8

Biological Effects of Static Magnetic Fields

Shoogo Ueno and Tsukasa Shigemitsu

CONTENTS

8.1 Introduction 204
8.2 Mechanisms of Biological Effects of Static Magnetic Fields 204
8.3 Experimental Studies on Static Magnetic Field Effects 207
8.3.1 *In Vivo* Studies 207
8.3.1.1 Animal Behavior: Recognition and Analgesia 207
8.3.1.2 Reproduction and Development 210
8.3.1.3 Circulatory System Effects 212
8.3.1.4 Neuroendocrine, Visual, and Neurophysiological Systems 214
8.3.1.5 Magneto-Mechanical Systems 215
8.3.1.6 Musculoskeletal System 215
8.3.2 Tissue, Molecular, and Cellular Studies 216
8.3.2.1 DNA and Chromatin 216
8.3.2.2 Cell Growth, Cell Proliferation, and Cell Cycle 216
8.3.2.3 Cell Membrane and Cell Metabolic Activity 220
8.3.2.4 Gene Expression and Signal Transduction 221
8.3.2.5 Genotoxicity 222
8.3.2.6 Cell-Free System, Free Radical, Enzyme Activity 223
8.4 Miscellaneous 225
8.4.1 Biological Sensing and Magnetite 225
8.4.2 Plant Growth, Response, and Magnetotropism 227
8.4.3 Magnetotaxis 229
8.4.4 Others 230
8.5 Medical Applications 230
8.5.1 Biomagnetic Phenomena 230
8.5.2 Transcranial Magnetic Stimulation 232
8.5.3 Magnetoencephalography 234
8.5.4 Magnetic Resonance Imaging 235
8.5.5 Magnetic Orientation for Tissue Engineering 238
8.5.6 Treatments of Pain, Cancer, and Other Diseases 240
8.6 Conclusion 242
Acknowledgments 243
References 244

8.1 Introduction

In ancient times, magnetism, especially permanent magnets, were a symbol of mystique because of the magnetic force that remains even after numerous attractions of iron. Although William Gilbert was called the pioneer of modern magnetics, he was surprised by the magnetism associated with living organisms. Magnetism, in contrast to transient static electricity, has been used as an explanation for various invisible effects and is expected to possess miraculous healing powers. Although people have been using magnetism for healing purposes without any scientific evidence, there have not been significant problems concerning the side effects of magnetism. As permanent magnets have improved in quality and achieved higher magnetic strength, magnetism has become more commonly used in modern medicine. For example, magnetism is commonly used in the correction of dentures.

In the society today there are many sources of electromagnetic fields. Humans are exposed daily to man-made and naturally originated fields. During the past decade, questions about whether the exposure to electromagnetic fields may be linked to adverse health effects have been raised. Although the interaction of electromagnetic fields with biological systems has been investigated, there are no biophysical mechanisms that can explain many of the observed biological effects of low-level of magnetic fields. Proposed mechanisms include effects on currents, direct forces on biomagnetic materials, effects on free radicals, ion cyclotron resonance, charge transfer processes, stochastic resonance, etc.

Recent developments in medical instrumentation such as magnetic resonance imaging (MRI) and transcranial magnetic stimulation (TMS) have raised questions as to whether or not strong (in the tesla range) magnetic fields influence human health. Medical applications of weak (1–200 mT) magnetic fields for the purpose of pain reduction and tissue healing have also been studied for many years. Therapeutic applications of permanent magnets and other magnetic devices have recently been expanded to various areas such as treatment of pain and diseases like rheumatoid arthritis and cancer.

The objective of this chapter is to describe some of the more recent information on biological effects and medical applications of static magnetic fields. This chapter consists of four sections. Each section has a comprehensive review of a recent topic of interest. A short summary of the mechanism of static magnetic field action on biological systems is described in the second section, which includes a brief review of well-known mechanisms that are discussed before mentioning the interactions of weak static magnetic fields with biological systems. The third section reviews and summarizes more recent *in vivo* and *in vitro* experimental results of the effects of static magnetic fields, including near-zero magnetic fields, geomagnetic fields, and MRI fields. The fourth section covers special topics including magnetic sensing, magnetite, and plant response to magnetic fields. In parallel with the comprehensive review of biological effects, the development and medical application of the static magnetic field phenomena are introduced in the fifth section and reviewed with emphasis on the applications that are currently under investigation.

8.2 Mechanisms of Biological Effects of Static Magnetic Fields

The biological effects of static magnetic fields are not well understood. Magnetic fields exert a force on moving charged particles at right angles to both the field and the velocity, $\vec{F} = q\vec{v} \times \vec{B}$, where $\vec{F}$ is the force, q is the charge, $\vec{v}$ is the velocity, and $\vec{B}$ is the magnetic flux density. In vacuum, the magnetic flux density is given by $\vec{B} = \mu_0 \vec{H}$, where $\vec{H}$ is the magnetic field strength and μ_0 is the magnetic permeability of a vacuum. (In this section we will be careful to distinguish between $\vec{B}$ and $\vec{H}$, although in subsequent sections we will be less careful, using ''magnetic field'' as a general term that often is used to describe flux density.) Additionally, these fields exert a torque on particles with both fixed and induced magnetic dipole moments. This torque tends to align the dipoles along the magnetic flux density and is given by $\vec{T} = \vec{M} \times \vec{H}$ where $\vec{M}$ is the magnetic dipole moment. For paramagnetic and diamagnetic materials, $\vec{M}$ is proportional to the magnetic flux density. The magnetic susceptibility, χ, is given by the equation, $\vec{M} = \chi \vec{H}$, where $\vec{H}$ is the local value of the magnetic field strength and χ is dimensionless. All materials may be mainly divided into three categories based on their susceptibility values. Materials with negative susceptibility are called diamagnetic. Materials with positive values are referred to as paramagnetic. Materials with large susceptibility include both ferro- and ferrimagnetic materials. Recognition of the role of diamagnetic, paramagnetic, and ferro- or ferrimagnetic materials in the body helps in the understanding the underlying mechanisms of biomagnetic effects.

Table 8.1 shows three types of well-known mechanisms of the biological effects of magnetic fields including time-varying magnetic fields. As shown in Table 8.1, there are two basic mechanisms of static magnetic fields: first, the magnetic torques on objects and second, the mechanical force effects. A radical pair mechanism is also proposed.

When biological materials or systems are exposed to a spatially homogenous magnetic field, they tend to rotate to a stable direction, which is determined by the anisotropy of magnetic susceptibility of the materials and magnetic torque acting on the materials, as described by the following equation:

$$T = -\frac{1}{2\mu_0} B^2 \Delta\chi \sin 2\theta$$

where B is the magnetic flux density, $\Delta\chi$ is the anisotropy of magnetic susceptability of the materials, θ is the angle between the direction of the magnetic field and the long axis of the materials, and μ_0 is the magnetic permeability of a vacuum. The magnetic orientation of diamagnetic materials such as fibrin and collagen can be observed and explained by this principle (Torbet et al., 1981).

Next, when biological materials or systems are exposed to a spatially inhomogenous magnetic field, the materials or systems tend to move along the direction of the steepest

TABLE 8.1

Well-Known Mechanisms of the Biological Effects of Magnetic Fields

1. Time-varying magnetic field	
Eddy currents $J = -\sigma \frac{B}{t}$	Nerve stimulation
Heat SAR $= \sigma \frac{E^2}{\rho}$	Thermal effects
2. Static magnetic fields	
a. Homogenous magnetic field	Magnetic orientation of biological cells
Magnetic torque	
$T = -\frac{1}{2\mu_0} B^2 \Delta \chi \sin 2 \theta$	
b. Inhomogenous magnetic field	Parting of water by magnetic fields (Moses effect)
Magnetic force	
$F = \frac{\chi}{\mu_0} (\text{grad } B) B$	
3. Multiplication of magnetic fields and other energy	Yield effect of cage product and escape product
Photochemical reactions with radical pairs	
Singlet–triplet intersystem crossing	

gradient of magnetic force. The magnetic force acting on the materials is proportional to the multiplication of the magnetic flux density B, the gradient of the magnetic flux density B (grad B), and the magnetic susceptibility χ of the materials, as described by the following equation:

$$F = \frac{\chi}{\mu_0}(\mathrm{grad}B)B$$

where μ_0 is the magnetic permeability in a vacuum.

Dramatic demonstrations of these forces can be seen when water is parted by magnetic fields using magnetic field exposures of 4–8 T with a gradient of 50 T/m (Ueno and Iwasaka, 1994a,b). Magnetic levitation of diamagnetic materials such as wood and other organic materials, is realized in magnetic fields of more than 20 T (Beaugnon and Tournier, 1991). This phenomenon can also be explained by the principles of magnetic force.

Oxygen is a paramagnetic molecule, and its behavior under magnetic field gradients has an important role both as a gas and when dissolved in solution. The blockage and disturbance of gas flow by magnetic fields have been observed (Ueno and Harada, 1987). This phenomenon, called a magnetic curtain, can be explained by the action of magnetic force on a paramagnetic molecule. The magnetic curtain in this example is a wall of oxygen or air. Experimentation with this principle has demonstrated the quenching of burning candle flames (Ueno, 1989), where the interception of oxygen by the magnetic curtain has a quenching effect on the flames. As a second example, when a human subject is positioned inside a space shielded by the magnetic curtain, one may expect the respiratory function, evaporation of water molecules, body temperature, blood circulation, and other physiological functions to be disturbed or modulated.

The effect of static magnetic fields on water vaporization rate was investigated (Nakagawa et al., 1999). This study demonstrated that the water vaporization rate was found to be significantly influenced when both air and oxygen were in the presence of magnetic fields, and the observed effect was dependent on the field–field gradient product rather than on the B field itself. It should be noted that this magneto-enhancement of vaporization might be the indirect cause of certain physiologic effects on living organisms.

For example, skin temperature decreases in rats exposed to magnetic fields have been observed (Ichioka et al., 2003). This observation can be explained in terms of the effects of the magnetic field on air convection. That is, high magnetic field gradients (135–140 T^2/m) push the diamagnetic water molecules toward the magnet bore. This increases the movement of water molecules in the air around the animal body and the vaporization rate. The heat of vaporization leads to a decrease in skin temperature. The decrease in the blood flow of the skin microcirculation is assumed to be a secondary change to the decrease in skin temperature.

Oxygen dissolved in water is also affected by magnetic fields. Changes in dissolved oxygen concentration were observed for magnetic field exposures on the order of 1 T (Ueno and Harada, 1982; Hirota et al., 2000; Kishioka et al., 2000). The changes in oxygen concentration are accelerated or regulated by gas transport of oxygen and water molecules inside and outside the water surface.

