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T.S. Tenforde

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Abstract - The interaction mechanisms and biological effects of time-varying magnetic fields in the extremely-low-frequency (ELF) range are reviewed. Although several models have been proposed of both linear and nonlinear mechanisms through which ELF fields could perturb the functions of biological systems, it is concluded that the induction of Faraday currents in tissue is the only established physical interaction mechanism at the present time. The one biological effect of these fields that has been independently replicated in many laboratories is the induction of magnetophosphenes in the visual system during exposure to sinusoidal or pulsed magnetic fields with frequencies in the ELF range. Time-varying magnetic fields that induce tissue current densities in excess of approximately 10 mA/m^2 have also been observed in many laboratories to perturb the function of living systems, most notably in the case of pulsed fields with rapid rise times. These findings suggest that magnetic induction of tissue electrical currents which exceed the endogenous level can produce measurable biological effects. A summary and critical evaluation is given of several recent epidemiological reports which suggest that residential and/or occupational exposure to ELF fields may lead to an increased risk of cancer. It is concluded that these studies generally suffer from both dosimetric and methodological deficiencies, and that definitive conclusions cannot be drawn at the present time concerning the possible relationship of ELF field exposure and cancer risk.

Introduction

Time-varying magnetic fields in the ELF range (less than 300 Hz) originate from both natural and man-made sources [57]. 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 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 [50]. 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 [132,166]. The ELF magnetic fields from video display terminals at typical operator locations [143] and the ambient field levels at most locations within a household environment [24,95] 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 [91].

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 [8,9,171]. 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 [74,103]. The rapidly switched gradient fields used in nuclear magnetic resonance (NMR) imaging devices also produce human exposure to time-varying magnetic fields [19,97,151]. 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 paper. Various aspects of this subject have been summarized in recent review articles and monographs [3,18,134,147-149]. The principal topics that will be discussed in this paper 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

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ELF electric and magnetic fields with living matter are reviewed in the paper by W. T. Kaune in this volume. 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

$$\oint \vec{E}\cdot d\vec{\ell} = - d/dt \iint \vec{B}\cdot d\vec{S} \qquad (1)$$

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, $d\vec{\ell}$ 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

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

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

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

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 σ_{av}, is given by

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

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 [13] 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 transversely 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 [131]. 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 of 0.1 S/m [13] 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_o 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 [66]. A time-varying field with a frequency exceeding approximately 1 Hz would therefore be unable to induce a "flickering" orientational 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 [121]. 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 [81]. 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.

A factor of major importance in determining the response of living systems to ELF magnetic fields with any type of waveform is the fundamental field frequency. The phenomenon of magnetophosphenes, which is discussed in the next section of this paper, 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 [123]. A comprehensive discussion of these ELF field effects is given in the paper by M. L. Swicord in this volume. 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 [36,157]. 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 [30]. 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 [14]. 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 [123].

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 [14-16,127]. 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 [68]. In such weak fields, several biologically relevant electrolytes such as potassium, chloride, and lithium ions may exhibit resonant frequencies in the ELF range. Preliminary studies in which rats were exposed to a 26 μT static field at right angles to a 60-Hz magnetic field have shown a change in operant behavior that was not observed when either field was applied separately [83]. The authors hypothesized that a possible mechanism underlying this behavioral effect might be the cyclotron resonance condition for lithium ions in the central nervous system that was present during exposure to the combined fields. Several theoretical models have been proposed in an effort to explain how an ion cyclotron resonance effect, in which the interaction energy is significantly less than the thermal noise level, could perturb the function of living systems [27,82,99]. These models involve the concept that ion motions and ligand binding interactions in cell membranes could be influenced by a magnetic resonance effect. However, because the collisional damping of ion motion is large in the physiological temperature range [121], it is presently unclear that ion cyclotron resonance orbits could be established or sustained over significant distances at the membrane surface or within pores that traverse the membrane. 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. In subjects with normal vision, the maximum visual sensitivity to sinusoidal magnetic fields has been found at a frequency of 20 Hz [89]. At this frequency the minimum field intensity required to elicit phosphenes is approximately 10 mT [89], which lies well above the range of ELF magnetic field levels generally encountered by man. 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 [6]; (2) pressure on the eyeball abolishes sensitivity to magnetically-induced phosphenes [6]; (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 [89]; 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 [89].

