evidence of ELF fields below about 20 kV/m affecting plants, interpretation of data sometimes was confounded by uncontrolled environmental variables such as climatic factors. Results of the studies, however, gain credence when compared with the results of laboratory experiments. Several thousand plants representing 85 different species were exposed to electric fields from 0 to 50 kV/m in growth chambers under carefully controlled environmental conditions (McKee et al. 1978, 1982). Except for limited damage at leaf tips from coronal discharge, even the maximum field strength of 50 kV/m failed to affect overall growth, viability, yield, or reproduction of exposed plants. Findings of these studies are complemented by experiments on plant root growth (Miller et al. 1980; Robertson, Miller, and Carstensen 1981) and seed germination (Marino, Hart, and Reichmanis 1983). Reduction in root tip growth in peas was reported at field strengths above 250 V/m for fields aligned parallel to the root tip. Germination rates of sunflower seeds were reported to be depressed 5 percent by exposure to electric fields in air of 1 to 5 kV/m. These data are more fully discussed in Chapter 5 which deals with cellular effects of ELF electric and magnetic fields. If the projected intensity of horizontal ground currents for the ELF Communications System are correct (0.07 to 1.5 V/m), it appears unlikely that either plant root systems or germination of seeds would be affected. Although there is no evidence to suggest that plants will be affected by operation of the ELF Communications System, there is a paucity of information regarding possible effects on lower plants or species occurring at the sites.

Effects on Mammals. No effects attributable to electric or magnetic fields were found in small mammals occupying the right-of-way of an 1100-kV prototype transmission line (Warren et al. 1981). Rogers and Lee (1985) concluded that it was unlikely that small mammals would be affected by overhead lines because similar electric field characteristics did not produce significant effects in laboratory studies, and small animals are partially screened from electric fields by an overhead canopy of plants. Studies of livestock maintained near high voltage power lines suggested that the likelihood of any effect on behavior of large native animals also was low (Amstutz and Miller 1980; Hennichs 1982; Rogers et al. 1982; Williams and Beiler 1979). Indeed, no effects were detected in the patterns of deer and elk movements attributable to the presence of a 500-kV transmission line in Idaho (Goodwin 1975) nor to the apparent abundance of mule deer and pronghorn antelope in the vicinity of a high voltage DC transmission line in Oregon (Griffith 1977).

Effects on Birds. Bird studies also failed to reveal adverse effects of high voltage transmission lines except for changes in land use brought about by the clearing of vegetation from the transmission line right-of-way (Anderson, Mann, and Shugart 1977). Bird studies have included monitoring of hawks nesting atop transmission line towers (Lee et al. 1982). Eggs and young were exposed to electromagnetic fields during substantive portions of their development, apparently without detrimental effect. Pardoxically, in the laboratory, Delgado et al. (1982) report significant embryological changes in chick embryos induced by weak ELF fields.

Effects on Honeybees. Studies of honeybees in the vicinity of high voltage transmission lines generally reveal normal foraging behavior outside the hive but abnormal behavior and, in some cases, reduced honey production and reduced overwintering survival inside the hive (Rogers et al. 1982). The effects appear to be due to currents induced in the hive by electrical fields above 2 kV/m (Greenberg et al. 1981). Again it is unlikely that such a phenomenon will occur at the ELF Communications System sites. The known effect of low intensity magnetic fields on honeybee orientation (Martin and Lindauer 1977) may justify the intended study of honeybees in conjunction with ELF communications. It should be noted, however, that the effects that have been observed in bees were attributed to electric, not magnetic, fields.

Summary. In summary, none of the biological observations on plants, birds, mammals, or insects in the vicinity of high voltage transmission lines suggest areas of concern for the operating the ELF Communications System. It is true that no studies were conduced below ground with burrowing or fossorial forms. However, the intensities of electromagnetic ground fields anticipated for the ELF Communications System are low (0.07 to 1.5) V/m; 0.03 G) and unlikely to be of significance. This is an area of uncertainty but of low enough risk to warrant study in conjunction with, rather that preceding, operation of the ELF Communications System. Current plans are to study lower life forms closely coupled to surface and subsurface soils (IITRI 1984).

Other Animal studies

There are two ways in which electromagnetic fields might affect animals. The first is by covert biochemical or physiological changes of which the animal is unaware but may alter its chance of survival in the wild. Examples of covert changes are mutagenesis, changes in activity levels of enzymes and hormones, changes in cell cycles, embryological effects, calcium efflux in nerve tissue, and alteration of the circadian system (Albert and Slaby 1985; Goodman and Greenebaum 1985; Marino 1985; Sikov 1985; Sulzman 1985; Tompkins et al. 1985; Winters and Phillips 1985). These kinds of effects are primarily observed in laboratory experiments probing for the mechanism of interaction of electromagnetic fields with biological material. For the most part, the experiments have been conducted under conditions very different from those anticipated at the ELF Communications System sites. The following are examples of attempts to extrapolate laboratory findings to the ELF sites made in reviewing the recent literature:

> If there are covert mechanisms regulating the basic biological processes sensitive to the effects of magnetic or EM fields, at present, no one understands them sufficiently. (Winters and Phillips 1985).

> Geomagnetism may be used in direction finding, but the geomagnetic effect is like the Cheshire Cat encountered by Alice in Wonderland: it has "the disconcerting habit of appearing without warning and then vanishing, in part or in whole, only to reappear at some later time" (Graves, Long, and Poznaniak 1979). (Gauthreaux 1985).

> At this time, the available data will not permit one to extrapolate whether a cell would show altered cation fluxes at the field intensities actually encountered in the vicinity of a power line or a communication's antenna. (Goodman and Greenebaum 1985).

> In conclusion, the data reviewed in this paper suggests that exposure to ELF fields can cause alterations in the immune system, although generally transient and mild in nature. We interpret this to indicate that ELF field exposures represent a near threshold "non-specific stressor" phenomenon to which the response is, by definition, unpredictable and subject to

> individual, as well as, species variation. (Tompkins et al. 1985).
>
> There have been no studies which clearly demonstrate deleterious effects of ELF electromagnetic field exposures during either prenatal or postnatal development of any mammalian species. (Sikov 1985).
>
> On the basis of an analysis of the literature on biological effects of ELF electric and magnetic fields on cellular systems, and despite the considerable uncertainties on issues of biological interest and importance, there is essentially no probability of deleterious biological effects on organisms exposed to the Project ELF in air. (Chapter 5).

Laboratory findings cannot be summarily dismissed. They may indeed represent mechanisms that underlie effects expressed in the wild. For the most part, however, the end points are covert and cannot be measured directly in nature. Their detection depends on some secondary effect such as reduced fecundity, change in behavior, or death of an indicator species.

Detection of a biological response to ELF electric and magnetic fields in a natural setting depends largely on a second kind of change. This is an overt behavioral response resulting from detection and reaction to the ELF fields. Overt behavioral changes are dependent upon the integrity of the nervous system. A distinction is made between detecting and reacting to a stimulus because it appears that in vivo detection of electric or magnetic fields can occur at a lower field intensity than do changes in nerve tissue in vitro. This implies that a receptor (in many cases unidentified) acts as a transducer to trigger the rest of the nervous system to process the information. Piloerection (i.e., hair or feather erection) is a candidate receptor for electric fields (Cooper and Graves 1981), and cells containing magnetite particles are candidate receptors for detection of magnetic fields (Walcott et al. 1979). Actual biological mechanisms for detecting electromagnetic fields, however, are poorly understood except in electrosensitive fish (Albert and Cohen 1985; Albert and Slaby 1985; Chapter 6; Goodman and Greenebaum 1985; Lovely 1985; Sikov 1985; Stern and Laties 1985). Regarding the integrity of the nervous system exposed to ELF fields,

> There is no convincing evidence that ELF E or B fields of environmental intensity harm the nervous system, exceed its adaptive capacities, or produce significant functional changes. The available evidence suggests that any effects which do exist

are modest and well within physiological limits. (Wolpaw, Seegal, and Dowman 1985).

Given that fields produced by the ELF Communications System are unlikely to produce adverse effects to the nervous system, it is uncertain how the species that do sense the field will react. The possibilities are numerous and range from habituation to aversive behavior in which the organism purposefully avoids further exposure (Lovely 1985; Stern and Laties 1985). The best guess is that mobile species that find the ELF field unpleasant will simply cease to occupy space close to the antenna corridors. It should be noted that there was no evidence of aversive behavior by native birds and large mammals studied in the vicinity of high voltage power transmission lines (Rogers and Lee 1985).

It is unlikely that the majority of species at the ELF Communications System sites will detect, let alone be influenced by, the operation of the system. However, the responses of those few species especially adapted for detection of low intensity electric or magnetic fields are difficult to predict. Conceivably, ELF transmissions could disrupt use of geomagnetic fields as navigational aids by some birds (Larkin and Sutherland 1977), orientation of bees to geomagnetic fields (Martin and Lindauer 1977), use of weak electric fields by some fish to locate prey or position (Kalmijin 1966), or use of weak electric AC fields for communication between termites (Becker 1977). The first three examples are the focus of research projects to be undertaken during future operation of the ELF Communications System (IITRI 1984).

Projections of possible effects of ELF communications on any of the examples above are confounded by lack of agreement between investigators of the role played by geomagnetic fields in behavior. The navigational apparatus of migratory and homing birds is apparently a redundant system. Depending on the species and circumstances, it can involve sun orientation, celestial navigation, biological clocks, landmark recognition, geomagnetic fields, and olfaction (Gauthreaux 1985; Papi and Wallraff 1982). Even though migratory birds have been observed to deviate from their flight path when crossing an operating ELF antenna, it is not clear that the event interferes with migratory success (Williams and Williams 1979). Neither is it clear that the homing experiments with pigeons encumbered with various magnets, brass bars, or Helmholtz coils do more than delay arrival at the home roost (Papi, Meschini, and Baldaccini 1983; Keeton n.d.). One investigator has even questioned (perhaps facetiously) whether or not the geomagnetic field served any useful purpose to migratory birds.

The literature published since 1977 does not present convincing evidence that any of the effects produced by ELF fields in the laboratory can be extrapolated to organisms living in the vicinity of the ELF Communications System. Neither does the literature prove that similar effects will not occur there. Each critique in companion document (Assessments and Opinions of the Biological and Human Health Effects of Extremely Low Frequency Electromagnetic Fields. Compilation of Commissioned Papers for the ELF Literature Review Project) has its own set of disclaimers, but all authors agree that under some circumstances, at some times, electric and magnetic fields will produce changes at the cellular, organ, or whole organism level of complexity. The significance of the changes is speculative. The interaction of electric and magnetic fields with living material is viewed by all as an intriguing scientific problem with many practical ramifications. Additional research is recommended.

COMMENTS ON THE NAVY ELF COMMUNICATIONS SYSTEM'S ECOLOGICAL MONITORING PROGRAM

If biological effects of ELF fields are detected as a result of operating the communication system, it is likely that they will be subtle not catastrophic. It is likely that several years of study will be required to establish a cause and effect relationship because similar effects may be produced by other environmental variables, and several comparable seasons of observation may be required to determine natural seasonal responses.

There are two predominant philosophies on which ecological monitoring strategies are based. The first emphasizes study of the habitat(s) present. The rationale is that if the critical elements of the habitat are preserved, the species typically occurring in the habitat will be relatively undisturbed (Boyce 1978; Gysel and Lyon 1980). The studies of herbaceous plant cover and trees proposed for the ELF Ecological Monitoring Program are representative of this approach (IITRI 1984).