The magnetic field effects for large fields can be explained by these well-known mechanisms. With ever-increasing evidence indicating that weak static magnetic fields have profound effects on biological systems, a number of mechanisms for the action of these static magnetic fields, including geomagnetic fields, on biological systems have been proposed.

Possible biomagnetic and chemical effects can be expected when biological systems are exposed to both static magnetic fields and other forms of energy such as light and radiation (Ueno and Harada, 1986). Photochemical reactions produced by a radical pair intermediate can be expected to show magnetic field effects that arise from an electron Zeeman interaction, electron-nuclear hyperfine interaction, or a hyperfine interaction mechanism including an electron-exchange interaction in a radical pair intermediate (Hata, 1976; Schulten et al., 1976; Tanimoto et al., 1976; Nagakura and Molin, 1992; Natarajan and Grissom, 1996; Hayashi, 2004).

The magnetic field effect observed with radical pair recombination is one of the well-known mechanisms by which magnetic fields interact with biological systems. Throughout the past decades there have been several experimental results describing the effects of magnetic fields on radical pair recombination. Mohtat et al. (1998) examined the behavior of radical pairs derived by hydrogen abstraction of triplet benzophenone and some of its derivatives from bovine serum albumin, human serum albumin, and calf thymus DNA. The magnetic field strength was as high as 150 mT with durations as long as 10 μs. This result indicated that radical pair behavior is sensitive to magnetic fields, and this effect can be interpreted by using the theory of free radical recombination. Using the triplet state of benzophenone as a convenient source of pairs, Eveson et al. (2000) examined the effects of weak (>1 mT) magnetic fields on radical recombination reactions in micells. They found that the concentration of free radicals escaping from the micelle was both affected and depended on the conditions surrounding the radical pair.

Timmel and Till discussed the weak magnetic field effects on free radical recombination reactions (Till et al., 1998; Timmel et al., 1998). Vink and Woodward (2004) described the effects of a weak magnetic field, 21 mT, on the recombination reaction of neutral free radicals in isotropic solution.

Ritz et al. (2002) reviewed the physiological basis of animal magnetoreception. They suggested that there was a link between photoreception and magnetoreception, from their findings in behavioral and theoretical studies. Migratory birds have the ability to sense the geomagnetic field and use it as a source of compass information. The candidates for a biophysical mechanism of this magnetoreception are magnetite and magnetically sensitive chemical reactions in animals. Ritz et al. (2000) postulated the possibility that magnetoreception involves radical pair processes as a biophysical mechanism.

8.3 Experimental Studies on Static Magnetic Field Effects

This section focuses on *in vivo* and *in vitro* studies of the effects of static magnetic fields. It covers the field effects observed on behavior, the cardiovascular system, reproductive system, cellular and tissue development, the neuroendocrine system, and the magneto-mechanical system, utilizing molecular, cellular, tissue, and cell-free systems.

8.3.1 *In Vivo* Studies

8.3.1.1 Animal Behavior: Recognition and Analgesia

Scientific interest in behavioral changes has led to the development of a psychology of learning that studies the effects of various external stimuli, and this research has further led to the development of behavioral pharmacology to observe the effects of drugs on the central nervous system. There have been several investigations for studying the effects of magnetic fields on behavior and the central nervous system using techniques developed specifically in these research fields. Behavioral research directed toward the effects of magnetic exposure of living organisms mainly addresses two questions: whether magnetic fields are sensed and avoided and whether magnetic fields have any influence on the functions of leaning and memory. Magnetic field experiments designed to address both questions have been conducted using several indicators, such as open-field behavior, operant behavior, and spontaneous motor activity, as tools of observation and measurement. (See also Chapter 4 on behavioral effects by Johnston and D'Andrea.)

8.3.1.1.1 Animal Behavior and Recognition

Nikolskaya et al. (1996) investigated the influence of inhomogeneity of natural magnetic fields on rat cognition with regard to whether or not magnetic fields could serve as an informational factor for cognition. Under three natural magnetic field conditions, $37 \pm 2\,\mu T$ (condition 1; horizontal component (N–S) is 14 μT, and vertical 34 μT), 16–118 μT (condition 2), and 55–240 μT (condition 3), rats were subjected to a food-operant behavior study. All rats in conditions 2 and 3 were unable to form operant behavior, while rats in condition 1 demonstrated the behavior. Using the combination of an original behavioral model and a multiple alternative maze, an impact of Opilong, which is an analog of dermorphine and μ-receptor agonist, on rat sensitivity to $38 \pm 2\,\mu T$, in the static magnetic field has been investigated by the same authors (Nikolskaya et al., 1999). They concluded that chemical modulation of the opioid system in rats induced both an increased magnetic field sensitivity and an allowed perception of magnetic field parameters. In the following study (Nikolskaya and Echenko, 2002), it was reported that cognitive activity in the natural magnetic field of 38 μT caused an increase of ethanol intake in 34.8% of rats.

During the 1980s, Liboff (1985) argued favorably for the combined effects of static (DC) with extremely low-frequency (ELF) magnetic fields (see also Chapter 9 resonance phenomena by Liboff on). A surprising effect was observed at the ELF magnetic field frequency close to the cyclotron frequency of a calcium ion. Thomas et al. (1986) reported the disruption of operant behavior in rats after exposure to low-intensity magnetic fields. The protocol developed by them in the report has been reexamined by Stern et al. (1996) in a two-part experiment. In the first part, the vertical component of the static field was reduced to 0.0261 μT. In the second part, both the horizontal and the vertical components were matched to those used by Thomas et al. The results obtained in these experiments were found to be inconsistent with the results reported by Thomas et al. Effects of the combination of static (DC) and AC magnetic fields at the cyclotron frequency on rat open-field behavior have been investigated (Zhadin et al., 1999). Levels of locomotor and exploratory activities were decreased after exposure to DC and AC magnetic fields at the calcium cyclotron frequency, whereas field exposure at the magnesium cyclotron frequency increased levels of these activities.

Studies have been conducted to determine whether rats could acquire a two-choice discrimination based on a specified discrimination stimulus (Creim et al., 2002). The specified discriminative stimulus used in this study was tested both in ambient illumination as well as in a combination of an oscillatory field of 50 μT at 60 Hz and a static field of 26 μT. The results demonstrated that rats were able to discriminate between two-choice tasks easily during the period of changing illumination and that the presence or absence of the static and oscillatory fields had no observed effect on these findings.

Tsuji et al. (1996) evaluated physiological consummatory behavior by observing intakes of food and water and changes in the body weight using BALB/c mice exposed to magnetic field levels of 5 T for a period of 24 and 48 h. Exposure to a 5-T magnetic field for 48 h suppressed eating and drinking behavior. The decreased body weight, the increased blood urea nitrogen (BUN) level, and the slightly increased BUN–Cr ratio observed in this experiment might be attributed to the loss of body fluid secondary to decreased food and water intake.

For the purpose of observing changes caused by magnetic field exposure, MRI systems and application of their high-strength static magnetic fields have been useful and widely used to obtain intact images. There have been three reports describing the behavioral effects observed as a result of high-strength static magnetic field exposure of rats and mice. Using a conditioned taste aversion technique, it was shown that rats developed a conditioned taste aversion after exposure to a high magnetic field of 9.4 T for 30 min (Nolte et al., 1998). Following this report, similar experiments were carried out. Restrained rats and both unrestrained and restrained mice were exposed to magnetic fields of 7 and 14 T generated by superconducting magnets (Houpt et al., 2003). In the report, it was found that exposure of rats to high magnetic fields suppressed rearing and locomotor circling and induced conditioned taste aversion and expression of c-Fos in vestibular neclei. The rat's orientation in magnetic fields is a key factor for the direction of circling. Similar results were obtained with mice (Lockwood et al., 2003). All tested mice showed development of conditioned taste aversion, and a significant number showed tight circling and rearing suppression. Effects were observed more significantly in unrestrained mice than in restrained mice. Snyder et al. (2000) have identified brain stem regions that were activated by exposure to static magnetic field levels of 9.4 T for 30 min, of restrained rats, by using a c-Fos immunohistochemisty detection assay. Increased expression of c-Fos and neural activation in visceral and vestibular nuclei by magnetic field exposure have been reported. It has been suggested that the neural activation response might be a factor in promoting conditioned taste aversion learning.

Superconducting high magnetic field exposures of 7 T have been reported to have reduced the trehalase enzyme activity in honey bees (Kefuss et al., 1999). There were no changes found in the level of fatty acids, triacyglycerols, and steroids in this study.

8.3.1.1.2 Analgesia

Effects of a hypogeomagnetic environment with a flux density of 4 μT inside a Mu-metal box on stress-induced analgesia in C57 male mice have been investigated (Del Seppia et al., 2000). This study consisted of three consecutive parts: (1) maintaining the mice under various magnetic exposure conditions: hypogeomagnetic, altered magnetic field, and Earth's geomagnetic field of 46 μT for 90 min; (2) immobilizing the animals in a tube for 30 min under each exposure condition; and (3) recording nociceptive responses of the restraint-stressed mice as the latency of front-paw lifting to hot-plate stimulus. Stress-induced analgesia was significantly reduced in the animal group exposed to the hypogeomagnetic field, and this result was comparable with that in the mice exposed to altered magnetic fields or treated with prototypic opiate antagonist naloxone. It has been suggested that the exposure period in a hypogeomagnetic environment might be responsible for the inhibition of stress-induced analgesia. They also demonstrated that exposure to altered magnetic fields induce more rapid habituation to a novel environment (open field) (Del Seppia et al., 2003). The experiment was carried out to investigate effects of irregularly varying (<1 Hz), 20–70-μT or regular 37-Hz, 80-$\mu T_{p\text{-}p}$ magnetic fields with a 2-h exposure of mice. The nociceptive response was measured by a hot-plate test and showed that the nociceptive sensitivity was significantly greater in magnetically treated mice than in controls.