Although the available evidence strongly implicates the retina as the site of magnetic field action

Table 1. Magnetophosphene Studies

Reference	Principal Findings
[33] d'Arsonval, 1896	Initial report of magnetophosphenes produced by a 42-Hz field
[152] Thompson, 1909	Described magnetophosphenes produced by a 50-Hz field as a colorless, flickering illumination that is most intense in the peripheral region of the eye
[46] 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
[94] 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
[6] Barlow et al., 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 60-Hz magnetic 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
[133] Seidel, 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
[86-90] Lövsund 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
[20] Budinger et al., 1984	Found minimum time rate of change of pulsed magnetic field to be 1.3 to 1.9 T/s to produce magnetophosphenes

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, Lövsund et al. [90] 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 Lövsund et al. [90] 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 [72] 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 Lövsund et al. [90] 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 et al. [71] 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. Lövsund et al. [90] 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.

Several phenomena related to the sensitivity of the visuosensory system to time-varying magnetic fields have been studied by Silny [137,138]. In experiments with more than 100 human subjects, he found that distinct flickering could be elicited in the visual field by sinusoidal magnetic fields in the frequency range 5 to 60 Hz. The threshold field intensity varied with the field frequency and background light level, but was as low as 5 mT under optimal conditions. Silny [137,138] also reported that alterations in visually evoked potentials (VEP) occur in sinusoidal ELF magnetic fields at intensity levels that are 5 to 10 times greater than those which produce magnetophosphenes. The change in VEP is characterized by a reversal of polarity and a decreased amplitude of the three major evoked potentials. These effects were observed within 3 min following onset of the magnetic field exposure, and the VEP returned to normal only after a recovery period of approximately 30 to 70 min following termination of the exposure. The existence of any relationship between changes in the VEP and the mechanism of magnetophosphene induction is not clear from the evidence that is presently available.

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 [13], 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 [169]. In a subsequent study with *Aplysia* [135], 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 et al. [163] 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 et al. [75] were able to stimulate frog nerve-muscle preparations at field frequencies of 60 and 1000 Hz. Öberg [108] and Ueno et al. [162]] 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 [67] and the sciatic nerves of dogs and rabbits [93] has been reported to occur in response to pulsed magnetic fields. Based on electromyographic recordings from the human arm, Polson et al. [122] 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 [168]. 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 [167].

During the past two decades, a large number of studies on animal behavioral responses to ELF magnetic fields have been reported. 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 [58,59,80,142] 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 [59]. 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 [23]. 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 [80,142]. 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 [150], and very weak oscillating magnetic fields have also been claimed to affect avian orientation [112]. 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 [55,170]. 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 report. 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 32 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 9 of the 13 investigations in which no behavioral effect was observed [11,31,32,34, 38-41,51,56,62,63,156], the time rate of change of the applied magnetic field was sufficient to induce peak intracranial current densities at or above the endogenous level of approximately 1 mA/m^2. In contrast, only one of the positive findings of behavioral alterations in mammals [4] 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

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

	Reference	Subject	Exposure Conditions*	Results
[48]	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
[23]	Caldwell and Russo, 1968	Honeybee	60 Hz, 2.2 to 30 mT; 10-min exposures	Altered exploratory behavior
[115]	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
[116]	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
[63]	Grissett and deLorge, 1971	Monkey	45 and 75 Hz, 0.3 mT; fields applied in 10 daily sessions of 1 h duration	No effect on reaction time
[62]	Grissett, 1971	Monkey	45 Hz, 1.0 mT; continuous exposure for 42 days	No effect on reaction time
[117]	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
[118]	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
[110]	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
[38-43]	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, inter-response time, overall lever responding, or match-to-sample performance
[11]	Beischer et al., 1973	Human	45 Hz, 0.1 mT; 22.5-h exposure	No effect on reaction time
[51]	Gibson and Moroney, 1974	Human	45 Hz, 0.1 mT; 24-h exposure	No consistent effect on cognitive or psychomotor functions
[96]	Mantell, 1975	Human	50 Hz, 0.3 mT; 3-h exposure	No effect on reaction time
[100]	Medvedev et al., 1976	Human	50 Hz, 10 to 13 μT; acute exposures	Increased latency of sensorimotor reactions
[139]	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
[4]	Andrianova and Smirnova, 1977	Mouse	100 Hz, 10 mT; acute exposures	Heightened motor activity
[17]	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
[156]	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
[10]	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
[28] Clarke and Justesen, 1979	Chicken	60 Hz, 2.4 mT; aperiodic exposures during 1-h interval for 10 days	Increased variability of response to electric shock stimulus when 60-Hz magnetic field used as conditional stimulus
[37] 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
[112] 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
[56] Graham et al., 1983	Human	60 Hz, 40 μT; acute exposures	No perception of field
[31] Creim et al., 1984	Rat	60 Hz, 3.03 mT; 1-h exposure	No field-associated avoidance behavior
[34] 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 agent
[83] Liboff et al., 1985	Rat	60 Hz, 56 μT (with a transverse 26 μT static field); 30-min exposures	Changes in timing discrimination
[32] Creim et al., 1985	Rat	60 Hz, 3.0 mT; 1- to 23-h exposures	No avoidance of applied field in a shuttlebox test

* The magnetic fields were sinusoidal unless otherwise indicated.