The second philosophy emphasizes study of critical or indicator species. The rationale is that the species chosen for study is particularly sensitive to the environmental insult of concern and that an effect detrimental to its survival is an early warning of more widespread ecological impacts. A species particularly sensitive to electromagnetic fields characteristic of the ELF Communications System has not been identified. However, the proposed studies on slime mold, pollinating insects, small mammals, and nesting birds are representative of the second philosophy (IITRI 1984).

The proposed ecological studies at the ELF Communications System sites will use paired plots. That approach requires the selection of plots as nearly alike as possible with one set exposed to the ELF fields and the others at some distance. The rationale is that if the ELF fields produce an effect, it will occur in the plots closest to the source, and that the effects will be attributed solely to ELF because all other environmental variables will be the same. The approach is conventional but does not recognize a second set of variables produced by clear-cutting, brushing, and trenching during construction of the antenna systems. Although these kinds of impacts are beyond the scope of this review, they must be considered as a confounding factor to interpretation of ecological data (Lee et al. 1979). Because the electromagnetic field strengths are so low, the experimental plots must be in, or close to, the antenna corridor to produce a significant exposure. Because the effects of construction and maintenance are anticipated to be so much greater than effects of ELF transmission, it may be essential to maintain a nonoperating "dummy" span of antenna installed and maintained in the same manner as the operating system as an additional experimental control for some studies.

CONCLUSIONS

- The ecological risk of operating the redesigned USN ELF Communications System is low. The risk is probably less than that projected in the National Academy of Sciences 1977 evaluation.

- The complexity of ecological systems makes it impossible to rule out the possibility of some component of the ecosystem responding to electromagnetic fields generated by the ELF Communications System. The prediction of low risk is an assumption that should be verified through ecological research conducted in concert with operation of the ELF Communications System.

- Research published since 1977 does not alter the conclusions drawn by the National Academy of Sciences in 1977 nor does it negate their recommendations for additional research on the effects of ELF electromagnetic fields on biological systems.

- Ecological effects, if detected, in the vicinity of the operating ELF systems will be subtle not catastrophic; may require a long time to develop; and are of secondary importance to changes produced by the construction of the Communications System.

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APPENDIX A

EXTREMELY LOW FREQUENCY (ELF) COMMUNICATIONS SYSTEM AND ITS ELECTROMAGNETIC FIELDS

NAVAL ELECTRONIC SYSTEMS COMMAND
COMMUNICATIONS SYSTEMS PROGRAM OFFICE
WASHINGTON, D.C. 20363-5100

FEBRUARY 1985

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THE ELF COMMUNICATIONS SYSTEM

SUBMARINE COMMUNICATIONS

Present submarine communications systems use numerous portions of the radio frequency spectrum, ranging from the Very Low Frequency (VLF) band to the Ultra High Frequency (UHF) band. Each system and band has certain desirable capabilities (for example, high transmission data rate), but also inherent limitations (depth of signal penetration in sea water, for instance). This limitation, depicted in Figure 1, requires submarine receiving antennas to remain at or near the surface to maintain communications.

The Extremely Low Frequency (ELF) Communications System will fulfill an important and immediate submarine command and control requirement. The ELF System, transmitting signals that penetrate sea water to great depths, will provide a capability to free submarines from the vulnerabilities and limitations of near-surface operations as shown in Figure 1. The ELF System will allow communications with submarines at high operating speeds and great depths and provide almost worldwide coverage.

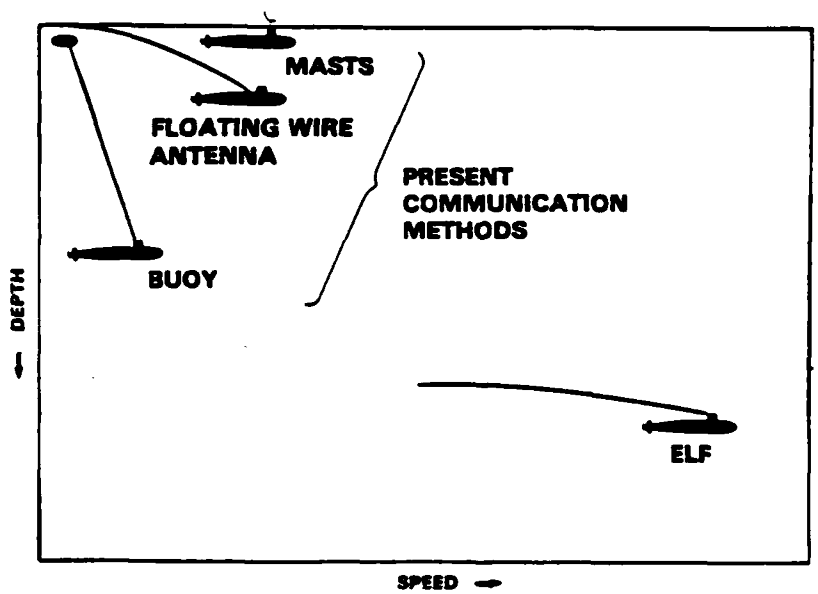


Figure 1. Comparison of ELF Communications Capability with Present Submarine Communications Sytems.

ELF SYSTEM TESTS

An ELF Test Facility located in northwestern Wisconsin was used to demonstrate the practical feasibility of ELF communications in 1976 through 1978 and 1981 through 1984 using experimental receivers aboard submarines. These tests demonstrated that the ELF Communication System has essentially world-wide coverage and that performance was as predicted. Some of the locations where ELF reception has been successfully demonstrated are indicated by the circles in Figure 2.

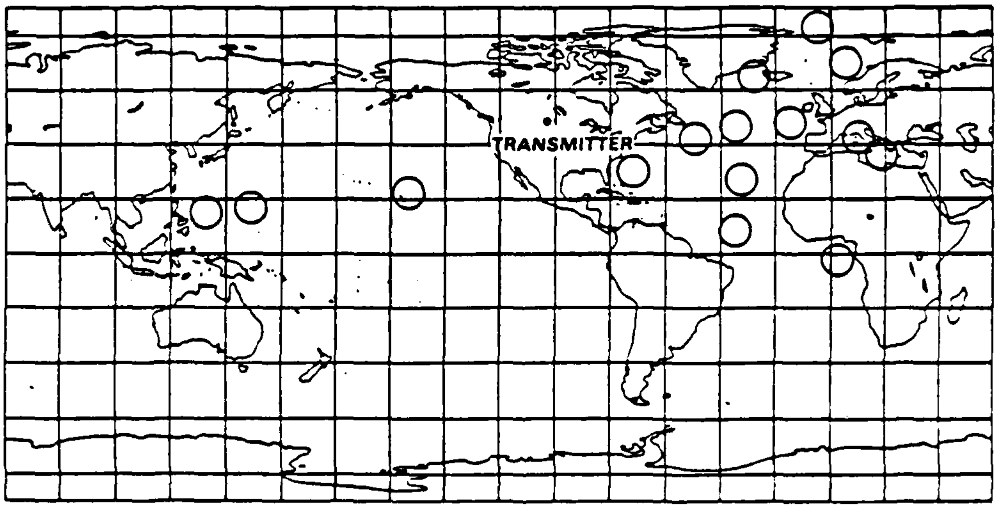


Figure 2. Areas of Successful ELF Communications Reception

THE ELF TRANSMITTER

The ELF transmitter will consist of two transmitter facilities, one in the Chequamegan National Forest near Clam Lake in Wisconsin and the other near Republic in the Upper Peninsula of Michigan, as shown in Figures 3 through 5. The transmitters are approximately 148 miles apart and the EM fields near one transmitter will therefore not be significantly influenced by the fields of the other transmitter. The Wisconsin Transmitter Facility will consist of the existing Wisconsin Test Facility upgraded to meet operational requirements. The two existing 14 mile long antennas, one oriented essentially north-south and the other essentially east-west, will remain. Each antenna carries 300 amperes of current. The Michigan transmitter has one essentially north-south and two essentially east-west antennas. The total antenna length is 56 miles and each antenna carries 150 amperes. Antenna construction at both sites resembles a rural power distribution line. The antenna will consist of two conductors in Wisconsin and one in Michigan mounted on 30 to 55 foot high utility poles and a 35 to 75 foot wide cleared right-of-way. Each transmitter site has two power amplifiers, rated at 650 kilowatt, one for the north-south antenna and one for the east-west antenna(s). Each antenna is terminated in a distributed ground system at each end. The ground system designs vary according to local geology and employ two to four miles of bare wire buried 6 to 8 feet deep and several well type grounds, each approximately one hundred feet deep. Figure 6 shows the design for one of the Mighigan ground systems. The Wisconsin and Michigan ELF Transmitter Facilities will provide 2 watts signal strength when operated independently in the 70-80Hz band and 1 watt in the 40-50Hz band. When operated synchronously as a single source, the power of the signal will be 8 and 4 watts, respectively.

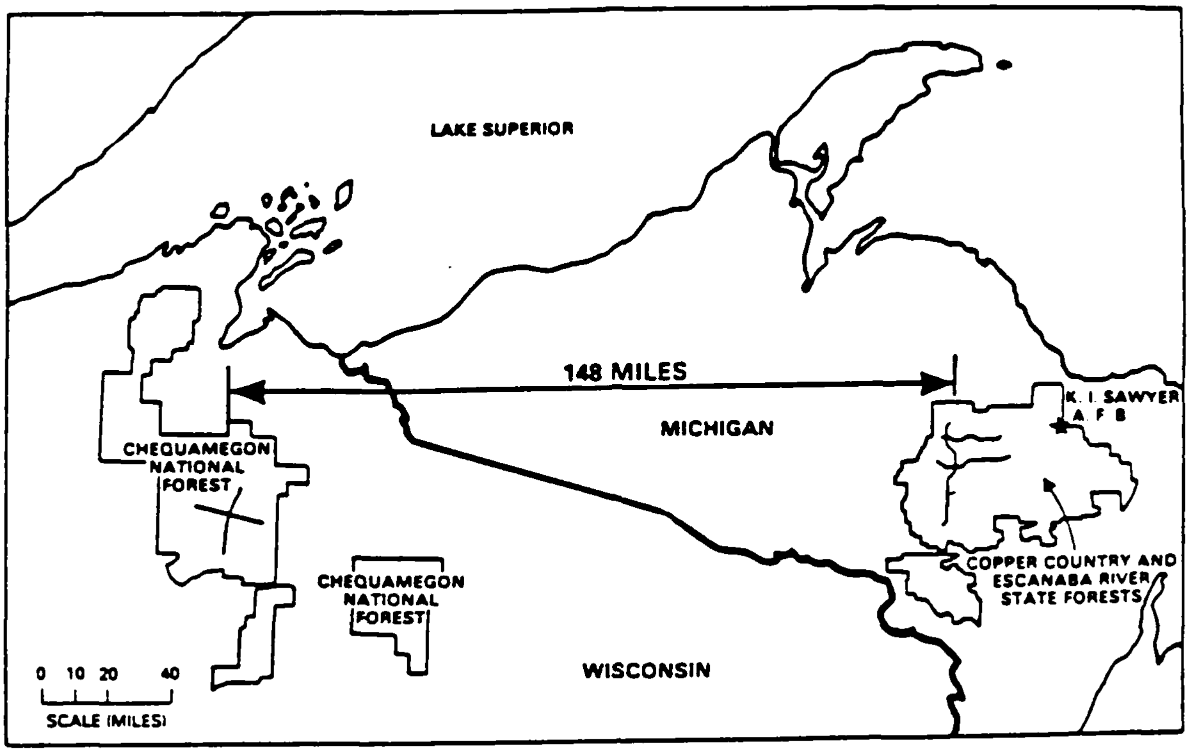


Figure 3. Geographical Siting of the ELF Transmitter Facilities.