Various sensing-transduction mechanisms have been proposed to explain the biological effects of magnetic fields. Prato et al. (1996a). showed inhibitory effects of 60-Hz magnetic fields at levels of 299 $\pm$ 1 $\mu T_{p\text{-}p}$ and static magnetic fields at levels of 78 $\pm$ 1 μT on opioid-mediated analgesia in the land snail, *Cepaea nemoralis*. It has been reported that the effects were dependent on the relative direction of both the weak static and the 60-Hz magnetic field, as well as on the presence of light. In a following study, indirect and direct mechanisms of ELF magnetic fields on an endogenous opioid peptide-mediated analgesic response have been proposed. It was shown that the energy transduction mechanism did not involve induced electric currents or magnetite (Prato et al., 1996b), and the results indicated that a direct magnetic field detection mechanism was consistent with the parametric resonance model. In a later study to reexamine the results obtained and further clarify the role of light, it was found that reduction of the opioid-induced analgesia by magnetic field exposure was enhanced by the presence of light. It was reported that the reduction rate of analgesia was not dependent on ELF frequency; however, the effect of the ELF magnetic field was in fact mediated by direct magnetic field detection.

In order to detect static magnetic field-induced functional changes in brain tissue, Veliks et al. (2004) carried out an investigation to identify the effects of static magnetic fields on rat brain structures using heart rate and heart rhythm as physiologic indicators. Rats put under ketamine–xylazine anesthesia were exposed to magnetic field levels of 100 mT for 15 min. Before and after the exposure, an electrocardiogram was recorded for analysis of heart rate and heart rhythm. Static magnetic fields were found to evoke changes in both heart rate and heart rhythm in 80% of the subject animals.

McLean et al. (2003b) examined the effects of inhomogenous static magnetic fields, alone or in combination with the chemical agent phenytoin (PHT), on audiogenic seizures (AGS) in DBA/2 mice. In experimental studies where the static magnetic fields ranged from 0.26 to 10.5 mT, with a field gradient ranging between 0.012 and 0.48 T/m, seizure severity decreased as the magnetic flux density and exposure duration period increased. It was found that the magnetic field pretreatment enhanced the effect of PHT, and it was also found that a static magnetic field alone had some anticonvulsant effects as well. Further investigation is required to clarify the anticonvulsant effects of magnetic fields in AGS.

8.3.1.2 Reproduction and Development

The effects of static magnetic fields, including MRI fields (static, gradient, and RF), on fertility, the developing embryo, and the fetus have been investigated. There have been a series of reports describing the effects of 10- and 35-day exposures to a magnetic field level of 0.7 T on mice, in terms of sperm motility, maturation, and production and morphological and developmental changes (Tablado et al., 1996, 1998, 2000). In the first report, mice were exposed to a magnetic field level of 0.7 T for time periods between 1 and 24 h/d, over 35 d. It was found that sperm motility, maturation, and production were not affected. Two years later, it was reported that the size of sperm heads was still intact; however, the animals that had undergone continuous exposure demonstrated increased sperm head abnormality. In a study by Tablado et al. of magnetic effects during developmental changes, experiments were carried out to investigate the *in utero* exposure effects from magnetic field levels of 0.5 to 0.7 T on testis and epididymis development in mice. After mating, female mice were exposed from day 7 of gestation until the day of birth. Results showed that there were no significant differences between exposed and sham-exposed animals in terms of body weight gain of dam, litter size, body weight of male pups, and testis–epididymus weight gain of pups up to 35 d of age. In addition, there were no detectable changes found during a histopathological evaluation of the testis and epididymis of pups.

Narra et al. (1996) reported the biological effects of a static magnetic field on spermatogenesis and embryogenesis in Swiss Webster mice. Male and pregnant female mice were exposed to a magnetic field level of 1.5 T for 30 min. There was no increase in sperm head shape abnormality and no reduction in testicular sperm numbers; however, a decreased survival rate of preimplantation embryos was indicated.

It has been reported that there were no harmful effects detected in a static magnetic field of 4.7 T on ICR mice (Okazaki et al., 2001). Pregnant ICR mice were exposed to the field from days 7.5–9.5 of gestation and sacrificed on day 18.5 of gestation. There were no significant differences in the incidence of prenatal death or malformations between the exposed and control groups. The investigation has been conducted for potential adverse effects of a 10-week exposure to a 9.4-T magnetic field on the development of male and female rats as well as their offspring (High et al., 2000). All rats were exposed to 9.4 T for 3 h twice a week with an intermittent duration of 5 week on, 2 week off, and 5 week on. The results demonstrate hematological, biochemical, pathological, and behavioral changes in both adults and their offspring; however, there were no adverse effects observed in either male or female adult rats, as well as in their offspring.

Effects of long duration and high magnetic field exposure on fetal growth and postnatal development in mice have been investigated (Magin et al., 2000). One group of mice was exposed for 9 h on day 9 or on day 12 postcoitus (or both) to MRI conditions (static magnetic field of 4 T with 5-T/s gradient and whole-body SAR of 0.2 W/kg at 170 MHz). A second group was exposed to a combination of ultrasound and MRI fields. There were no significant changes in fetal growth in animals exposed to MRI or ultrasound fields individually. The average fetal weight of animals exposed to combined fields was lower than that of the other group. Carnes et al. (1996) investigated the effects of static magnetic field levels of 4.7 T, which is equivalent to the level used in MRI, on fetus, adult growth, and testicular development in mice.The 8-h exposure was carried out on day 9 or day 12 of gestation (or both). Effects of the combined application of 1 MHz ultrasound on day 9 and MRI on day 12 was also investigated. The average fetal weight of the exposed groups was found to be less than that of the control groups. It was found that the postpartum death rate was higher after the MRI exposure, and sperm production was reduced; however, no changes were detected in embryonic death rate, sex ratio, body weight at day 50, spleen weight, and seminal vesicle weight.

Jove et al. (1999) studied the effects of static magnetic field levels of 18 and 36 mT on the development of chick embryo, including the pineal gland. They found that static magnetic fields affected the development and growth of embryos, and this effect was dependent not only on the intensity but also on the length of exposure time. Ruggiero et al. (2004) reported the effects of a 3-h exposure to a magnetic field level of 0.2 T generated by a clinically used MRI system on the angiogenesis of chick embryo. Angiogenesis was evaluated using a chick embryo chorioallantoic membrane assay. Results indicated that static magnetic field exposure inhibited angiogenesis in chick embryo. Effects of a uniform static magnetic field of 29 mT on cell migration and differentiation in the cerebellum of chick embryo have been studied (Espinar et al., 1997). The cerebella of chick embryos was exposed to the magnetic field on 6 d of incubation and sacrificed at day 13 of incubation. Results showed that static magnetic field exposure could induce irreversible developmental effects on cell migration and differentiation. Clear signs of cell degenerations and delay in the process of neuronal differentiation were indicated.

There have been a series of reports describing the effects of static magnetic field on fish embryos (Formicki and Winnicki, 1996, 1998; Winnicki et al., 1996; Formicki et al. 1997; Formicki and Perkowski, 1998). First, it was reported that during a prolonged transportation of fertilized salmonid eggs and trout (*Salmo trutta* L. and *Oncorhynchus mykiss*), a magnetic field of 4 mT lowered the mortality rate and enhanced the conservation condition (Winnicki et al., 1996). Effects of static magnetic fields ranging from 50 to 70 mT on the cardiac muscle activity of carp (*Cyprinus carpio* L.) embryos and larvae have been investigated (Formicki and Winnicki, 1996). An increase in heart rate was observed after exposure to these fields. Effects from both the strength and the direction of the geomagnetic field and static magnetic fields of 0.5 and 1 mT on the orientation of trout embryo

(*S. trutta*) and rainbow trout (*O. mykiss*) have also been investigated. Results have shown that the embryos were sensitive to the static magnetic fields, with a preference for a certain field direction. Further investigation has been conducted to clarify the response of fish embryos and larvae from the same type of trout to a static magnetic field (Formicki and Winnicki, 1998). Eggs were placed in magnetic fields during the period from fertilization to hatching. The exposure of eggs resulted in slower embryonic development; thus, eggs were incubated for a prolonged period of time. Embryos of rainbow trout (*O. mykiss*) and trout (*S. trutta*) exhibited orientation both in the natural magnetic field and in artificial magnetic fields of 0.5 and 1 mT. In a supplementary paper, Formicki and Perkowski (1998) showed the effects of static magnetic fields of 5 and 10 mT on the gas exchange in rainbow trout (*O. mykiss*) embryos. An increase of oxygen uptake was observed. It was determined that the impact of magnetic field exposure on the respiratory system was significant in the periods of advanced morphogenesis.

It has been reported that the exposure to static magnetic fields of 10–100 mT could alter the early embryonic development in two species of sea urchin embryo, *Lytechinus pictus* and *Strongylocebtrotus purpuratus* (Levin and Ernst, 1997). Results suggested that static magnetic fields delayed the onset of mitosis in both species. A static magnetic field of 30 mT caused an eightfold increase in the incidence of exogastrulation in one species. Static magnetic field effects of 4 and 8 mT and effects of exposure to 60-Hz AC magnetic fields of 6 and 8 mT on the first division of two sea urchin embryos, *Sphaerechinus granularis* and *Paracentrotus lividus*, have been studied (Pagnac et al., 1998). No differences were found in the time of the first cleavage in both exposures.

In a static magnetic field of 35 mT, the fruit fly (*Drosophila melanogaster*) was reared through several generations to investigate the width and length variability of both wings (Stamenkovic-Radak et al., 2001). In the second-generation exposure, there was a significant difference between sexes in the context of directional change of wing size variability. In the sixth generation, the differences in wing size between the magnetic field exposure group and control groups showed the same directional pattern in both sexes. Pan and Liu (2004) reported the effects of high static magnetic fields of 9.4 and 14.1 T on the hatching behavior of fresh mosquito eggs. Hatching was delayed, and the delay time depended on the intensity of the magnetic field.

Effects of exposure to high static magnetic field with levels up to 16.7 T on the first three cleavages of *Xenopus laevis* embryos have been investigated (Denegre et al., 1998). Results have indicated that cleavage furrows aligned parallel to the magnetic field. The most significant effects on the second and third cleavages have been observed in homogenous fields, not in the gradient fields. It has been suggested that this phenomenon was caused by interactions between the magnetic fields and the diamagnetic materials in the *Xenopus* embryo. Further studies have shown that after exposure to static magnetic fields of 17–22 T during either or both of the first two cell cycles, the third cell cycle mitotic apparatus at metaphase could be induced, and the third cleavage furrows aligned perpendicular to their nominal orientations (Valles, 2002; Valles et al., 2002). Valles et al. (1997) investigated the magnetic field gradient levitation (MFGL) as a technique for simulating low gravity for biological systems.They levitated living biological specimens, embryos of the frog *X. laevis*, using a large inhomogenous magnetic field. MFGL of embryos reduced the body forces and gravity-induced stress on them.