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 [156], 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 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 deLorge [40], 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 [114]. Based on coroner and police records from various urban and rural regions within a 5000-km^2 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 [140]. 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. [114] 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 report. (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 [64]. 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 [85].

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 [11], but comparable effects were not observed in monkeys [41].

Regardless of the inadequacies that exist in the available database, the existing literature reports summarized in Table 3 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 [1,9,53,60,61,125,144,177];
- decreased rate of cellular respiration [53,60,61,

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

Reference		Test Specimen	Exposure Conditions*	Results
[109]	Odintsov, 1965	Mouse	50 Hz, 20 mT; 6.5-h single exposure or 6.5-h daily for 15 days	Increased resistance to <u>Listeria</u> infection
[45]	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 capacity of brain, kidney, and liver tissues
[126]	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)
[126]	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
[145]	Tarakhovsky et al., 1971	Rat	50 Hz, 13 to 14 mT; exposure for 1 month	Changes in serum chemistry, hematocrit, and tissue morphology
[78]	Krueger et al.,	Chicken	45 Hz, 0.14 mT, and 60 Hz, 0.12 mT; exposure for 1 month	Reduced growth rate in young animals
[111]	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
[11]	Beischer et al., 1973	Human	45 Hz, 0.1 mT; 22.5-h exposure	Elevated serum triglycerides; no effects on blood cell counts or serum chemistry
[41]	deLorge, 1974	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)
[155]	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 system
[158]	Udintsev and Moroz, 1974	Rat	50 Hz, 20 mT; 1 to 7 days exposure	Increase in adrenal 11-hydroxy corticosteroids
[104]	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

* 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
[12]	Beischer and Brehl, 1975	Mouse	45 Hz, 0.1 mT; 24-h exposure	No change in liver triglycerides
[96]	Mantell, 1975	Human	50 Hz, 0.3 mT; 3-h exposure	No hematological changes
[159]	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
[9]	Batkin and Tabrah, 1977	Mouse neuroblastoma	60 Hz, 1.2 mT; 13-day exposure	Decreased tumor growth rate
[128]	Sakharova et al., 1977	Rat	50 Hz, 20 mT; 1-day exposure	Increased catecholamines in tissue
[70]	Kartaskev et al., 1978	Yeast (Saccharomyces cerevisiae)	0.1 to 100 Hz, 0.025 to 0.40 mT; 20- to 30-min exposure	Changes in rate of anaerobic glycolysis
[73]	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
[144]	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
[120]	Persinger et al., 1978	Rat	0.5 Hz, 0.1 μT 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
[119]	Persinger and Coderre, 1978	Rat	0.5 Hz, 0.01 μT to 1.0 mT, rotating field; 5-day exposure	No significant change in thymus mast cell numbers in animals exposed prenatally and postnatally or exposed as adults
[160]	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
[161]	Udintsev and Khlynin, 1979	Rat	50 Hz, 20 mT; 1-day exposure	Metabolic changes in testicle tissue
[79]	Kronenberg and Tenforde, 1979	Cultured mouse tumor cells	60 Hz, 2.33 mT; 4-day exposure	No effect on cell growth rate
[25]	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
[26]	Chiabrera et et al., 1979	Frog erythrocytes	Single bidirectional pulses at 40 to 70 Hz, or 4-kHz bursts of bidirectional pulses with 10 to 20 Hz repetition rate; 2-mT peak intensity; 12- to 24-h exposures	Dedifferentiation and morphological changes
[53] [60,61]	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_2 uptake)
[76]	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
[47]	Fam, 1981	Mouse	60 Hz, 0.11 T; 23 h daily for 7 days	Decreased body weight and increased water comsumption; hematology, organ histology, and reproduction not affected