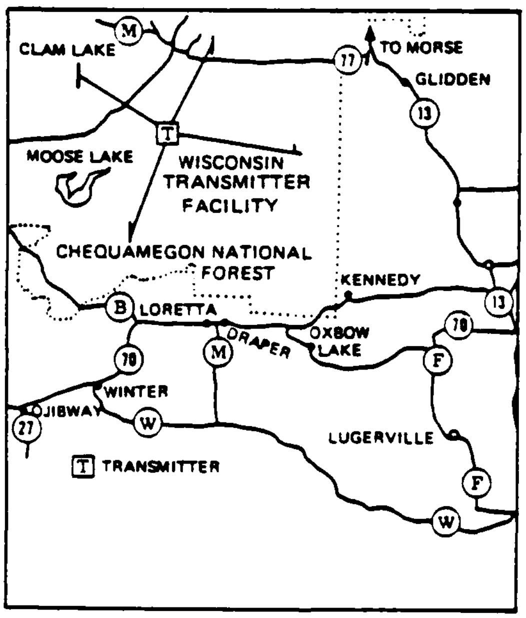


Figure 4. Wisconsin Transmitter Facility Layout

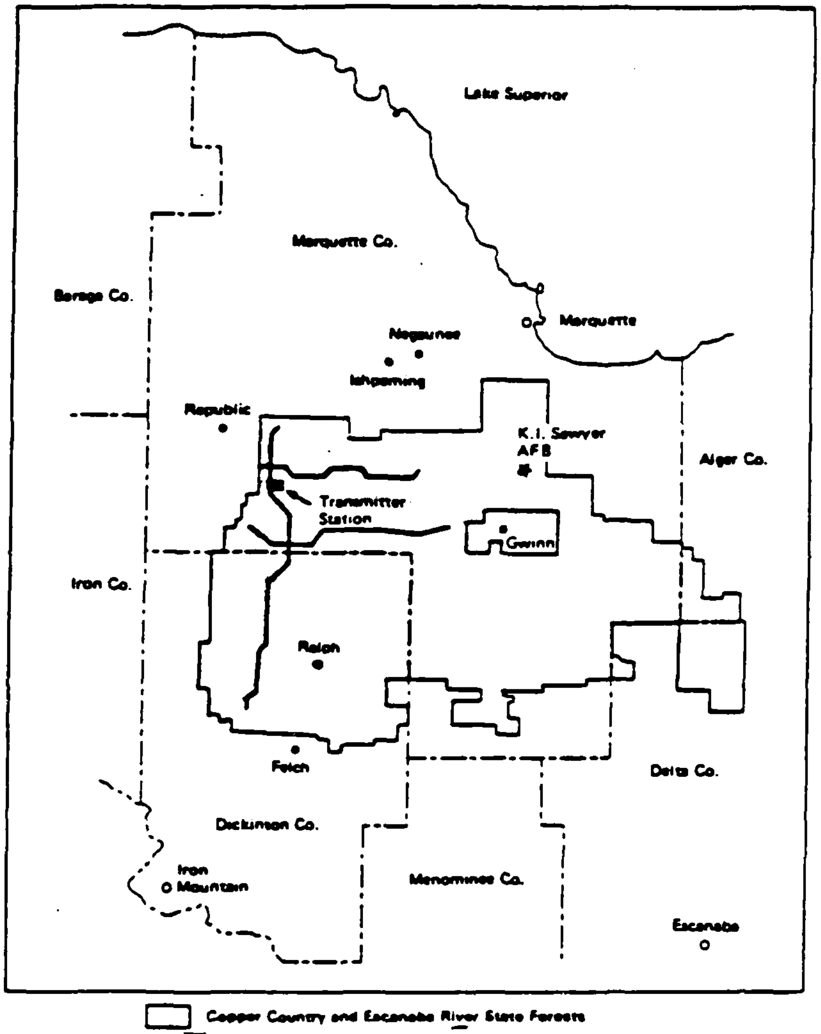


Figure 5. Mighigan Transmitter Facility Layout

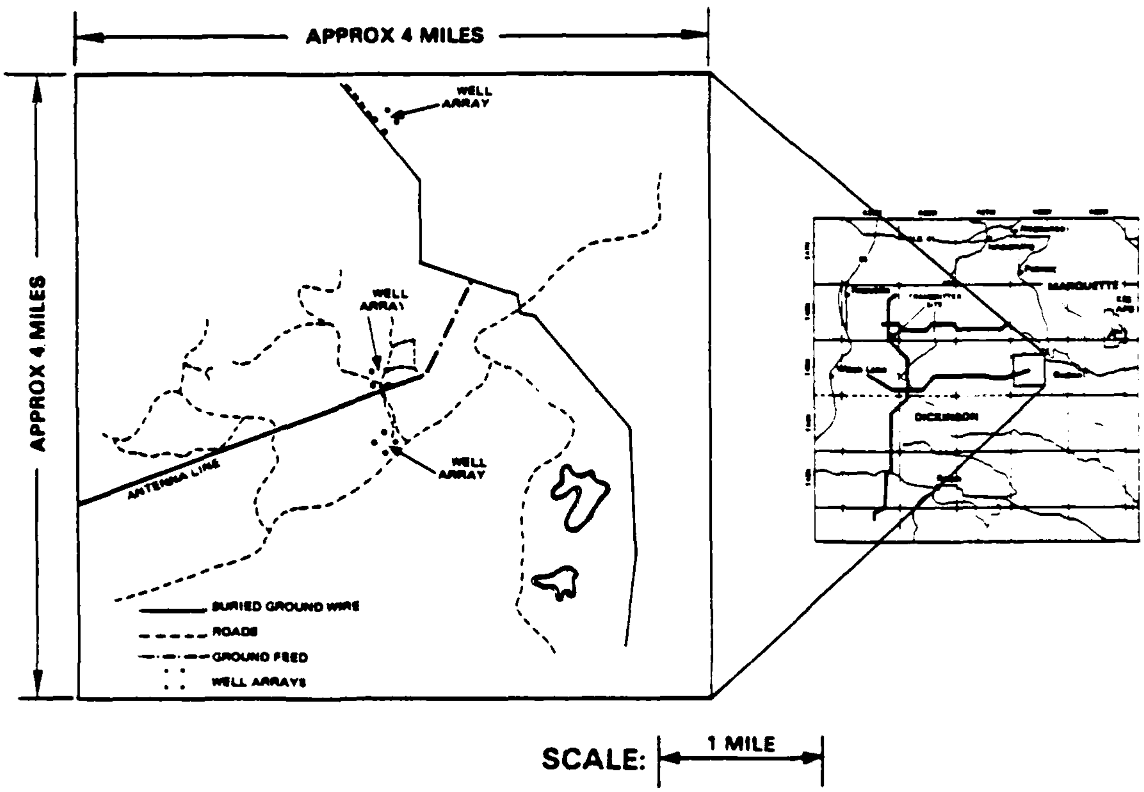


Figure 6. Detailed Design of One of the Michigan Antenna Ground Systems

THE ELF COMMUNICATIONS SPECTRUM

THE ELF COMMUNICATIONS SIGNAL

The ELF communications signal uses a modulation scheme known as Minimum Shift Keying (MSK), shown in Figure 7. It is a special case of Frequency Shift Keying (FSK) that provides a spectrally efficient (compact spectrum) phase-continuous envelope signal, which minimizes transients in the transmitting system. The frequency is shifted between $f_o + \Delta f$ and $f_o - \Delta f$ depending of whether a 1 or a 0 chip is to be transmitted. Although the phase is continuous, shifting may occur at peaks or zero crossings or anywhere in between as required for antenna pattern steering.

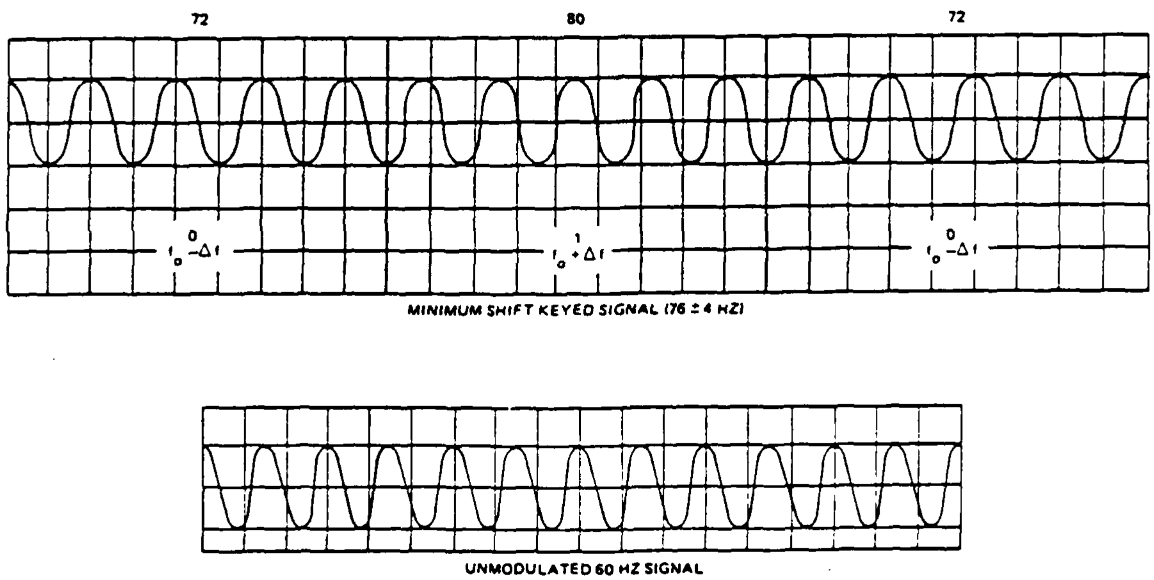


Figure 7. Minimum Shift Keyed ELF Signal and Unmodulated 60Hz Power Line Signal.

THE ELF SIGNAL SPECTRUM

Based on an analysis of numerous possible modulation codes, the broadest spectrum of an MSK ELF signal would be expected if random switching between two frequencies were replaced by alternately switching between the frequencies at zero crossings. For the case of 72Hz and 80Hz (i.e., 72Hz, 80Hz, 72Hz, 80Hz, etc.) and a 16Hz chip rate, the frequency components of the spectrum are separated by 8Hz. The envelope described by this line spectrum is depicted in Figure 8 and conservatively represents the spectrum for a 72/80Hz pseudorandom MSK signal with a 16Hz chip rate. The antenna bandwidth is approximately 15Hz. Frequency components outside this band will be substantially attenuated by the antenna and other hardware components.