8.3.1.3 Circulatory System Effects

Recently, effects of static magnetic field applications on the circulatory system have been reviewed in experimental animals (Tenforde, 2005) and in humans (Chakeres and de Vocht, 2005; Crozier and Liu, 2005; van Rongen, 2005). Most of the studies have been related to MRI systems, and it has been reported that in MRI-related studies using strengths of up to 8 T, there were little or no significant changes in cardiovascular and circulatory parameters. In contrast, it was found that moderate-intensity static magnetic fields ranging from 1 to 350 mT can have significant circulatory system effects, most notably on cutaneous microcirculation and arterial blood pressure.

8.3.1.3.1 Microcirculation

Ohkubo and Xu (1997) studied the acute effects of 1–10-mT static magnetic fields applied for 10 min on the microcirculatory changes in conscious rabbits using a rabbit ear chamber (REC) and microphotoelectric plethysmography (MPPG). The static magnetic fields induced biphasic changes in vasomotion in a non-dose-dependent manner. Static magnetic fields suppressed vasomotion when the vascular tone was high, while the same level fields enhanced vasomotion when the tone was low. To clarify these effects, the same group, Okano et al. (1999), investigated the effect of a 1-mT static magnetic field for 10 min on microcirculation in conscious rabbits using pharmacological manipulation together with REC and MPPG. The results showed that the static magnetic field enhanced vasodilatation and increased vasomotion under norepinephrine, which induced high vascular tone and, in contrast, induced vasoconstriction and decreased vasomotion under acetylcholine, which induced low vascular tone.

These studies are strongly supported by another independent study that examined the effect of a moderate-intensity static magnetic field on microcirculation, suggesting that the static magnetic field could modulate the biphasic responses of relatively smaller-diameter blood vessels (arterioles). Morris and Skalak (2005) studied the acute effect of a 70-mT static magnetic field for 15 min on the diameter of microvessels in rat skeletal muscle placed under pentobarbital anesthesia, using intravital microscopy. This study suggested that the static magnetic field could modulate microvascular tone in a restorative fashion, thereby acting to normalize the tone.

Gmitrov and colleagues reported the acute effects of 250–350 mT static magnetic field exposures for a time period of up to 80 min on microcirculation within cutaneous tissue of the rabbit ear lobe placed under pentobarbital anesthesia using REC and MPPG (Gmitrov and Ohkubo, 1999a,b; Gmitrov et al., 2002). They demonstrated that application of static magnetic fields to the carotid sinus baroreceptor region for a period of 65–80 min increased microcirculation. The static magnetic fields suppressed or recovered a Ca^{2+} channel blocker, verapamil, which reduced microcirculation.

Xu et al. (1998) observed the subchronic effects of a 180-mT static magnetic field, with length of exposure times for up to 4 weeks, on cutaneous microcirculation in conscious rabbits, using REC and MPPG. The static magnetic field significantly increased the long-lasting vasodilatation and enhanced the vasomotion. The same authors found that exposure to static magnetic fields at 1 mT or higher for 10 min enhanced microcirculation and increased peak blood velocity (Xu et al., 2000).

Mayrovitz et al. (2001, 2005) investigated the effects of static magnetic fields with strengths as high as 100 mT and exposure periods of up to 36 min on skin blood flow in humans, using a laser-Doppler flowmeter. They showed that the static magnetic fields have no significant effect on the normal, unstressed circulation or vasoconstrictive response in conjunction with skin temperature. Steyn et al. (2000) also indicated that there are no effects observed on blood flow in horses after exposure to static magnetic fields.

In a series of studies that observed the effects of ultrastrong (>5 T) static magnetic field exposure, Ichioka et al. (1998, 2000) investigated the acute effect of an 8-T static magnetic field exposure for a period of 5 min on blood flow in rat by using a laser-Doppler flowmeter and thermistor-derived measurements.They demonstrated that blood flow and skin temperature decreased during the field exposure, through the movement of water vapor over the animal and the decreased humidity in the air.

8.3.1.3.2 Blood Pressure

Gmitrov and colleagues studied the influence of both a 350-mT static magnetic field and geomagnetic field activity on mean arterial blood pressure (MAP) in pentobarbital-anesthetized rabbits (Gmitrov and Ohkubo, 2002; Gmitrov et al., 2002). Application of the static magnetic field to the baroreceptor region for 65–80 min decreased MAP. In testing geomagnetic field applications, they found that there was a positive correlation of this field's activity with MAP, and this result implied that magnetic storms could increase the incidence of severe cardiovascular events.

Okano and Ohkubo (2001) examined the acute effect of a 1-mT static magnetic field applied for 30 min on pharmacologically altered blood pressure in conscious rabbits. It was found that (1) the static magnetic field reduced the vasodilatation effect from enhanced vasomotion and antagonized the reduction of blood pressure under a Ca^{2+} channel blocker, nicardipine, which induced low vascular tone, and (2) the static magnetic field attenuated vasoconstriction and suppressed the elevation of blood pressure while under the influence of a nitric oxide (NO) synthase inhibitor, L-NAME, which induced high vascular tone. However, two of their experiments, which were carried out under normal conditions without pharmacological drugs, showed that static magnetic fields did not induce any significant effects on hemodynamics and blood pressure (Okano and Ohkubo, 2001, 2003a). With regard to these undetectable effects, Muehsam and Pilla (1996) speculated that physiologically significant bioresponses to therapeutic signals appear to occur only when the physiologic state of the target system is far from homeostasis.

In contrast to the experiments done without pharmacological manipulation, Okano and Ohkubo (2003a) found that exposure to a 5.5-mT static magnetic field for 30 min caused the suppression of norepinephrine- or L-NAME-induced vasoconstriction and hypertension in rabbits. Furthermore, they tested exposures of 5–10-mT static magnetic fields for a period of several weeks on the development of hypertension in spontaneously hypertensive rats (Okano and Ohkubo, 2003b; Okano et al., 2005a). Experimental results indicated that the static magnetic fields suppressed and retarded the development of hypertension because of the reduction in plasma levels of both angiotesin II and aldosterone together with lower levels of NO metabolites (NO_x).

In addition, the antihypotensive effects of static magnetic fields on reserpine-induced hypotensive rats were investigated (Okano et al., 2005b). The result suggested that exposure to a 25-mT static magnetic field for several weeks suppressed the reserpine-induced hypotension and bradykinesia through the inhibition of norepinephrine depletion.

Saunders (2005) commented that most of these studies were undertaken in the context of the potential therapeutic effects of static magnetic field on various disorders. Further studies with some independent replications are required even if the effects of static magnetic field on both blood flow and blood pressure indicate possible medical applications.

8.3.1.4 Neuroendocrine, Visual, and Neurophysiological Systems

Effects of static magnetic field exposures of 0.05 μT to 80 mT, and 7 T on the level of melatonin in rat have been examined (Kroeker et al., 1996). The first experimental exposure using field strengths of up to 80 mT for 12 h/d and 8 d showed no significant changes in night-time pineal and serum melatonin levels, as did the second experimental exposure using 7 T for 45 min. The visual system of the fruit fly (*D. melanogaster*) was investigated after an exposure to a zero magnetic field (Creanga et al., 2002). Adults from pupae maintained in a zero magnetic field for 20 h were used for the electroretinogram. A significant increase in sensitivity of neural cells from the first optic ganglion was indicated.

Osuga and Tatsuoka (1999) tested the effects of a 1.5-T static magnetic field by using an MRI system application on neuroconduction in a partially active nerve in the bullfrog (*Rana catesbeiana*). The action potential and nerve impedance measurements indicated that a field strength of 1.5 T had no effect on neuroconduction; therefore, it was determined that neuroconduction in damaged nerves was not affected by the exposure.

8.3.1.5 Magneto-Mechanical Systems

Testorf et al. (2002) studied the influence of homogenous static magnetic fields of 8 and 14 T on melanophore aggregation in black tetra (*Gymnocorymbus ternetzi*). The result showed no significant field effects on the aggregation after exposure to magnetic fields.

Effects of a 0.2-T static magnetic field on a normal human neuronal cell culture, FNC-B4, has been investigated with MCF-7 and WEHI-3 cells as controls (Pacini et al., 1999b). FNC-B4 cells changed their morphology after the exposure. Cells became elongated and formed vortexes, while controls did not show any alteration. The morphological changes in MRC-5 fibroblasts were evaluated as well (Pate et al., 2003). The cells were screened for cell mobility, cell distribution, and cellular morphology (size, shape, lysis, and background). These cells were exposed to both a static magnetic field and a pulsating magnetic field for a period of 0, 24, 48, and 72 h. Although the static magnetic field-exposed cells showed cell membrane damage and morphological change, as well as other interesting findings that were included in the report, this report may not be useful because it did not provide essential dosimetric data, such as strength of the field.

Danielyan et al. (1999) examined the effects of a 0.2-T static magnetic field on binding of ouabain-H^3, which is a specific inhibitor of Na^+-K^+-ATP-ase, in normal glandular breast tissue and in cancerous breast tissue. The static magnetic field-induced decrease of binding was considered as evidence for the dehydration effect of the field. This study has indicated that the static magnetic field tested could influence the cancer cell's metabolism through cell hydration changes. They investigated the effects of a 0.2-T static magnetic field on the hydration of rat tissues (Danielyan and Ayrapetyan, 1999). They assumed that the target for magnetic field action was the structured water of the cell. Decreases in hydration and adaptation of brain, liver, and spleen and an increase in the case of kidney were observed.

8.3.1.6 Musculoskeletal System

Yan et al. (1998) investigated the effects of static magnetic fields on bone formation of rat femurs. They implanted magnetized samarium cobalt rods with a field strength of 180 mT into rat femurs. The bone mineral density (BMD) and bone calcium content were measured 12 weeks after implantation. Results indicated that the femurs adjacent to the magnetized specimens had significantly higher BMD and calcium content. However, BMD and calcium content levels were found to be normal in both magnetized and unmagnetized specimen groups. The same research group further studied the effects of a 180-mT static magnetic field on bone formation, using an ischemic rat femur model (Xu et al., 2001). It was reported that the enhancement of the femoral bone formation was due to the improved blood circulation in the femur.

Satow et al. (2001) observed the effect of a 0.65-T static magnetic field on muscle tension in the neuromuscular preparation of the sartorius muscle of bullfrog (*R. catesbeiana*). The tension development was obtained by stimulation of the sciatic nerve or of the sartorius muscle itself for a duration of 30 min. A decrease in muscle tension was observed. The results indicated that application of the static magnetic field was responsible for tension development.