* 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
[1]	Aarholt et al., 1981	Bacteria	16.66 and 50 Hz, 0 to 2.0 mT; 10- to 12-h exposure	Decreased growth rate
[125]	Ramon et al., 1981	Bacteria	60 and 600 Hz, 2 mT; 17- to 64-h exposure	Decreased growth rate and cytolysis
[155]	Toroptsev and Soldatova, 1981	Rat	50 Hz, 20 mT; 1- to 24-h exposures	Pathomorphological changes in brain
[77]	Kolodub 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
[129]	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
[35,36]	Delgado et al., 1981, 1982	Chicken embryo	10, 100, and 1000 Hz; 0.12, 1.2 and 12 μT; 0.5-ms rectangular pulses; 2-day exposure	Morphological abnormalities in nervous tissue, heart, blood vessels, and somites
[2]	Aarhott et al.,	Bacteria (E. coli)	Square-wave pulses at 50 Hz; 0.20-0.66 mT; 2- to 3-h exposures	Changes in rate of β-galactosidase production
[141]	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
[130]	Sander et al., 1982	Human	50 Hz, 5 mT; 4-h exposure	No changes in ECG, EEG, hormones, blood cell counts, or blood chemistry
[92]	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
[136]	Shober et al., 1982	Mouse	10 Hz, 1 mT; 1-day exposure	Decreased sodium ion content of liver
[107]	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
[44]	Dixey and Rein, 1982	Rat phaeochromocytoma cells	500-Hz bidirectional pulses; 160 to 850 μT; 3-h exposure	Stimulation of noradrenalin release
[30]	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
[54]	Goodman et al., 1983	Dipteran salivary gland chromosomes	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
[69]	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
[124]	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

* 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
[157]	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
[5]	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 and DNA synthesis
[81]	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
[21]	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
[177, 178]	Winters and Phillips, 1984a, 1984b	Cultured human colon tumor cells	60 Hz, 0.14 mT; 1-day exposure	Increase in growth rate, number of transferrin receptors, and expression of tumor-specific antigens
[146]	Temur'yants et al., 1985	Rat	8 Hz, 5.2 μT; daily 3-h exposures for up to 45 days	Transient hyperlipemia in blood serum
[105]	Murray and Farndale, 1985	Cultured chicken fibroblasts	15-Hz bidirectional pulses; 2.2 mT peak intensity; daily 12-h exposures for 1 to 8 days	Enhanced collagen and total protein synthesis, and decreased cAMP after 6 days of exposure
[22]	Cain et al., 1985	Cultured mouse calvarium	Single bidirectional pulses at 15 Hz; 0.8-mT peak intensity; 15- to 60-min exposures	Decreased cAMP production and increased ornithine decarboxylase activity in response to parathyroid hormone
[164]	Ueno et al., 1985	Toad embryos (xenopus laevis)	20 Hz, 2 kHz and 20 kHz; 10 to 15 mT; 15-min to 8-h exposures	Teratogenic effects
[65]	Gundersen and Greenebaum, 1985	Rat muscle	60 and 70 Hz (linear and circular polarization); 0.1 mT; 10-min exposure	Effects on miniature endplate potentials
[179, 180]	Winters et al., 1985a, 1985b	Human and dog leukocytes	60 Hz, 0.1 mT; 24-h exposure	No effect on mitogen responses, DNA, RNA or protein synthesis, or levels of cell surface receptors

* The magnetic fields were sinusoidal unless otherwise indicated.

76];

- altered metabolism of carbohydrates, lipids, proteins, and nucleic acids [5,54,70,76,77,81,105,107, 146,160,161];
- endocrine alterations and altered hormonal responses of cells and tissues [21,22,44,69,73,92,126,128,129, 158,160];
- altered immune response to antigens and mitogens [30,104,109];
- morphological and other nonspecific tissue changes in adult animals, frequently reversible with time after exposure [45,129,136,141,154,155];
- effects on gene expression and genetic regulation of cell functions [2,26,54];
- teratologic and developmental effects [35,36,78,111, 124,157,164].

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 [145], all of the published studies on hematological parameters in exposed animals have shown no consistent field-associated effects [11,41,47,96, 130]. 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 [25,45,47,73,76,77,104,109,128,129,141,145,154, 155,158-161]. 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 [25], 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 [13]. It is also notable that positive findings of biological effects were obtained in all of the 16 studies listed in Table 3 in which square waveforms and pulsed fields with repetition frequencies in the ELF range were used [2,5, 21,22,26,30,35,36,44,54,69,92,105,107,124,157]. 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 [69,92]. 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 [11,96,130]. With the exception of one unconfirmed report of an elevation in serum triglycerides in the exposed subjects [11], 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 et al. [130], 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 six 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 [29,49,52,84,98,101,102,106,113,153, 165,172-176,181]. These studies are discussed in detail in the paper by D. A. Savitz in this volume. 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.