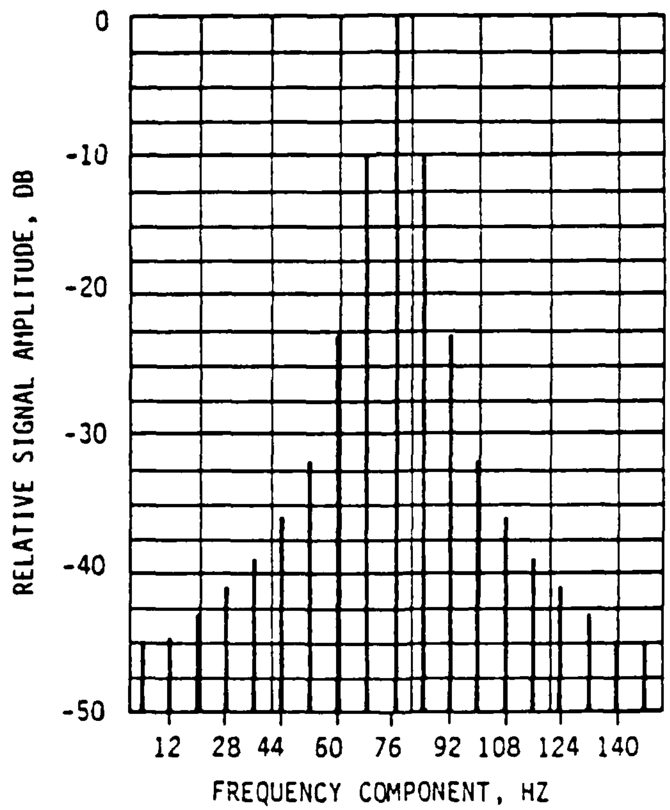


Figure 8. Frequency Spectrum for a 72/80Hz Repeating MSK Signal with 16Hz chip rate.

ELECTROMAGNETIC FIELD CONCEPTS

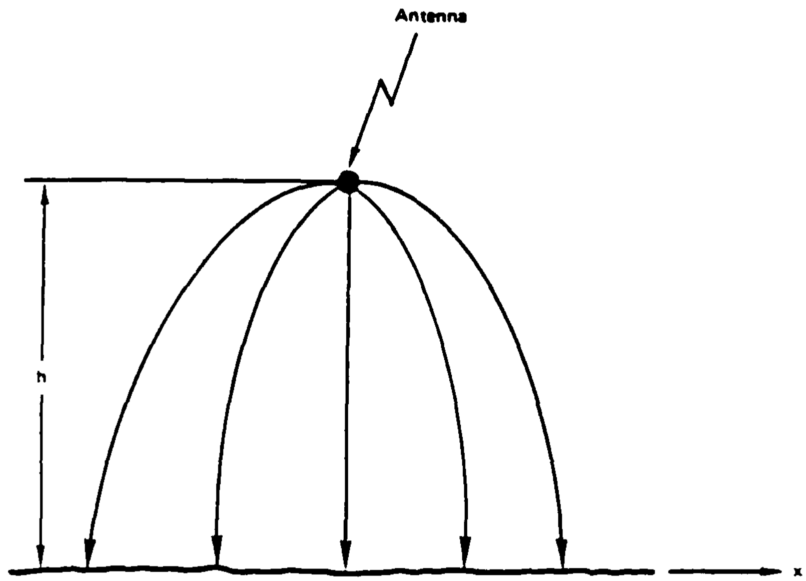
ELF COMMUNICATIONS SYSTEM ELECTROMAGNETIC FIELD COMPONENTS

The ELF electromagnetic fields near the ELF transmitters are most easily described as consisting of four separate components:

- o Transverse electric fields due to antenna voltage,
- o Magnetic fields due to antenna current,
- o Longitudinal electric fields induced by the magentic field, and
- o Electric fields near the ground terminals.

TRANSVERSE ELECTRIC FIELDS

The voltage on an overhead ELF antenna produces an electric field in air in a plane transverse to the antenna direction as illustrated in Figure 9. This transverse field does not penetrate the earth to any significant extent. The field intensity is proportional to antenna voltage, which is highest at the feed point. It also depends on the distance between the antenna and the observer as shown in Figure 10.



At the Earth's Surface:

$$E = \frac{2V}{h\ln\left(\frac{2h}{a}\right)}\left[\frac{1}{1+\left(\frac{x}{h}\right)^2}\right] \quad \text{VOLTS/METER}$$

v = antenna voltage, volts
h = antenna height, meters
x = transverse distance from antenna, meters
a = antenna diameter, meters

Figure 9. Transverse Electric Fields At Ground Level Produced by an ELF Antenna

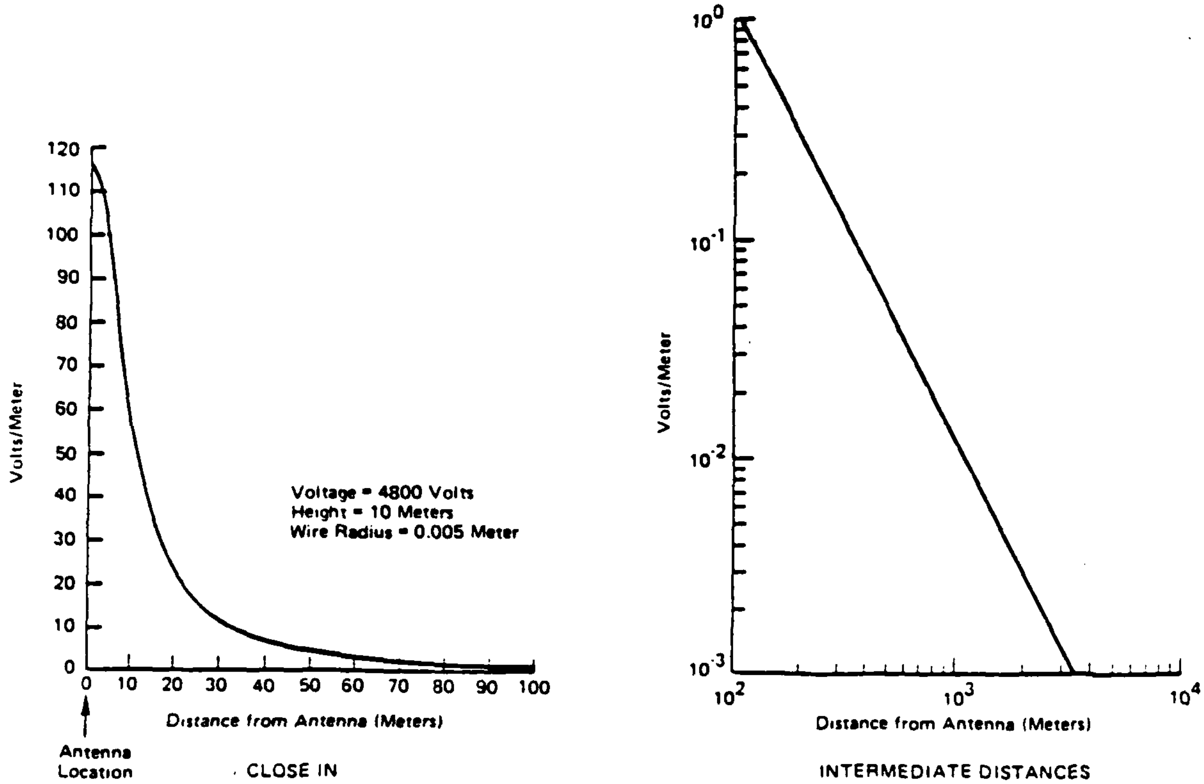


Figure 10. Transverse Electric Field Intensity as a Function of Horizontal Distance From Antenna.

TRANSVERSE ELECTRIC FIELD COMPARISONS

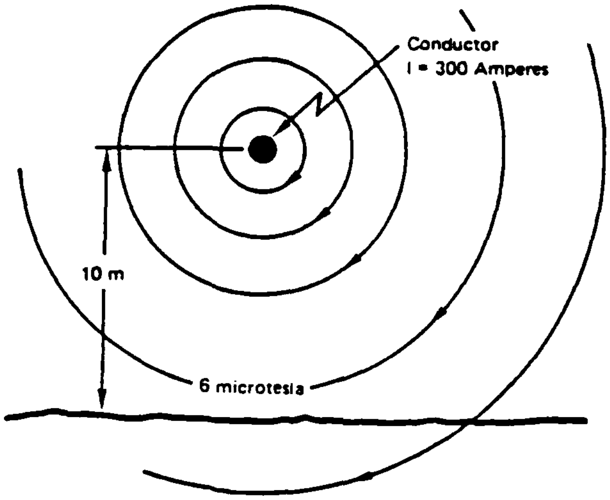
The transverse electric field produced by ELF antennas has, as shown in Table 1, about the same intensity as fields produced by commercial 60Hz power distribution lines serving customers' homes in northwestern Wisconsin and the Upper Peninsula of Michigan. Extra High Voltage (EHV) cross-country power transmission lines produce transverse electric fields more than 10 times as intense as those produced by ELF antennas and local power lines. Transverse electric field intensities near the Earth's surface are affected (shielded) by the presence of vegetation and buildings, and diminish rapidly as a function of distance beyond antenna and powerline rights-of-way.

Table 1. Transverse Electric Field Intensities from the ELF Antenna and Typical 60Hz Power Distribution and Transmission Lines.

SOURCE	ELECTRIC FIELD (VOLTS/METER)
ELF Antenna (calculated at feedpoint)	120
7.2KV Distribution Line	130
69KV Transmission Line	500
345KV Transmission Line	5000
765KV Transmission Line	8000

MAGNETIC FIELDS

Magnetic flux is produced by current-carrying conductors. The magnetic flux surrounds the conductor having the same magnitude at all points on a circle around the conductor as depicted in Figure 11. Magnetic flux density is directly proportional to current, inversely proportional to the distance from the conductor, as shown in Figure 12, and is independent of voltage on the conductor.



$$\beta = \frac{\mu_0 I}{2\pi r} \text{ tesla}$$

$\mu_0 = 4\pi \times 10^{-7}$ henry/meter, permeability of free space

I = current, in amperes

r = distance from conductor, in meters

Figure 11. Magnetic Field Intensity Produced by 10 meter high Overhead Conductor Carrying 300 Amperes