8.3.2 Tissue, Molecular, and Cellular Studies

8.3.2.1 DNA and Chromatin

The exposure of isolated rat lymphocytes to a static magnetic field of 7 mT for 3 h did not increase the number of damaged cells (Zmyslony et al, 2000). Although incubation with 10 μg/ml $FeCl_2$ did not cause DNA damage, the number of damaged cells increased when the $FeCl_2$-incubated lymphocytes were simultaneously exposed to the field. A hypothesis for these observations was that the number of reactive oxygen species generated by iron ions in cells might increase after the exposure to the magnetic field (Jajte et al., 2002).

Binhi et al. (2001) have reported the effect of a weak static magnetic field on *Escherichia coli* K12 AB1157 cells, by using anomalous viscosity time dependence (AVTD) assay methods. The AVTD changes were found when the cells were exposed to static magnetic field levels up to 110 μT. These results were consistent with the calculations of individual rotations of the ion–protein complexes Ca^{2+}, Mg^{2+}, and Zn^{2+}, provided that all complexes rotated at the same speed. They suggested that the rotation for all ion–protein complexes is on the same carrier, such as DNA.

The effect of a zero magnetic field on the conformation of chromatin in human VH-10 fibroblasts and lymphocytes was investigated by the AVTD method (Belyaev et al., 1997). A decrease in the AVTD peaks was observed within 40–80 min of exposure to fibroblasts, and this decrease was transient, disappearing 120 min after the beginning of exposure. A similar effect of zero field was observed when cells were exposed for 20 min and kept at an ambient field. They concluded that both zero field and γ-rays caused hypercondensation and decondensation of chromatin. Zero field effects were more significant in the beginning of the G_1-phase than in the G_0-phase in human lymphocytes.

Okuda et al. (1998) evaluated the effects of a 6.34-T static magnetic field on the instability of microsatellite repetitive sequences in DNA mismatch repair (MMR)-proficient and MMR-deficient cell lines, HeLa S3, and HCT116, respectively. After exposure to the field, both cell lines exhibited no significant microsatellite sequence changes. This result suggested that the static magnetic field might not induce the genetic changes in microsatellite sequences.

8.3.2.2 Cell Growth, Cell Proliferation, and Cell Cycle

Potenza et al. (2004b) showed that *E. coli* cell growth and gene expression were affected by a static magnetic field exposure level of 300 mT. Cell proliferation at the stationary phase was increased by exposure to those cells growing in a modified medium culture containing glutamic acid; however, cell proliferation was not affected in those cells growing in traditional Luria–Bertani (LB) medium. Gene expression differences were estimated by differential display assays using arbitrary primers, and four genes were found to be responsive to the static magnetic field. One clone, expressed only in the exposed cells, corresponded to a putative transposase. Potenza et al. suggested that the static magnetic field exposure might stimulate transposition activity.

Stansell et al. (2001) reported that antibiotic (piperacillin) resistance of the clinically isolated *E. coli* was increased by the heterogenous static magnetic field exposure level of

8–60 mT for 45 min. They suggested the observation may be unique to the particular strain of *E. coli* or the specific antibiotic used. They did not suggest any mechanistic implication for this observation.

Poiata et al. (2003) reported zero magnetic field effect on the antibiotic resistance of *E. coli* strains isolated from human subjects. They used 26 *E. coli* strains and 5 different antibiotics, ampicillin, ceftazidine, tetracycline, ofloxacin, and kanamycin. Approximately one third of the tested strains was sensitive to the zero field treatment. Minimum inhibitory concentrations (MICs) of each antibiotic for some strains were decreased by zero magnetic field exposure, while the MICs for other strains were increased by the exposure. Their mechanistic hypothesis, based on magnetic particles, did not support these observations.

Ruiz-Gomez et al. (2004) showed that growth of the haploid yeast strain *Saccharomyces cerevisiae*, a eukaryotic cell, was not affected by exposure to static magnetic field levels of 0.35 and 2.45 mT.

Effects of a 0.2-T static magnetic field, generated by MRI alone or in combination with vitamin D treatment, on cell damage and proliferation in the human breast cancer cell MCF-7, human neuronal cell FNC-B4, and murine leukemia cell WEHI-3 have been investigated (Pacini et al., 1999a). Three-hour exposures to the 0.2 T field had no effect on the cell colony formation number in all three cell lines. Results demonstrated that [^{3}H] thymidine incorporation level decreased in MCF-7 and FNC-B4 cells, while no changes were observed in WEHI-3. It was also demonstrated that the treatment of cells using vitamin D had a permanent antiproliferative effect.

Long-term effects on proliferation of human fetal lung fibroblast (HFLF) cells of repetitive exposure to a 1.5-T static magnetic field with exposure periods of 1 h/d for 3 weeks have been investigated (Wiskirchen et al., 1999). Results showed no changes in clonogenic activity, DNA synthesis, cell cycle, and proliferation kinetics. In a following paper, effects of static magnetic field levels of 0.2, 1.0, or 1.5 T on the cell cycle in both synchronized and nonsynchronized HFLF cells were evaluated (Wiskirchen et al., 2000). The exposure condition was 1 h/d for 5 consecutive days. Results showed no significant differences in cell cycle events between synchronized and nonsynchronized cells.

A series of research studies on growth enhancement by strong inhomogenous static magnetic fields have been reported. Tsuchiya et al. (1996) showed that the growth of *E. coli* was affected by both a strong homogenous static magnetic field strength of 7 T and inhomogenous field strengths of 5.2–6.1 or 3.2–6.7 T. In the stationary phase, the cell number under a high magnetic field was about two to three times higher than that of a control. The effect of the inhomogenous field was much stronger than that of the homogenous field. They also showed that the transcription activity of *E. coli* was enhanced by the strong inhomogenous static magnetic field levels of 5.2–6.1 T (Tsuchiya et al., 1999). The transcription levels of the *rpoS*, gene which encodes sigma factor of RNA polymerase, was increased in the stationary phase by the static magnetic field exposure. This transcription factor is specifically activated during the stationary phase and plays an important role in the transcription control of other genes in the stationary phase.

Horiuchi et al. (2001) showed that *E. coli* cell death in the stationary phase was suppressed by strong inhomogenous static magnetic field levels of 5.2–6.1 T with a gradient of 24 T/m and that the suppression was dependent on the addition of amino acids to the LB medium. The addition of glutamic acid enhanced cell death as pH increased in the stationary phase, and cell death was dramatically suppressed by the field exposure. At the same time, *rpoS* gene expression was increased 20% by the field exposure. They suggested that the increase of *rpoS* gene expression in the stationary phase by the field exposure might be related to the base resistance because the *rpoS*-disrupted strain showed a lower base resistance than the wild-type strain (Ishizaki et al., 2001). It has been shown that the medium supernatant, when used after the static magnetic field exposure, could enhance the suppression of cell death (Horiuchi et al., 2002). The pH of the medium after the static magnetic field exposure was only slightly different from that of the control (by a factor of 0.07 pH), and pH-adjusted medium from both exposed and control supernatants still had the suppression effect characteristics from the exposure to static magnetic fields. It has been suggested that other factors also were involved in the full suppression effect of cell death by the field exposure.

The growth advantage in stationary phase (GASP) phenomenon is described as follows. When *E. coli* cells grown for 10 d (aged culture) and *E. coli* cells grown only for 1 d (young culture) were mixed, the cell number of the young culture decreased, and the population of the young culture was taken over by the aged culture, and eventually only aged cells predominantly survived in the system. It has been found that the GASP phenomenon disappeared with the exposure to strong inhomogenous static magnetic field levels of 5.2–6.1 T (Okuno et al., 2001). They suggested that the disruption of the GASP phenomenon might be related to an effect on the *rpoS* gene by the static magnetic field exposure.

Gray et al. (2000) evaluated static electric and magnetic field effects on the action enhancement of the chemotherapeutic agent adriamycin in transplanted mammary adenocarcinoma in female B6C3F1 mice. Treatment consisted of using 10 mg/kg of adriamycin in combination with a 4-h exposure to a 110-mT field. Tumor regression in the groups exposed to a static magnetic field was greater than in the group treated with adriamycin only.

Tanioka et al. (1996) evaluated the effects of a 6.34-T static magnetic field on proliferation and metastatic activity in the B16 melanoma and EL-4 T-lymphoma cell lines. Cell cultures were incubated in the presence of magnetic fields for 12, 24, 36, or 48 h at 37°C. It was found that the proliferative and the metastatic activities of both cell lines were promoted under certain conditions.

Tofani et al. (2003) exposed immunocompetent mice bearing either the murine Lewis lung carcinoma or the B16 melanotic melanomas to static field levels of 3 and 4 mT and treated them with two commonly used anticancer drugs, cisplatin and cyclophosphamide, respectively. The survival time of mice treated with cisplatin and exposure to the magnetic fields was significantly longer than that of mice treated only with cisplatin or only exposed to the magnetic fields, surpassing that of mice treated with 10 mg/kg i.p. of the drug and showing that the magnetic field acts synergically with the pharmacological treatment. When mice treated with cyclophosphamide were exposed to the magnetic field, no synergic effects were observed. No clinical signs or toxicity were seen in any of the mice exposed to the magnetic field alone or along with cisplatin or cyclophosphamide treatment.

Raylman et al. (1996) studied the effects of exposure to a static magnetic field of 7 T for 64 h on cell viability in three malignant human cell lines, melanoma (HTB 63), ovarian carcinoma (HTB 77IP3), and lymphoma (Raji; CCL86). It has been reported that the static field exposure reduced the viable cell count and appeared to inhibit cell growth.

Using two types of mammalian cells, mouse leukemia cells P388 and Chinese hamster fibroblast cells V79, Sakurai et al. (1999) tested the effects on cell growth patterns of exposure to a 7-T static magnetic field for up to 5 d. No significant magnetic field effects on cells were found.

In a series of papers (Kula, 1996; Kula and Drozbz, 1996a,b), the magnetic field effects on cultured fibroblasts isolated from the BALB/c mouse have been investigated. The fibroblast cultures were exposed to a static magnetic field of 0.49 T and a 50-Hz AC magnetic field of 0.02 T for a time period of 2–64 min/d over four consecutive days. The following parameters were studied: the dynamics of culture growth; protein content;

thymidine incorporation; Zn, Fe, and Cu ion content; the activity of superoxide dismutase (SOD) and catalase (CT); and glycosaminoglycan metabolism. The static magnetic field exposure had no effect on both the vital functions and glycosaminoglycan metabolism and did not show any changes in the free-radical process in fibroblasts. Kula et al. (2000) further evaluated the activities of SOD, CT, glutathione peroxidase, and malondialdehyde (MDA) in the livers and kidneys of rats exposed to a static magnetic field of 0.49 T and a 50-Hz AC field of 0.018 T. While the 50-Hz magnetic field was found to influence free-radical processes in both liver and kidney tissue, the static magnetic field showed no effects. Magnetic field effects on the lipid peroxidation product, MDA, in mouse subcellular fibroblast have been evaluated by the same protocol in a previous report (Kula et al., 2002). It was found that exposure to a static magnetic field caused no changes in peroxidation of membrane structures.