Fourteen reports on this subject published since 1979 are summarized in Table 4. The initial publication by Wertheimer and Leeper [172] 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

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
[172]	Wertheimer and Leeper, 1979	Children (< 19 yr); residential fields [344 cases; 344 controls]	(+)
[49]	Fulton et al., 1980	Children (< 20 yr); residential fields [119 cases; 240 controls]	(-)
[153]	Tomenius et al., 1982	Children (< 18 yr); residential fields [716 cases; 716 controls]	(+)
[174]	Wertheimer and Leeper, 1982	Adults; residential fields [1179 cases; 1179 controls]	(+)
[176]	Wiklund et al., 1981	Adults; telecommunication workers [Swedish Cancer Registry with 385,000 cases for 1961-1973]	(-)
[101]	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]	(+)
[181]	Wright et al., 1982	Adults; male workers in 10 electrical/electronic occupations [Cancer Surveillance Program in Los Angeles County, 1972-1979]	(+)

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

Reference	Subjects	Correlation Between Increased Cancer Incidence and Residential or Occupational Exposures
[98] McDowall, 1983	Males aged 15-74; workers in 10 electrical/electronic occupations [Survey of occupational mortality in England and Wales, 1970-1972	(+)
[29] Coleman et al., 1983	Males aged 15-74; workers in 10 electrical/electronic occupations [South Thames Cancer Registry from 1961-1979]	(+)
[165] Vågarö and Olin, 1983	Males and females aged 15-64; workers in electrical/electronic occupations [Swedish Cancer Registry with 385,000 cases from 1961-1973]	(+)
[113] Pearce et al., 1985	Adults; male workers in 8 electrical/electronic occupations [546 cases; 2184 controls]	(+)
[102] Milham, 1985	Adults; male members of American Radio Relay League in states of Washington and California [1691 male cancer deaths in these two states compared with U.S. age-specific white male death frequencies in 1976]	(+)
[84] Lin et al., 1985	Adults; white male workers in 3 electrical/electronic occupations [Brain tumor decedents in state of Maryland from 1969 through 1982]	(+)
[52] Gilman et al., 1985	Adults; white male workers in underground mines [40 cases and 160 age-matched controls selected from the National Institute for Occupational Safety and Health cohort mortality study]	(+)

epidemilogical survey by Tomenius et al. [153] of childhood leukemia incidence in the County of Stockholm produced results that were consistent with the Wertheimer and Leeper [172] study.

In a study conducted in Rhode Island, Fulton et al. [49] 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 [173] were critical of the study by Fulton et al. [49] on the basis that the control and case groups had not been matched for interstate migration, for years of occupancy in 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. [49], Wertheimer and Leeper [173] 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 five brief epidemiological reports were published during the period 1982 to 1985 in the format of letters to journal editors [29,98,101,113, 181], all of which showed an apparent association between the incidence of leukemia in males and occupational exposure to ELF electric and magnetic fields. Two of these studies were conducted in the United States [101,181], two in England [29,98], and one in New Zealand [113]. 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 [165]. Based on an epidemiological survey of white male residents of the state of Maryland who worked in three electrical/ electronic occupations, Lin et al. [84] reported a statistically significant elevation in the incidence of brain tumors relative to the general population. Using years of employment as a surrogate for exposure to electromagnetic fields, Gilman et al. [52] reported a statistically significant increase in the incidence of all forms of leukemia, acute myelogenous leukemia and chronic lymphocytic leukemias among underground miners employed for more than 25 years. Because the risk for chronic lymphocytic leukemia has not previously been associated with exposure to chemicals or other environmental agents, they suggest that the electromagnetic fields from power distribution lines, transformers, electric trolleys, etc., should be considered as a possible factor in the elevated risk for this disease class among underground miners.

In an epidemiological study of telecommunications workers that was based on the Swedish Cancer-Environment Registry, Wiklund et al. [176] found no increased risk for this occupational group as compared to the Swedish population as a whole. Milham [102], however, has reported that amateur radio operators who were members of the American Radio Relay League in the states of Washington and California had a significantly higher leukemia incidence than the general population.

Overall, 12 of the 14 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 deficiencies 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 group 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 and Conclusions

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 from power lines or other sources. 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.

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