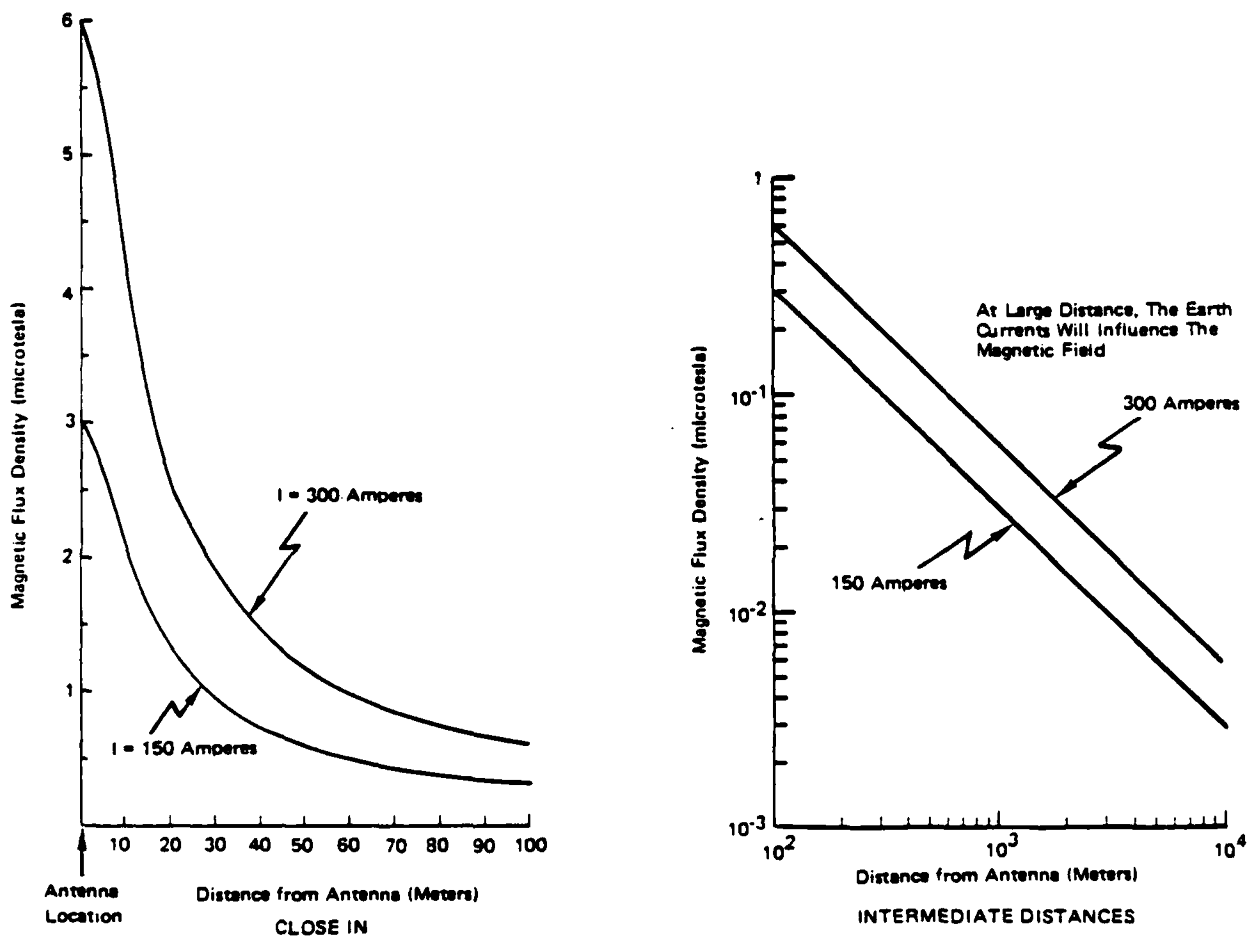


Figure 12. Magnetic Field Intensity as a Function of Horizontal Distance from an Antenna 10 Meters Above Ground.

MAGNETIC FIELD COMPARISONS

Magnetic field intensity diminishes rapidly as a function of distance from any current conductor or electric appliance. As shown in Table 2, the magnetic fields produced in ELF antenna rights-of-way are lower than fields in cross-country EHV transmission line rights-of-way, and comparable to magnetic fields produced by appliances used in the home. Magnetic fields produced by power distribution lines near homes are highly variable due to neighborhood characteristics and individual electric usage (hourly, daily and seasonal changes).

Table 2. Magnetic Field Intensities from the ELF Antenna, 60Hz Power Lines and Appliances and the Earth's Magnetic Field.

SOURCE	MAGENETIC FIELD (MICROTESLA)
AC	
ELF Overhead antenna	
Wisconsin (300A)	6.0
Michigan (150A)	3.0
EHV transmission line	30.0
Household appliances, at 3 feet	0.3 - 3.0
Shop tools, at 1 foot	1.0 - 25.0
Personal appliances, at 1 inch	6.0 - 2000
DC	
Earth's DC fields	50.0

LONGITUDINAL ELECTRIC FIELDS

Magnetic flux density produced by current-carrying conductors induces current and an electric field in the Earth. The electric field is longitudinal (parallel to the conductor), and is affected by the near-surface electrical conductivity of the Earth. The intensity of the field is proportional to the current and frequency. It also depends on the distance between the conductor and the observation point. As a result, it is a function of the height of an overhead ELF antenna or power line as well as the lateral distance.

$$E = \frac{-j\omega\mu_0 I}{2\pi}\left[\ln \frac{1.85}{|\gamma r|} - j\frac{\pi}{4}\right] \text{ volts/meter}$$

γ = propagation constant $(j\omega\mu_0\sigma)^{1/2}$ $r \leq 0.25$

$\omega = 2\pi f$

f = frequency in hertz

σ = near surface earth conductivity, in siemens/meter

r = distance, in meters

Because variation in longitudinal electric field intensity is a logarithmic function of distance, as shown in Figure 13, the ELF antenna height has little effect on field intensity except very close to the antenna. The intensity is much more influenced by the operating frequency of the system and the current. Near surface Earth conductivity is a factor, but only radical local changes have a significant effect on intensity.

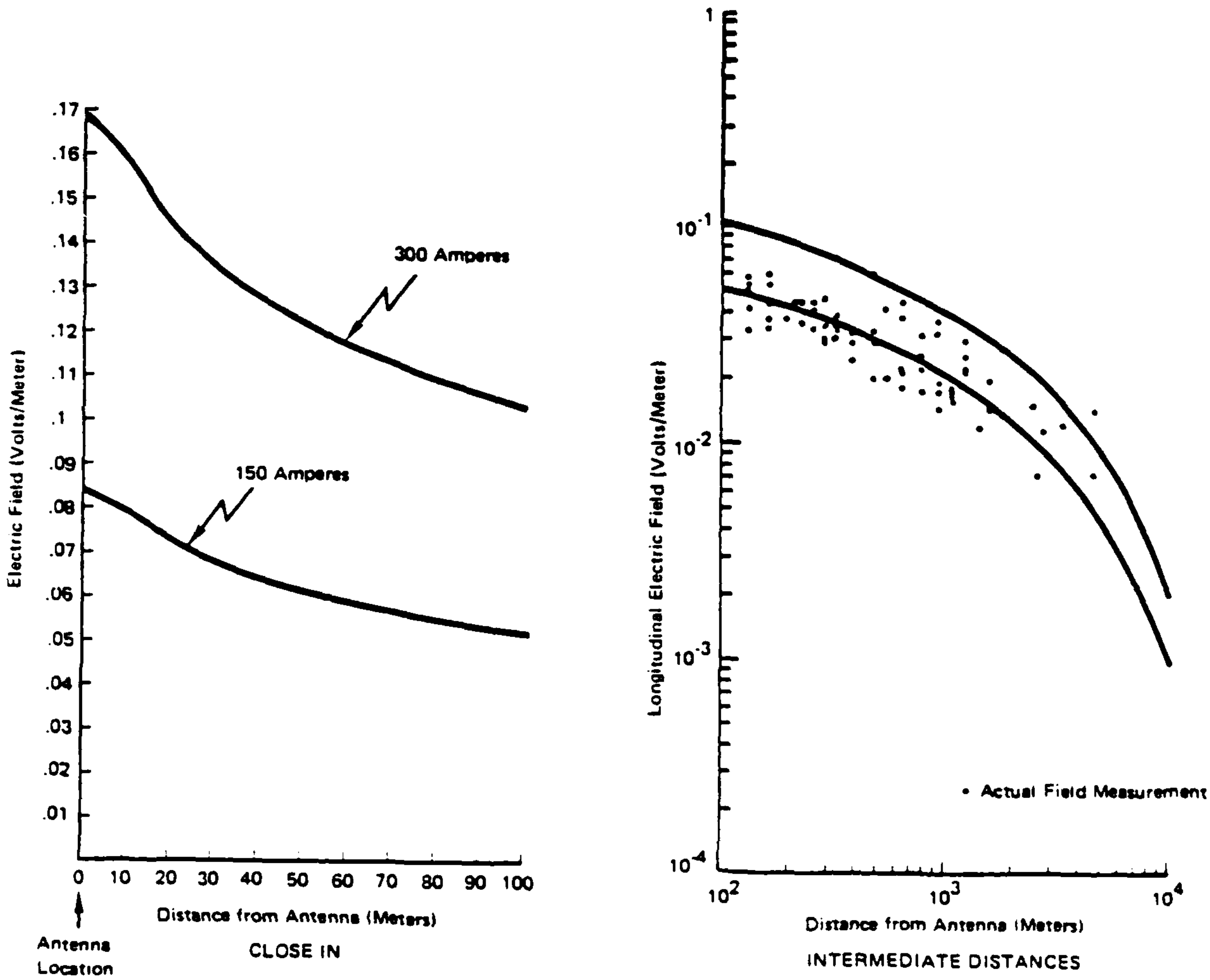


Figure 13. Intensity of Longitudinal Electric Field as a Function of Distance from a 10-foot high Antenna for f=76Hz and σ= .0005 s/m.

LONGITUDINAL ELECTRIC FIELD COMPARISONS

Longitudinal electric field intensities produced by ELF antennas are the same order of magnitude as longitudinal field intensities produced in EHV cross-country transmission line rights-of-way and near electric customers' homes, as depicted in Table 3.

Table 3. Longitudinal Electric Fields from the ELF Antenna and 60Hz Power Lines.

SOURCE	ELECTRIC FIELD (VOLTS/METER)
ELF Antenna	
Wisconsin (300A)	0.15 (NOM)
Michigan (150A)	0.07 (NOM)
EHV Transmission line	0.01-0.05
Near consumer's home (171 data points)	0.5 max 0.09 mean

ELECTROMAGNETIC FIELDS NEAR GROUND TERMINALS

The bare, horizontal buried cables are in continuous contact with Earth, and produce localized electric fields that are parallel to the Earth's surface. These fields are commonly known as "step potentials" since they produce voltage differences between any two points on the Earth's surface, as shown in Figure 14. The magnetic field produced by buried ground cables is proportional to the current in each cable segment comprising the ground system, and is not affected by Earth conductivity.

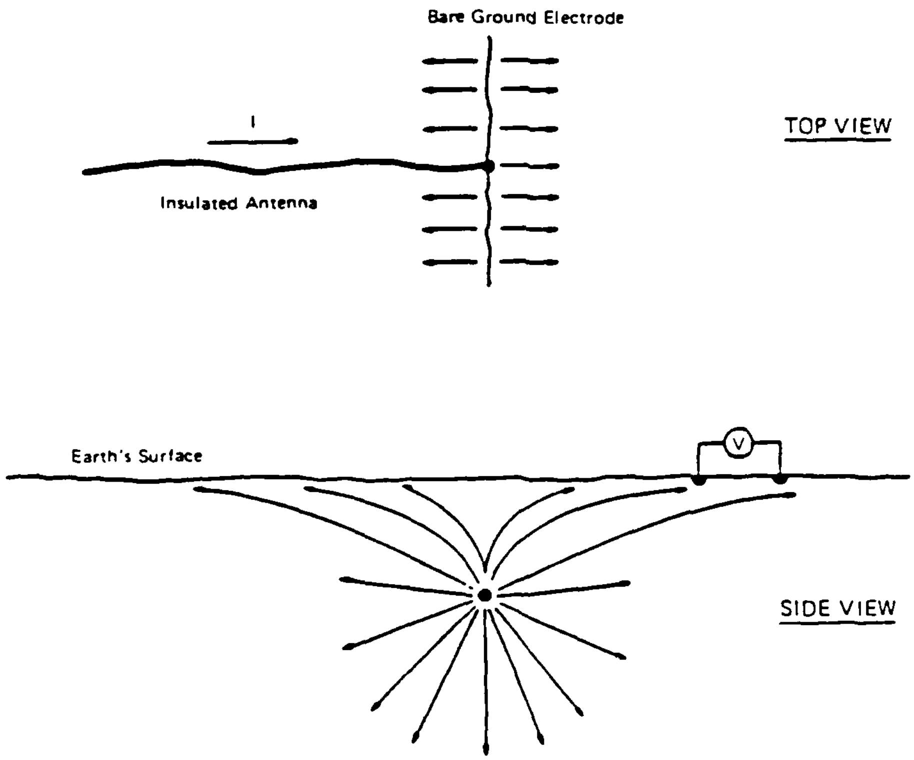


Figure 14. Electromagnetic Fields Produced by Ground Terminals.