Effects with a combination of static and alternating magnetic fields on cell attachment and induction of apoptosis in rat tendon fibroblast and rat bone marrow (RBM) osteoprogenitor cells have been reported (Blumenthal et al., 1997). Experiments utilized 60-and 1000-Hz AC magnetic fields of up to $0.25\,mT_{p\text{-}p}$ and static magnetic fields of up to 0.25 mT. It was found that AC fields and static magnetic fields tested with various combinations of field strengths and frequencies resulted in extensive detachment of preattached cells and prevented the normal attachment of cells not previously attached to substrates. Results suggested significant alterations in cell metabolism and cytoskeleton structure after the exposure.

Blanchard and Blackman (1994) proposed the ion parametric resonance (IPR) model for the prediction of the interaction between magnetic fields and biological systems (see also Chapter 9 on resonance phenomena by Liboff). According to the IPR model, the relationships among the strength of a static magnetic field, the AC magnetic field frequency, and the charge-to-mass ratio of ions of biological relevance were important key factors. Blackman et al. (1996) tested the influence of magnetic fields on neurite outgrowth in PC-12 cells and showed that the PC-12 cell response to perpendicular AC and static magnetic fields was distinct and predictably different from that found for parallel AC and static magnetic fields. It has been reported that the response to perpendicular fields was dominant in an intensity-dependent nonlinear manner.

The effects of the combination of AC and static magnetic fields on the behavior of Friend erythroleukemia cells have been studied (Eremenko et al., 1996). The combined fields were a geomagnetic field of 45 μT, together with a 70-μT field at 50 Hz which was produced in a solenoid coil, and 20-nT DC and 2.5-pT AC fields in a magnetically shielded room. It was found that the culture growth cycle of cells was slightly accelerated inside the solenoid, and the degree of acceleration appeared to depend on sensitivity of the cell cycle to the magnetic field. On the other hand, it was found that the culture growth cycle of cells inside the magnetically shielded room was slightly decreased.

Effects of a static magnetic field exposure of 10 T for up to 4 d on the rate of cell growth or cell cycle distribution in Chinese hamster ovary (CHO-K1) cells have been investigated (Nakahara et al., 2002). The exposure to the static magnetic field alone did not affect micronucleus formation. In x-ray irradiated cells, exposure to the 10-T static magnetic field resulted in a significant increase in micronucleus formation. Buemi et al. (2001) examined the effects of a 0.5-mT static magnetic field on the cell proliferation and cell death balance in monkey renal cells (VERO) and in rat cortical astrocyte cells. After 6 d of exposure to the magnetic field, they observed the effects on cell proliferation and cell death balance and suggested that the effects might vary depending on the cell type. Magnetic fields may also have a nephropathogenic effect.

Tofani et al. (2001) investigated the role of magnetic field characteristics on the growth of WiDr human colon adenocarcinoma, MCF-7 human breast adenocarcinoma, and MRC-5 embryonal lung fibroblast. Cell death induction was observed with a magnetic field exposure of greater than 1 mT when the combined static magnetic field and 50-Hz magnetic field was applied. The report showed that significant tumor growth inhibition appeared when the total field strength was greater than 3.59 mT.

Schiffer et al. (2003) studied the effects of four different types of magnetic field applications on the cell cycle progression in two different tumor cell lines, the human acute myeloid leukemia cell HL-60 and the mouse lymphoma cell EA2. The four types of magnetic field applications used were (1) the static magnetic field of 1.5 and 7.05 T, (2) the magnetic gradient field with ± 10 and ± 100 mT/m at 100 Hz; (3) the pulsed high frequency magnetic field (5.8 μT at 63.6 MHz); and (4) the combination of (1)–(3). The exposure duration ranged from 1 to 24 h. Cell cycle fractions at G_0/G_1, S, and G_2/M phases were analyzed by flow cytometry. Cell cycle analysis did not show differences between the exposed and control cells. In conclusion, during MRI, no influence of magnetic field on cell cycle progression was observed in these cell lines.

8.3.2.3 Cell Membrane and Cell Metabolic Activity

Chignell et al. (1998) studied the effects of static magnetic fields of 25–150 mT on the photohemolysis of human erythrocytes by ketoprofen. An application of a static magnetic field during UV (>300 nm) irradiation of ketoprofen and erythrocytes significantly decreased the time required for photohemolysis. It has been suggested that the magnetic field increases the concentration and lifetime of free radicals that escape from the radical pair.

Chionna et al. (2005) investigated the effects of a 6-mT static magnetic field, applied for 24 h, on cell shape, cell surface sugar residue, cytoskeleton, and apoptosis in the hepatic transformed cell line Hep G2. Significant modifications of cell shape and surface by the field exposure have been observed. The exposed cells were found to be elongated, with many irregular microvilli randomly distributed on the cell surface. The shape of the cells was found to be less flat at the end of the exposure, although the morphology of the organelles remained unmodified throughout the exposure period. It has been reported that cell proliferation was partially affected. Results suggested that the static magnetic field caused a time-dependent biological effect on Hep G2 cells.

Sonnier et al. (2000) found that there were no effects from the exposure of static magnetic field levels of 0.1, 0.5, 5, or 7.5 mT, applied for 5 sec, on resting potential in cultured neuroblastoma cells. They also used the patch-clamp technique to measure transmembrane Na^+, K^+ currents in neuroblastoma cells SH-Sy5Y exposed to static magnetic fields of up to 7.5 mT (Sonnier et al., 2003). The magnetic field exposure did not result in detectable changes in any of the action potential parameters.

Trabulsi et al. (1996) measured the excitatory postsynaptic potential (EPSP) after the exposure of a mouse hippocampal slice to static magnetic field levels of 2–3 mT and 8–10 mT for a period of 20 min. They observed biphasic effects at 2–3 mT and depression of EPSP at 8–10 mT. It has been suggested that changes in intracellular Ca^{2+} concentration were responsible for these effects. Isolated *Helix aspersa* neurons were exposed to static magnetic field levels of 0.07–0.7 T, and their action potential was measured (Azanza and del Moral, 1996). A decrease in the spike depolarization voltage has been observed, and it has been attributed to desensitization of the membrane Na^+-K^+-ATP-ase pumps through an anisotropic diamagnetism reorientation.

Wieraszko (2000) studied the effect of 2–3-mT static magnetic fields applied for 20 min on the evoked potential response in B57/J56 mice hippocampal slices. Results, which were based on measurements of hippocampal function, showed both an alteration of the evoked potential and an effect on the influence of dantrolene, an inhibitor of intracellular Ca^{2+} channels.

The voltage-activated calcium channel function in cultured GH3 cells has been investigated (Rosen, 1996). A static magnetic field of 120 mT was applied for 150 sec. Reversible changes in calcium channel function were observed and were found to be temperature dependent. Results indicated that these changes were a result of alterations in the membrane proper because of the magnetically induced deformation.

Using the whole-cell patch-clamp technique, voltage-activated Na^+ channels in GH3 cells were examined (Rosen, 2003). The effects of exposure to a static magnetic field of 125 mT for 150 sec on voltage-gated Na^+ channel kinetics included a slight shift in the current–voltage relationship, a 5% reduction in peak current, and an increase in the activation time constant, τ_m, during and at least 100 sec after the exposure to the field. Significant changes were only observed at 35°C and 37°C. It was suggested that the temperature dependence factor that affected this process was probably due to the greater ease with which the liquid crystal membrane was deformed. Results suggested that the changes might be due to the reorientation of diamagnetic anisotropic molecules in the membrane. Hinch et al. (2005) showed the effects of static magnetic fields on action potential propagation and excitation recovery in nerve. At a field level of 125 mT, which was the same condition previously used by Rosen, they did not observe major changes in the electrical functioning of neurons.

Aldinucci et al. (2003a,b) investigated the effects of a 4.75-T static magnetic field exposure applied for 1 h, and also a 1-h exposure using combined fields of 4.75 T with a pulsed field of 0.7 mT, on proinflammatory cytokines, in human peripheral blood mononuclear cells (PBMCs) and Jurkat cells. They measured Ca^{2+}, proliferation, and the eventual production of proinflammatory cytokines. The static magnetic field exposure alone did not show any effects on the physiologic behavior of normal lymphocytes; however, the combined static and alternating magnetic field exposure contributed synergistically to the increase of $[Ca^{2+}]_i$. The exposure of PBMCs was carried out in a static magnetic field of 10 T (Onodera et al., 2003). It was reported that the magnetic field exposure reduced the viability of phytohemagglutinin (PHA)-activated T cells in both CD4+ and CD8+ subclasses. Sabo et al. (2002) observed a decrease in the metabolic activity of human promyelocytic leukemic cells HL-60 when exposed to a field of 1 T for 72 h. The decrease was also observed in the presence of antineoplastic drugs, which included 5-fluorouracil, cisplatin, doxorubicin, and vincristine.

Miyamoto et al. (1996) studied the effects of strong 6-T homogenous magnetic fields on both active and passive Rb^+ influx into HeLa cells. Using field exposures of 1.6 T and lower, and of 2.0 T, at various temperatures did not cause any changes in active or passive Rb^+ influxes.

Mouse islet of Langerhans cells have a very regular oscillation of calcium concentration. Madec et al. (2003) showed no effects of combined AC and static magnetic fields on these calcium oscillations in mouse islet of Langerhans.

8.3.2.4 Gene Expression and Signal Transduction

Fanelli et al. (1999) found a decrease of apoptosis in the human cell lines U937 and CEM, following exposure to a static magnetic field of 600 μT. It was suggested that the protective antiapoptotic effect was due to cellular modifications from the static field exposure, which affected the ability of the cell to enhance Ca^{2+} influx from the extracellular medium. Cohly et al. (2003) examined the effects of a 0.618-mT static magnetic field on a human osteoblast cell line (MG-63) culture, in terms of proliferation, proline uptake, and gene expression. Results showed that the exposure might be detrimental to bone formation.

Mnaimneh et al. (1996) investigated the effects of static magnetic field levels from 1 to 100 mT and also an AC field of 1.6 mT delivered at 1 Hz on NO production by murine

BCG-activated macrophages. No significant differences were observed in NO levels after a 14-h exposure.

Brief exposure effects from a static magnetic field of 100 mT for 15 min on protein expression in cultured rat primary hippocampal cells have been reported (Hirai et al., 2002). Expression of DNA binding activator protein-1 (AP-1), neural marker protein (MAP2), and neural differentiation marker protein (GAP-43, c-Fos, Fos-B, Fra-2, c-Jun, Jun-B, and Jun-D) were examined. Cytoplasmic Ca^{2+} and lactate dehydrogenase activities were also analyzed. It was found that exposure to the static field increased AP-1 DNA binding through expression of Fra-2, c-Jun, and Jun-D in immature cultured hippocampal neurons.

Flipo et al. (1998) examined *in vitro* effects of the static magnetic field levels of 2.5–150 mT applied for 24 h on the mitogen response to concanavalin A, phagocytosis, apoptosis, and Ca^{2+} influx in C57Bl/6 murine macrophages, spleen lymphocytes, and thymic cells. The exposure resulted in a decrease of phagocytosis, an inhibition of mitogenic response in lymphocytes, and a marked increase of apoptosis in thymic cells.

Salerno et al. (1999) measured *in vitro* expressions of activation markers and interleukin release in human PBMCs after exposure to a static magnetic field of 0.5 T for 24 h. They observed that the expression of CD69 at 0.5 T was reduced after PHA stimulation. Increases in interferon-γ and interleukin 4L (IL-4L) releases were observed; however, no changes in tumor necrosis factor α (TNF-α), IL-6, and IL-10 releases were observed.

Effects of a static magnetic field of 1.5 T applied for 240 min on human L-132 cells have been investigated (Guisasola et al., 2002). Heat shock proteins hsp70, hsp27, and their corresponding messenger RNAs (mRNAs), along with cyclic AMP and Ca^{2+} ions were analyzed. No field exposure effects were observed.

Effects of the exposure of HL-60 cells to a 6-T spatially inhomogenous magnetic field with a strong gradient of 41.7 T/m and to a spatially homogenous magnetic field of 10 T have been studied (Hirose et al., 2003b). The expression of c-Jun protein increased in HL-60 cells after exposure to the 6-T static magnetic field for 24, 36, 48, and 72 h.

Using budding yeast (*S. cerevisiae*) as a model for an *in vitro* biological test system, Ikehata et al. (2003) examined the genome-wide gene expression profile of yeast cells after exposure to 5- and 10-T fields for periods of 2 and 24 h. Exposure to static magnetic fields did not affect gene expression. Slight changes in the expression of several genes were observed after exposure to 14 T for 24 h.

8.3.2.5 Genotoxicity

Previous studies have shown that static magnetic fields alone did not have a lethal effect on cell growth and survival under normal culture conditions, regardless of the strength of the magnetic field applied. Effects of 5-h exposures of HL-60 cells to 6-mT static magnetic fields, with or without camptothecin, which is a DNA topoisomerase I inhibitor, have been investigated (Teodori et al., 2002). Results indicated that the field exposure did not cause apoptogenic or necrogenic effects. It was reported that exposure to the static magnetic field alone or with camptothecin did not affect cell viability.

Potenza et al. (2004a) showed that the conformation of plasmid DNA was altered by exposure to static magnetic fields of 250 mT. Various DNA point mutations were found, while no DNA degradation was observed. It was shown that the DNA degradation from H_2O_2 was accelerated by simultaneous field exposure; however, the plasmid DNA in *E. coli* cells exposed to the same static magnetic field did not show any alteration. They suggested that the magnetic field could change DNA stability directly or by activating the reactivity of oxidant radicals. It has also been suggested that the genotoxic effect could be minimized in living organisms by the presence of protective cellular responses, such as the DNA repair system and the buffering action of heat shock proteins.

In order to reveal the genetic effects of a 0.6-T static magnetic field, mutagen-sensitive mutants of the fruit fly (*D. melanogaster*) were used for the somatic cell test (Koana et al., 1995). It was shown that the exposure resulted in damaging effects in larval cellular DNA, and somatic cells without normal DNA repair functions failed to continue cell division, which resulted in developmental lethality of mutant larvae. The genotoxic activity of the field exposure was estimated to be the same as that of UV irradiation with 0.14 mJ/m^2/sec. Further study has been conducted with *D. melanogaster* using a wing spot test to estimate possible mutagenic or carcinogenic activity of the static magnetic field (Koana et al., 1997). A DNA repair defective mutation *mei-41*^{D5} was introduced into the conventional *mwh/flr* test system to enhance mutant spot frequency. Third-instar larvae were exposed to a field of 5 T for 24 h. It was shown that the exposure significantly enhanced the somatic recombination, and the recombination was found to be suppressed by supplementation of vitamin E. Results indicated that the magnetic field enhanced the genotoxic effects of spontaneously produced free radicals (Takashima et al., 2004).

In a report describing the investigations of whether static magnetic fields have cytogenetic effects in BALB/c AnNCrj male mouse bone marrow cells, Suzuki et al. (2001) indicated that the frequency of micronuclei was significantly increased by exposure to a 3-T field for 48 and 72 or a 4.7-T field for 24, 48, and 72 h. The increase in micronucleus frequency was shown to be dose dependent.

Micronuclei in cells have been used as an indicator of DNA damage. A study for *in vitro* assessment of the effects of a 4.7-T static magnetic field on the frequency of micronucleated cells in the Chinese hamster CHL/IU cell line with preexisting damage induced by exposure to mitomycin C (MMC) has been carried out (Okonogi et al., 1996). Results indicated a decrease in the frequency of micronuclei formation after 6 h of exposure and also the influence of the static magnetic field on the DNA damage stage produced by MMC.

An *E. coli* mutation assay has been carried out to assess the mutagenic effects of strong static magnetic fields (Zhang et al., 2003). Results obtained with a wild-type *E. coli* strain GC4468 and several derivatives, which were defective in DNA repair enzymes or redox-regulating enzymes, showed no effects of the exposure in terms of the survival rate of cells. On the other hand, the mutation frequency was significantly increased by exposure to the 9-T static magnetic field for 24 h in *soxR* and *sodAsodB* mutants, which were defective in their defense mechanism against oxidative stress. Results indicated that static magnetic fields induced mutations by increasing the production of intracellular superoxide radicals.

Ikehata et al. (1999) reported that 2- and 5-T static magnetic fields did not have mutagenic potential in a bacterial mutation test using *Salmonella typhimurium* (TA98, TA100, TA1535, and TA1537) and *E. coli* (WP2 *uvrA*) strains. They also reported that the exposure resulted in an increased mutation rate of the WP2 *uvrA* strain when induced by the agents *N*-ethyl-*N*′- nitro-*N*-nitrosoguanidine (ENNG), *N*-methyl-*N*′-nitro-*N*-nitrosoguanidine (MNNG), ethylmethanesulfonate (EMS), 4-nitroquinoline-*N*-oxide (4NQO), 2-amino-3-methyl-3*H*-imidazo-[4,5-*f*]-quinoline (IQ), and 2-(2-furyl)-3-(5-nitro-2-fulyl) acrylamide (AF-2). The mutagenicities of 2-aminoanthracene (2-AA), 9-aminoacridine (9-AA), *N*-4-aminocytidine, and 2-acetoamidofluorene (2-AAF) were not affected by the exposure. The bacterial growth did not change after the exposure. They suggested that the mechanism of these effects might be related to *in vitro* interactions between the chemicals and DNA and to repair systems in the test strains.

8.3.2.6 Cell-Free System, Free Radical, Enzyme Activity

Markov and Pilla (1994, 1997) studied the Ca^{2+}/calmodulin-dependent myosin phosphorylation and observed magnetic field effects of 44-μT, ambient, and 200-μT vertical fields for 5 min on the Ca^{2+} binding property. Phosphorylation increased up to at 200 μT depending on the [Ca^{2+}] concentration. The magnetic field effect disappeared as [Ca^{2+}] approached saturation for calmodulin. They emphasized that very small alterations in ambient level static magnetic fields are sufficient to have a profound effect on a cell-free enzyme system. In an attempt to replicate the results of Markov and Pilla, Coulton et al. (2000) saw no effects on myosin phosphoration in a cell-free system in vertical static magnetic fields up to 400 μT. As a result, in this experiment, no effects of static magnetic fields on the calcium/calmodulin binding property were observed. Engstrom et al. (2002) investigated the effects of nonuniform static magnetic fields of 0.7–87 mT with a gradient of 0.4–20 T/m for a period of 5 min on myosin phosphorylation and reported that the magnetic field exerted an influence on the rate of myosin phosphorylation. Increased phosphorylation was observed. It can be seen that the magnetic field gradients played a specific role in this experiment. Liboff et al. (2003) investigated the effect of a 30-min exposure to a static magnetic field of 20 μT on calmodulin-dependent cyclic nucleotide phosphodiesterase activity in cell-free systems and reported that the activity was altered in comparison to zero magnetic field exposures.

After studying the theoretical background of a cell-free system—Ca^{2+}/calmodulin-dependent myosin light chain phosphorylation reaction—Markov (2004a,b) designed experiments to test the effects of a pulsed radio frequency (RF) field, pulsating magnetic fields, gradient magnetic fields, and homogenous static magnetic fields on this cell-free system. He suggested that the magnetic fields affect the cell-free enzyme system by modulating ion–protein interactions.

Watanabe et al. (1997) measured and evaluated lipid peroxidation in the liver, kidneys, heart, lung, and brain of 8-week-old male BALB/c mice. The mice were exposed to 3.0- and 4.7-T fields for 3–48 h. The lipid peroxidation level in the liver was increased after exposure to the 4.7-T field. In kidney, heart, lung, and brain, no changes in the level of lipid peroxidation were observed compared to the control. The exposure to the 3.0-T field showed no alteration of the lipid peroxide level in all the tissues. The combination of CCl_4 administration and 4.7-T field exposure increased the lipid peroxidation level in the liver. It was concluded that the exposure to high static magnetic fields could induce the increase of lipid peroxidation levels in the liver of mice and could enhance the hepatotoxicity caused by CCl_4 injection.

Using fireflies, *Hotaria parvula* and *Luciola cruciata*, as bioluminescence systems, Iwasaka and Ueno (1998a) studied the effects of 8- and 14-T static magnetic fields on the emission of light. They showed that changes in the emission intensities under a magnetic field were related to the change in certain biochemical systems of the firefly, systems such as the enzymatic process of luciferase and the excited singlet state responsible for subsequent light emission.