SURFACE ELECTRIC FIELD NEAR LINEAR HORIZONTAL GROUND

The surface electric field near a bare, buried horizontal ground cable is a function of current in the cable, its length, its burial depth, and the conductivity of the Earth in the locality.

As shown in Figure 15, the surface electric field is zero directly above a buried ELF ground cable, is symmetric about the center line of the cable, reaches a maximum on either side of the cable at a surface distance equivalent to the burial depth, and then diminishes rapidly as a function of distance.

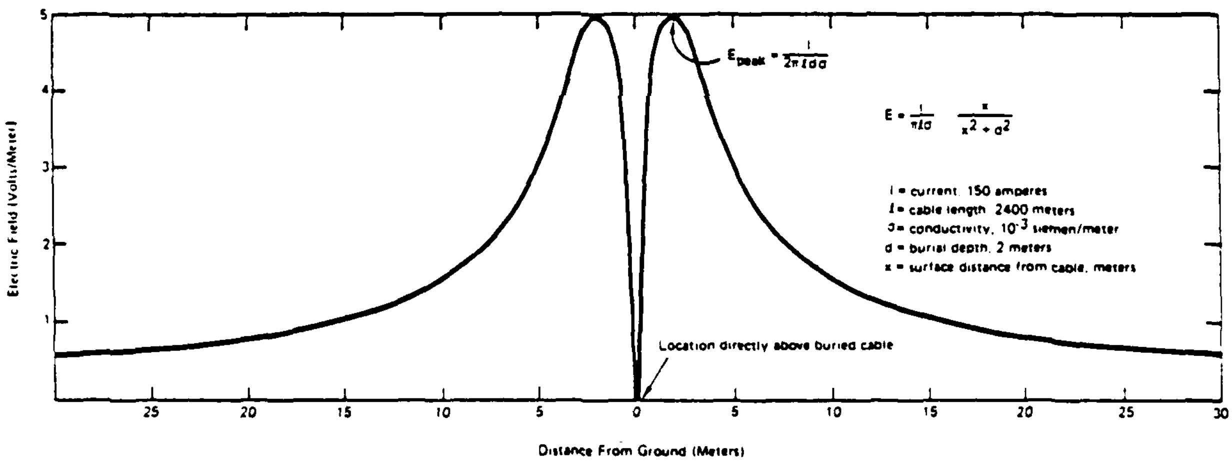


Figure 15. Surface Electric Field Strength as a Function of Distance from Buried Ground Cable.

STEP POTENTIAL NON-LINEARITIES

Since the surface electric field is localized and diminishes rapidly as a function of distance from the buried ground cable, step potentials are not linearly related to the distance between two points on the Earth's surface. Table 4 depicts how the magnitude of the step potential increases at a slower rate than the distance between two points.

Table 4. The Variation of Maximum Step Potential with Step Length.

MAXIMUM STEP POTENTIAL
(linear horizontal ground, 2 meter burial depth)

STEP LENGTH (meters)	MAX STEP POTENTIAL (volts)
1	E_{peak}
2	1.9 E_{peak}
4	3.5 E_{peak}
6	4.8 E_{peak}
8	5.8 E_{peak}
10	6.6 E_{peak}

SURFACE ELECTRIC FIELD NEAR VERTICAL WELL GROUND

The surface electric field near a vertical well ground is a function of the current into the electrode, length of insulated feed line, length of actual grounding electrode and conductivity of the earth.

The surface electric field is zero directly above the buried vertical well. Typically reaches a maximum within a distance approximately equal to the length of the insulated feedline and decreases beyond this distance, as shown in Figure 16. Contours of constant electric field at the earth's surface are circles centered over the well ground.

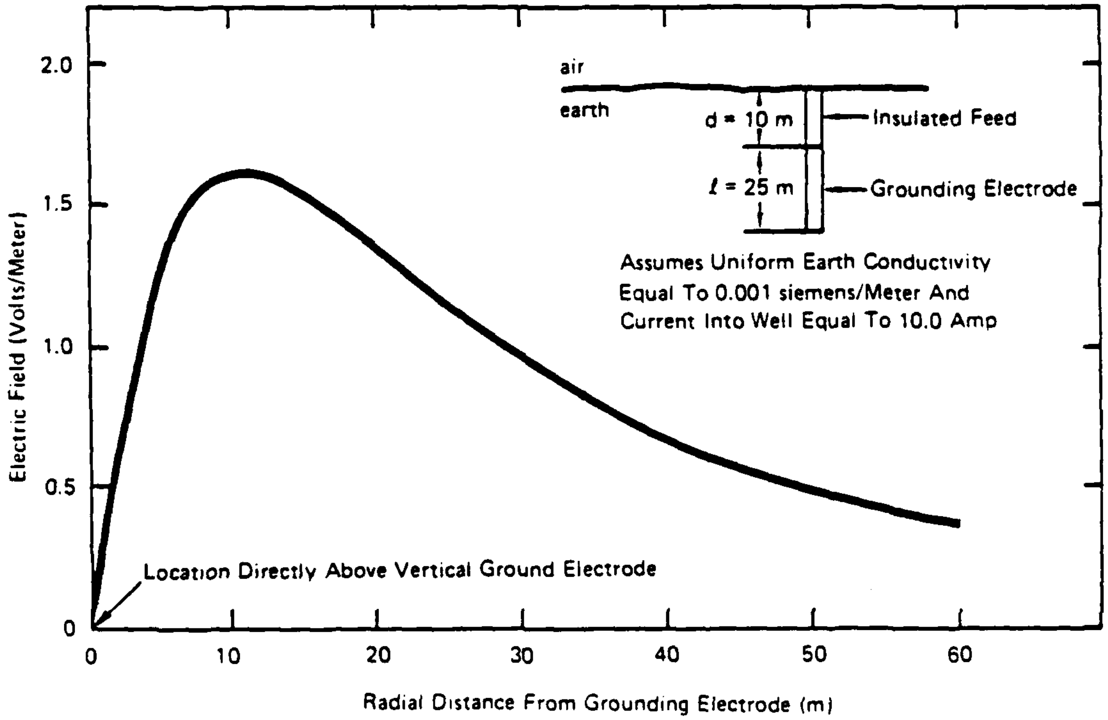


Figure 16. Surface Electric Field Strength Near a Vertical Well Ground.

GROUNDS SPECIFICATION

The ELF antenna terminal grounds systems are being designed in accordance with the requirements in ELEX-S-507B, the ELF System specification. Relevant paragraphs are as follows:

3.3.3.3.3 <u>Environmental criteria for antenna ground terminals</u> The design of antenna ground terminals shall be such as to limit the nominal body current that may be experienced in the vicinity to one milliampere (mA) and to ensure that there is a low probability that electric current will be perceived by a person traversing the area. Conformance with this requirement will be verified through a program of acceptance testing and monitoring, giving consideration to seasonal variations (see 4.4.2). The antenna grounding assemblies shall also be designed using IEEE-STD-81-1962 and IEEE-STD-80-1976 for guidance to ensure public safety and environmental compatibility.

4.4.2 <u>Antenna ground acceptance testing.</u> For acceptance tests, maximum body current in a given step shall be the current flowing in a 1000-ohm resistor when connected to two 0.5-inch diameter copper rods inserted into the earth to a depth of 7.5 inches and separated by the step length. Acceptance test data collected at intervals of 20 m (or less) along the length of the ground shall be analyzed statistically and shall conform to the following requirements:

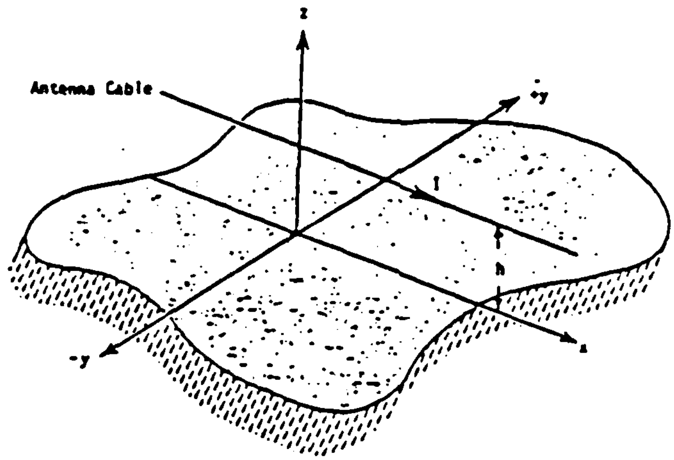
a. Step length shall be 1 m
b. Maximum current (I_{max}) measured shall be less than, or equal to, 2 mA
c. Current sample mean (I) plus standard deviation (S) shall be less than 1 mA.

ELECTROMAGNETIC FIELDS AT MIGRATORY ALTITUDES

The ELF Transmitter Facility in Wisconsin has been used for wildlife studies and other ecological research, including possible electromagnetic influences on migrating birds in flight. These studies have been supported by analytical descriptions of electric and magnetic fields at migratory altitudes (50-500 meters). The important field components at migratory altitudes may include both the transverse and longitudinal electric fields as well as the magnetic field, depending upon the location of birds in flight relative to the ELF antenna route.

MAGNETIC FIELDS AT MIGRATORY ALTITUDES

Magnetic flux density is in the order of tenths of microtesla at *migratory altitudes directly above an ELF antenna,* and is essentially independent of altitude at lateral distances of 1.5 kilometer or more as shown in Figure 18. Magnetic flux density beyond about 1.5 kilometers is only on the order of 10^{-10} tesla.



$$B_x = 0$$

$$B_y = \frac{\mu_0 I}{2\pi}\left[\frac{(d+z+h)}{y^2 + (d+z+h)^2} - \frac{z-h}{y^2 + (z-h)^2}\right] \text{ tesla}$$

$$B_z = \frac{\mu_0 I y}{2\pi}\left[\frac{1}{y^2 + (d+z+h)^2} - \frac{1}{y^2 + (z-h)^2}\right] \text{ tesla}$$

where: I = *antenna current, amperes*

h = antenna height

$\left.\begin{matrix} y \\ z \end{matrix}\right\}$ = coordinates of field point (meters)

μ_0 = permeability of free space ($4\pi \times 10^{-7}$), Henrys/meter

$d = \delta(1-j)$, $\delta = (2/\omega\mu_0\sigma)^{1/2}$

σ = earth conductivity, siemens/meter

Figure 17. The ELF Magnetic Fields at Migratory Altitudes.

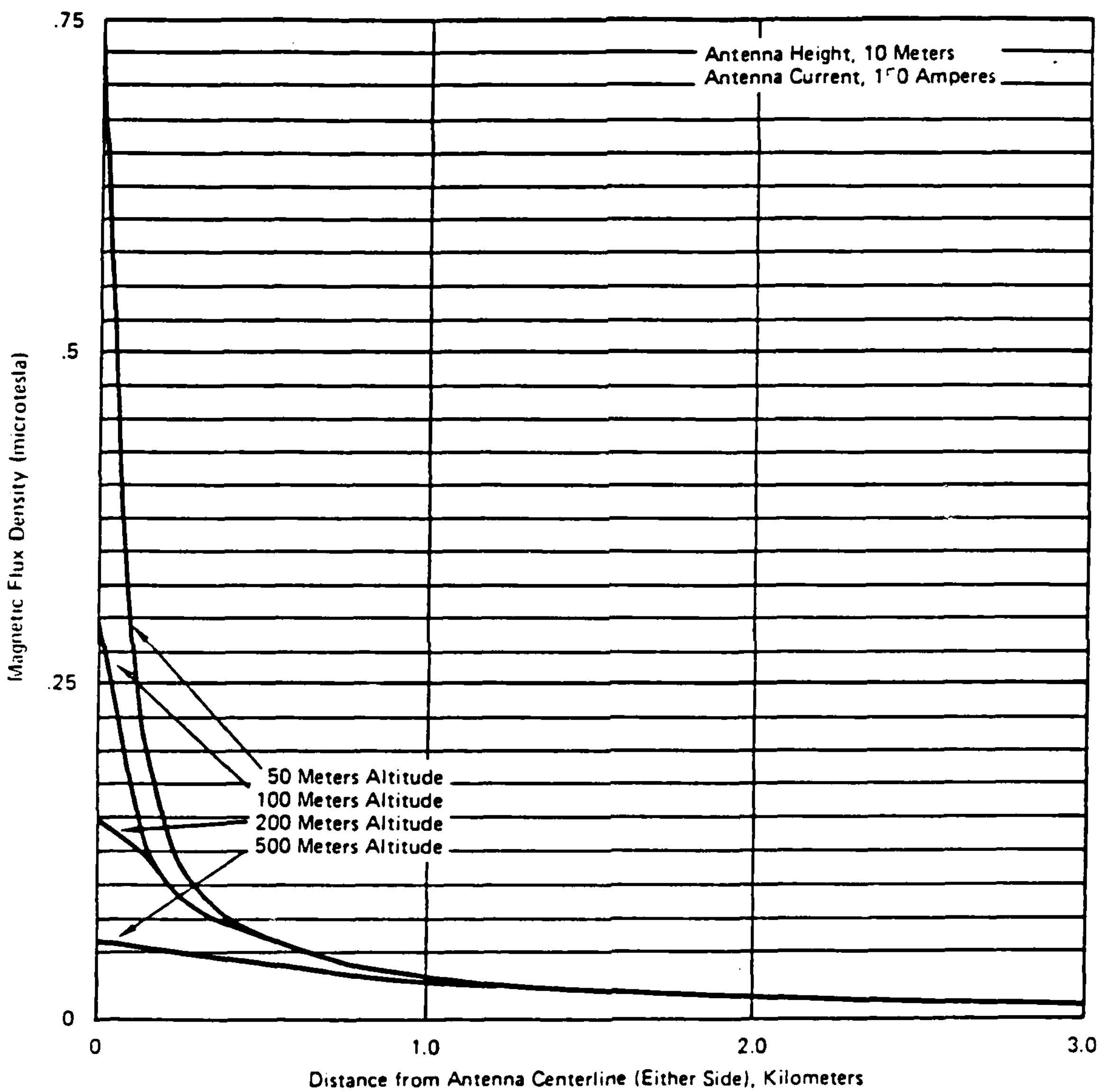
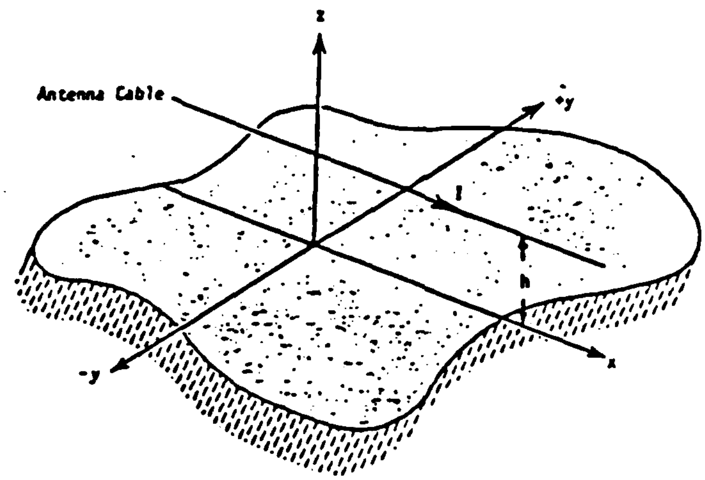


Figure 18. Magnetic Field Intensities at Migratory Altitudes.

TRANSVERSE ELECTRIC FIELDS AT MIGRATORY ALTITUDES

Transverse electric field intensities at migratory altitudes are low, and diminish rapidly as a function of distance from the ELF antenna. The field intensity is less than 1.0 volt/meter at distances greater than 100 meters from the antenna, and is practically independent of altitude at distances greater than 3 kilometers from the antenna. These fields are shown in Figure 20.



$$E_x = \frac{-j\omega\mu_0 I}{2\pi} \ln \sqrt{\frac{y^2 + (d+z+h)^2}{y^2 + (z-h)^2}}, \text{ volts/meter}$$

$$E_y = \frac{yV}{\ln\left(\frac{2h}{a}\right)} \left[\frac{1}{y^2 + (h-z)^2} - \frac{1}{y^2 + (h+z)^2}\right], \text{ volts/meter}$$

$$E_z = \frac{-V}{\ln\left(\frac{2h}{a}\right)} \left[\frac{h-z}{y^2 + (h-z)^2} - \frac{h+z}{y^2 + (h-z)^2}\right] \text{ volts/meter}$$

I = antenna current, amperes

ω = $2\pi f$, ELF angular frequency, radians/second

μ_0 = permeability of free space, $(4\pi \times 10^{-7})$, Henrys/meter

d = $\delta(1-j)$, $\delta = (2/\omega\mu_0\sigma)^{1/2}$

σ = earth conductivity, siemens/meter

z = altitude above surface, meters

h = antenna height, meters

y = surface distance from antenna, meters

a = antenna diameter, meters

V = antenna voltage, volts

Figure 19. The ELF Electric Fields at Migratory Altitudes.

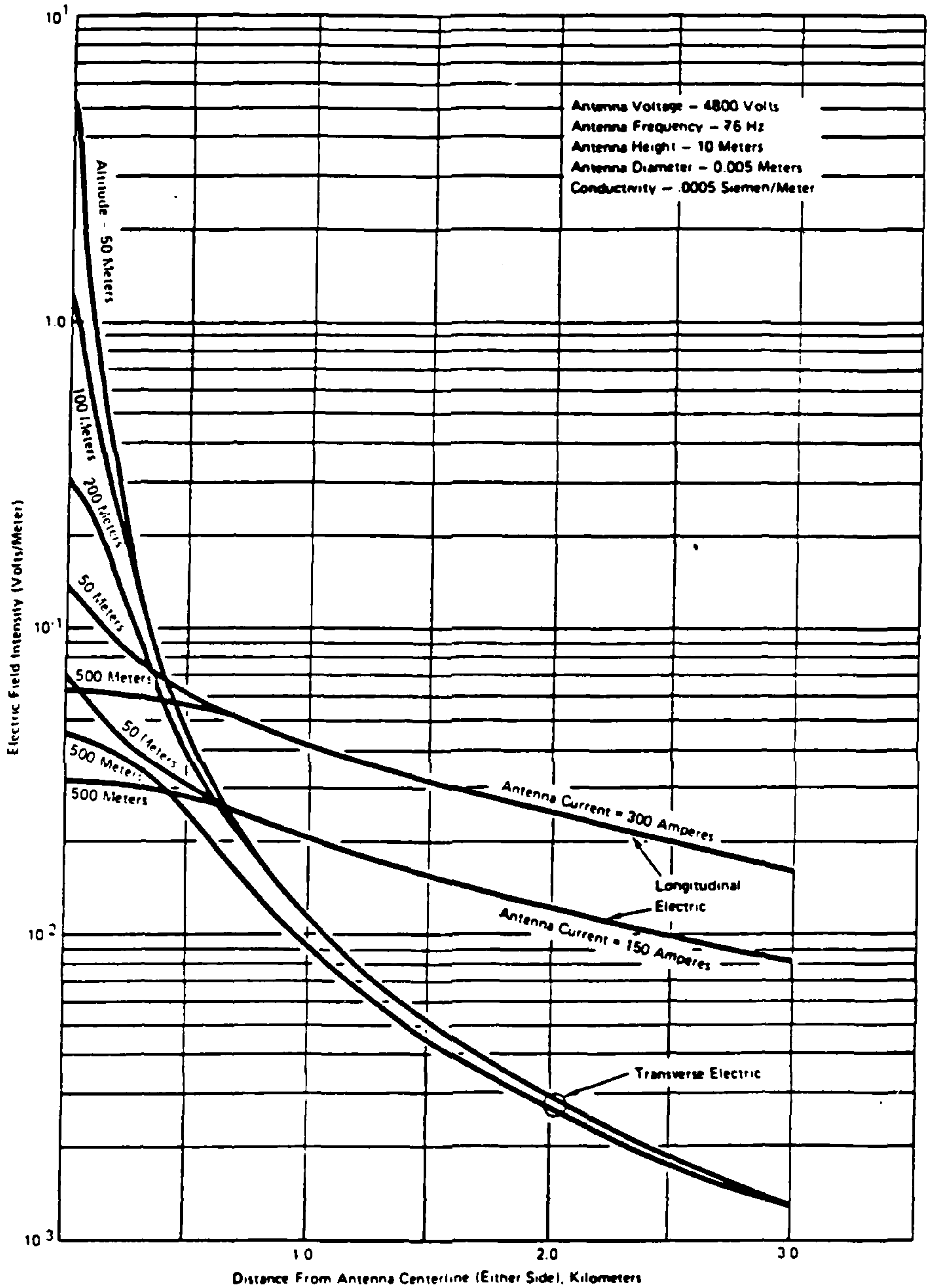


Figure 20. Electric Field Intensities at Migratory Altitudes.

MEASURED ELF ELECTROMAGNETIC FIELDS

MEASURED ELECTROMAGNETIC FIELDS NEAR OVERHEAD ELF ANTENNAS

Ecology studies of populations of soil organisms were conducted yearly from 1972 through 1977, and were supported by measurements of electromagnetic field intensities at each location and during each season(s). Study test plots were located in or adjacent to antenna rights-of-way (the latter to represent undisturbed forest conditions where necessary for ecology study). The data in Tables 5 through 7 describe electromagnetic field conditions near the Earth's surface close to ELF antennas, including ground terminals.

MEASURED MAGNETIC FIELDS NEAR THE OVERHEAD WISCONSIN ELF ANTENNA

Measured magnetic flux densities near the edge or adjacent to the ELF antenna rights-of-way in Wisconsin are less than the 6.0 microtesla predicted level at the Earth's surface directly under the antenna. Slightly higher densities can be measured near line sags and high topography where the antenna height is less than the nominal 35 feet. Order-of-magnitude higher densities can be measured where the ELF antenna passes under roads (6 foot burial depth). See reference 16 for test locations.

Table 5. Measured Magnetic Field Intensities Near the Overhead Wisconsin ELF Antenna.

TEST LOCATION	MAXIMUM MEASURED MAGNETIC FLUX DENSITY (microtesla)
7	4
11/12	5
13	4
14	7
15	14*
17	9**
18	9**
19	2
20	2
31	5

*directly under the antenna on high ground

**near mid-span (maximum cable sag) between poles at forest road overhead crossing

MEASURED TRANSVERSE ELECTRIC FIELDS NEAR OVERHEAD WISCONSIN ELF ANTENNA

Measured transverse electric fields in air near the edge or adjacent to the ELF antenna rights-of-way in Wisconsin are no more than several volts/meter regardless of operating frequency (40-50Hz, 70-80Hz) or modulation characteristics (unmodulated, MSK modulation). The field intensity in air directly under the antenna and 1.0 meter above the Earth's surface is typically about 120 volts/meter or less, except near antenna tuning capacitors, antenna feed points, and near hilltops (see below, for example). See reference 16 for test locations.

Table 6. Measured Transverse Electric Field Intensities Near Overhead Wisconsin ELF Antenna.

MAXIMUM MEASURED TRANSVERSE ELECTRIC FIELD STRENGTH

TEST LOCATION	VOLTS/ METER
7	2
11/12	2
13	0.2
14	4
15	157*
17	7**
18	11**
19	4
20	1

* Higher than theoretical 120V. Attributable to antenna sag.

** Near mid-span (maximum cable sag) between poles at forest road overhead crossing

MEASURED LONGITUDINAL ELECTRIC FIELDS NEAR WISCONSIN OVERHEAD ELF ANTENNAS

Variations between measured and theoretical longitudinal electric field intensities in Earth are caused by variations in local geology (conductivity) and parasitic conductors. See reference 16 for test locations.

Table 7. Measured Longitudinal Electric Field Intensities Near Wisconsin Overhead ELF Antenna.

TEST LOCATION	RANGE OF MEASURED ELECTRIC FIELD INTENSITY (VOLTS/METER)
11/12	0.10-0.12*
13	0.09-0.70**
14	0.08-0.16
15	0.10-0.23***
17	0.09-0.23
18	0.07-0.26

* bouldery surface condition

** 0.70 is considered to be a spurious point. Seven other measurements at the same location taken at different times and ELF frequencies were .1 v/m or less.

*** directly under antenna

REPRESENTATIVE ELECTROMAGNETIC FIELD INTENSITES NEAR THE CLAM LAKE (WI) ELF FACILITY

Electromagnetic field intensities produced by Extremely Low Frequency (ELF) communications antennas and commercial power distribution systems have been measured at numerous places near the Navy's ELF Communications Facility at Clam Lake, Wisconsin. The purpose of the measurements is to obtain a representative sampling of the field intensities where people live and work, and at places residents and visitors use for recreation. Tables 8 through 11 summarize the data contained in reference 16.

Table 8. MEASURED MAGNETIC FLUX DENSITIES AT BUILDINGS NEAR THE CLAM LAKE, WI, ELF FACILITY

MAGNETIC FLUX DENSITY (MICROTESLA) BUILDING USE	DISTANCE TO ELF ANTENNA (kilometers)	76HZ		60Hz	
		INDOORS	OUTDOORS	INDOORS	OUTDOORS
Residence	1.6	0.052	0.063	0.041	0.001
Residence	1.6	0.051	0.054	0.007	0.003
Residence	1.6	0.049	0.051	0.040	0.006
Retail	1.6	0.037	0.140	0.017	0.021
Retail	1.6	0.056	0.034	0.062	0.004
Resort	10	0.001	0.001	0.110	0.120
Residence	16	0.001	0.001	0.160	0.027
Office	16	0.001	0.004	0.021	0.027
Telephone Central	18	0.011	0.048	0.820	0.120
Office	21	0.0005	0.0008	0.034	0.087
Office	22	0.0002	0.0002	0.036	0.017
Residence	22	0.0005	0.0002	0.012	0.010
Residence	24	0.0002	0.0002	0.100	0.010
Office	26	0.0003	0.0004	0.030	0.033
Wholesale	42	0.0001	0.0001	0.026	0.006
Office	43	0.0001	0.0003	0.017	0.065

Table 9. MEASURED ELECTRIC FIELD INTENSITIES IN AIR AT BUILDINGS NEAR THE CLAM LAKE, WI, ELF FACILITY

BUILDING USE	DISTANCE TO ELF ANTENNA (kilometers)	ELECTRIC FIELD INTENSITY (volts/meter) 76HZ		60Hz	
		INDOORS	OUTDOORS	INDOORS	OUTDOORS
Residence	1.6	0.024	0.065	65.2	0.3
Residence	1.6	0.091	0.038	4.3	3.8
Residence	1.6	0.120	0.031	1.7	0.1
Retail	1.5	0.043	0.160	15.2	75.0
Retail	1.6	0.007	0.160	4.2	7.3
Resort	10	0.010	0.010	3.3	1.8
Office	16	0.008	0.003	2.8	1.8
Residence	16	0.003	0.003	18.7	2.1
Telephone Central	18	0.010	0.021	2.6	18.1
Office	21	0.003	0.003	1.5	16.1
Office	22	0.009	0.003	5.4	1.3
Residence	22	0.003	0.003	13.2	0.2
Residence	24	0.003	0.003	2.7	16.4
Office	26	0.003	0.003	3.6	0.1
Retail	42	0.003	0.003	2.2	3.3
Office	43	0.003	0.003	4.1	8.4

Table 10. MEASURED ELECTRIC FIELD INTENSITIES IN EARTH AT OCCUPIED PLACES NEAR THE CLAM LAKE (WI) ELF FACILITY

BUILDING	DISTANCE TO ELF ANTENNA (kilometers)	ELECTRIC FIELD INTENSITY (volts/meter) 76HZ	60Hz
Residence	1.6	0.0800	0.0049
Residence	1.6	0.0170	0.0038
Residence	1.6	0.0180	0.0008
Residence	15	0.0007	0.0210
Residence	22	0.0013	0.0820
Residence	24	0.0002	0.1500
Retail	1.6	0.0180	0.0110
Resort	10	0.0031	0.1600
Office	16	0.0003	0.0030
Telephone Central	18	0.0011	0.0035
Office	21	0.0003	0.0800
Office	22	0.0001	0.0250
Office	26	0.0001	0.0055
Retail	42	0.0001	0.0096
Office	43	0.0001	0.0064

Table 11. MEASURED ELECTRIC FIELD INTENSITIES IN EARTH AT CASUALLY-OCCUPIED PLACES NEAR THE CLAM LAKE (WI) ELF FACILITY

BUILDING	DISTANCE TO ELF ANTENNA (kilometers)	ELECTRIC FIELD INTENSITY (volts/meter) 76HZ	60Hz
Roadside Rest	1.6	0.0130	0.0039
Campground	1.6	0.0300	0.0001
Campground	1.6	0.0290	0.0002
Landfill	3	0.0140	0.0004
Campground	3	0.0089	0.0002
Campground	3	0.0320	0.0001
Campground	6	0.0130	0.0002
Campground	10	0.0003	0.0003
Pipeline R-O-W	21	0.0170	0.0084
Pipeline R-O-W	21	0.0070	0.0046
Forest	10	0.0016	0.0011
Forest	11	0.0012	0.0016
Forest	11	0.0003	0.0002
Forest	11	0.0003	0.0036
Meadow	11	0.0014	0.0001
Forest	13	0.0007	0.0017
Forest	13	0.0057	0.0002
Forest	14	0.0015	0.0055
Meadow	21	0.0001	0.0180

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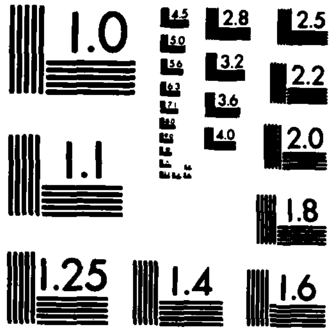

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SPECIAL SCIENCE PROGRAMS

July 1, 1985

Mrs. Crumbacker
Defense Technical Information Center
Cameron Station
Alexandria, VA 22304-6145

Dear Mrs. Crumbacker:

The Naval Electronic Systems Command has asked me to forward a erratum to the publication Biological and Human Health Effects of Extremely Low Frequency Electromagnetic Fields to you. A typographical error appears in the text of Chapter 1, page 3. The first line of the WHO quote currently reads "It is now possible from present knowledge . . ." The "now" should be changed to "not," making the sentence read "It is not possible from present knowledge . . ."

This document was sent to DTIC for processing and general distribution through NTIS. The NTIS accession number is ADA 152-731.

Thank you for your attention to this correction. If you need additional information, I can be reached at (202) 628-1500.

Sincerely,

Molly M. Frantz

Molly M. Frantz
Project Coordinator
ELF Literature Review Project

cc: Dr. Bodo Krueger

Attachment (1)

Most other reviews to date agree with Sheppard's (1983) statement made after he conducted a review of ELF biological effects literature (with a strong emphasis on 60-Hz research):

> Present scientific knowledge about the effects of 60-Hz electric fields does not permit unequivocal determination of the extent of possible hazard to human health, but to date no health hazards due to 60-Hz HVTL electric fields are established...as a group, the foregoing factors lead to the conclusion that a strongly expressed biological effect in humans is not very likely, and to the further conclusion that a pathological effect is even less likely.

In an environmental health criteria document on extremely low frequency electric and magnetic fields published by the World Health Organization (1984), one of the conlusions was:

> It is not possible from present knowledge to make a definitive statement about the safety or hazards associated with long-term exposure to sinusoidal electric fields in the range of 1-10 kV/m. In the absence of specific evidence of particular risk or disease syndromes associated with such exposure, and in view of the experimental findings on the biological effects of exposure, it is recommended that efforts be made to limit exposure, particularly to members of general population, to levels as low as can be reasonably achieved.

Another recent review of biological effects, including public health concerns, of electric and magnetic fields in the ELF range was conducted by a Florida State Science Advisory Commission, which included expertise in biology, psychology, engineering, medicine, physics, and risk assessment. The Commission (FEMFSAC 1985) concluded that it was not possible to make definitive statements that 60-Hz electric and magnetic fields do or do not pose a public health problem. They further concluded that:

> The Commission unanimously believes that the scientific information now available supports the conclusion that it is unlikely that 60-Hz electric and magnetic fields associated with high voltage transmission lines has led, or can lead, to public health problems. However, some ambiguities in the currently available science precludes our categorically concluding that absolutely no public health problem exists.

As one would expect of such a diverse area, the conclusion of no probable adverse public health effects of ELF electric and magnetic fields is not universal. Becker and Marino (1982) reviewed the literature concerning "electromagnetism and life" and concluded that

> Man-made EMFs are present in the environment at levels shown by experiment to be capable of affecting biological function. It

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