Zhadin et al. (1998) have undertaken experiments that investigated the combined action of static and AC magnetic fields on ionic current in aqueous glutamic acid solution. Results showed that the combined parallel static and AC magnetic field causes a rapid change in the ionic current flow when the AC frequency is equal to the cyclotron frequency.

During the last few years, Brocklehurst and McLauchlan (1996) discussed the free radical mechanism involved in the observed effects of environmental electromagnetic fields on biological systems. Grissom and Natarajan (1997) summarized the theory of magnetic field effects on chemical and enzymatic reactions. Magnetic field effects have been used as a powerful technique to study enzymatic and chemical reactions with radical pair intermediates. They suggested that the coenzyme B_{12}-dependent enzymes with radical pair intermediates are well suited for the study of this effect. Taoka et al. (1997) tested the magnetic field effects on coenzyme B_{12}-dependent enzymes. The end point was that ethanolamine ammonia lyase and human enzyme methylmalonyl–coenzyme A mutase catalyze coenzyme B_{12}-dependent rearrangement reactions. While the end point was affected, the authors speculate that the change would have little physiological significance.

Eichwald and Walleczek (1996) showed a model for magnetic field effects on radical pair recombination in enzyme kinetics. The magnetic field effects in radical pair chemistry have been reviewed (Grissom, 1995; Brocklehurst, 2002; see also Chapter 6 on free radicals by Engström).

8.4 Miscellaneous

8.4.1 Biological Sensing and Magnetite

Many studies have suggested that the magnetic field is an important marker for animal navigation and spatial discrimination (Wiltschko and Wiltschko, 1995). The blind mole-rat (*Spalax ehrenbergi*) was used as a model to examine the possibility of the perception and use of magnetic fields in their orientation in space (Kimchi and Terkel, 2001). Experiments were performed in an eight-arm maze under Earth's natural and artificial magnetic fields. Results showed that the blind mole-rat was able to perceive and use Earth's magnetic field to orient in space. Kimchi and Terkel showed that blind mole-rats spontaneously preferred to place their nests toward the south of the magnetic North. Deutchlander et al. (2003) showed that Siberian hamsters (*Phodopus sungorus*) used directional information from the magnetic field to set a position for their nests. In contrast to blind mole-rats, the directional preference for nest position demonstrated by Siberian hamsters appeared to be a learned response.

Since the neural substrate subserving magnetic orientation is not known, the combination of two techniques, a behavioral test for magnetic compass orientation and an immunocytochemical visualization of the transcription factor c-Fos as a neuronal activity marker, has been used to investigate magnetoreception in the mole rat (*Crytomys anselli*) (Nemec et al., 2001). Nemec et al. found that the superior colliculus of the hypothalamus contained neurons that would respond to magnetic stimuli, and thus determined the involvement of a specific mammalian brain structure in magnetoreception.

Edmond (1996) showed that a very sensitive magnetic compass is formed by the incorporation of a small quantity of ferromagnetic, single-domain crystals, such as magnetite, within a nematic liquid crystal. Winklhofer et al. (2001) localized high concentrations of Fe^{3+} in the upper-beak skin of homing pigeons (*Columba livia*), and identified the materials of magnetite nanocrystals as the core of a magnetic field receptor.

Lohman et al. (2001) found that hatchling loggerhead sea turtles (*Caretta caretta*), when they were exposed to magnetic fields found in three widely separated oceanic regions, swam in the direction that would help to keep them within the currents of the North Atlantic gyre and facilitate their migratory pathway. It was found that young loggerheads used a guidance system of magnetic fields to assist in their navigation.

Although the mechanism of magnetoreception has not been clearly identified, geomagnetic orientation has been well recognized. A biophysical model has shown that changes in the wavelength of light can influence magnetic field orientation through the interaction between the geomagnetic field and photoreceptors. Deutschlander et al. (1999a) found that light-dependent orientation in the newt (*Notophthalmus viridescens*), was mediated by extraocular photoreceptors located in the pineal complex or deeper in the brain. Using newts, Phillips et al. (2001, 2002b) showed the role of photoreceptors in magnetic compass orientation and the magnetic inclination for deriving map information. They investigated the possibility that the fixed-axis response of the newts was mediated by a magnetoreception mechanism involving single-domain particles of magnetite (Phillips et al., 2002a).

There are several explanations for the magnetic sensitivity in fish. The aquatic animal might perceive an electric voltage induced by the water current or by its own movement in the geomagnetic fields. Elasmobranch fish such as sharks, skates, and rays are known to possess a sensitivity to the induced electric field through the sensory organs called the ampullae of Lorenzini.

Yano et al. (1997) studied the migrating behavior of the chum salmon (*Oncorhynchus keta*) fitted with a magnet to investigate the role of magnetic compass orientation in the North Pacific off the coast of Kushiro, Hokkaido. The magnetic field strength was about 0.6 mT around the head area, with polarity changes every 11.25 min. There were no effects observed on the movement of salmon.

Effects of electric and magnetic fields have been observed in the behavior of marine animals and freshwater and terrestrial species. In addition, there are a growing number of questions concerning the effect on aquatic ecosystems of the growing spread of artificial techniques such as underwater sea DC cables. There are many underwater DC cables under various seas all over the world, which carry electrical currents (see also Chapter 1 on fields in the environment by Mild and Greenebaum). These electric currents induce static magnetic fields with intensities up to 3.5 mT around cables on the sea bottom, where there are many invertebrate and vertebrate species. Research has been carried out to examine whether the exposure to magnetic fields of 3.7 mT for several weeks could influence the survival rate and fitness of common benthic animals of the Baltic Sea (Bochert and Zettler, 2004). The investigation was carried out on the crustacean (*Crangon crangon*, *Rhithropanopeus harrisii*, and *Saduria entomon*); the mussel (*Mytilus edulis*); and the flounder (*Planthichthys flesus*). Results showed no differences between experimental and control animals. Since this is the first study for investigating the effects of static magnetic fields generated by sea-positioned DC cables, on aquatic organisms and marine benthic animals, further studies are required.

In a study to confirm the magnetite-based detection mechanism in rainbow trout (*O. mykiss*), magnetic crystals in the area of olfactory lamellae were found, and the arrangement of several magnetic crystals in a chain of about 1 μm has been confirmed (Diebel et al., 2000).

It was shown that magnetizable material abolishes the behavior of bobolink (*Dolichonyx oryzivorus*) by blocking the ophthalmic branch of the trigeminal nerve (Beason and Semm, 1996). The result was consistent with the hypothesis that magnetite is a constituent of the magnetoreceptors associated with the ophthalmic nerve.

It is suggested that migratory birds, amphibians, and reptiles may have the ability to sense the geomagnetic field and use it as a source of compass information. Phillips (1996) presented a graphical model that predicts qualitatively the changes in the direction of homing orientation. Munro et al. (1997) investigated the effect of pulse remagnetization on the orientation of inexperienced, juvenile migrant birds, such as the Australian silvereye (*Zosterops l. lateralis*). The ability of juvenile birds to maintain their normal magnetic orientation after pulse application indicated that the pulse does not impair the magnetic compass. On the other hand, the deflection observed in adult birds after pulse treatment appeared to reflect ''false'' map information, which leads to a change in course. This is consistent with evidence that the magnetic compass involves light-dependent magnetoreception mechanisms.

Wiltschko and Wiltschko (2001) studied the behavior of European robins (*Erithacus rubecula*), under monochromatic light of various wavelengths and intensities to investigate magnetoreception. At a quantal flux of 7×10^{15} quanta/sec/m^2, the birds were well oriented in their migratory direction under 424 nm blue, 510 nm turquoise, and 565 nm green, whereas they were disoriented under 590 nm yellow. Changes in behavior depended on increasing the light intensity. This finding suggested that light-dependent magnetoreception may involve receptors and a neuronal pathway of its own.

Ritz et al. (2000) postulated the possibility that magnetoreception involves radical pair processes as a biophysical mechanism. They first considered a system of radical pairs as a model for the magnetic sensory organ and evaluated the influence of the geomagnetic field on radical pair systems. European robins (*E. rubecula*), were used in this study, and the results showed the disruption of magnetic orientation behavior of robins when exposed to a vertically aligned broadband field of 0.1–10 MHz and 0.085 μT or the single frequency of 7 MHz and 0.47 μT, together with the geomagnetic field (Ritz et al., 2004). The disorientation observed was found to depend on the angle between the 7-MHz oscillating field and the geomagnetic field. The robins oriented in the migratory direction when the oscillating field was parallel to the geomagnetic field. The author suggested a magnetic compass based on a radical pair mechanism, due to the resonance effect on singlet–triplet transitions in the oscillating fields.

Fuller suggested the significance of the time constants of magnetic field sensitivity in animals (Fuller and Dobson, 2005). Conditioning experiments have had great success in the analysis of animal sensory physiology. Wiltschko and Wiltschko (1996) commented that the conditioning technique did not appear to be suitable for testing magnetic sensitivity.

Some insects are able to respond to magnetic fields, especially the geomagnetic field. Mosquitoes were tested for the presence of remanent ferromagnetic material and their behavioral response to magnetic fields. Most mosquitoes, when placed in a uniform static magnetic field of 0.1 mT, moved around until they were oriented parallel to the field. It was reported that a significant remanence found on the surface of both living and dead mosquitoes might be due to attraction of ferromagnetic dust onto the body (Strickman et al., 2000). It is well-known that magnetic fields influence honey bee behavior, moth navigation, beetle larvae, the behavior of hatchling loggerhead sea turtles, migration of birds, etc. Slowik et al. (1997b) speculated that the red imported fire ant (*Solenopsis invicta*) might use magnetic field information in their nesting activities and in orientation, since their first observation suggested that fire ant workers moved as a colony toward the magnetic field. In a second paper, Slowik et al. (1997a) suggested the presence of small amounts of ferromagnetic material in fire ants.

Many review papers have been published during the last few years. Deuschlander et al. (1999b) and Wiltschko and Wiltschko (2002) reviewed the light-dependent magnetoreception in animals. Lohmann and Johnsen (2000) described the difference between a magnetic directional sense and a magnetic map sense and reviewed the three hypotheses of vertebrate magnetoreception.

8.4.2 Plant Growth, Response, and Magnetotropism

The enhancement of plant growth using various magnetic field applications has been reported by many researchers (Phirke et al., 1996). Effects of magnetic fields on seed germination, crop growth, physiological response, sporulation, water uptake, and rate of seed have been studied; however, there has been no consistency in results among the various reports.

Studies directed toward investigating the effects of magnetic field treatment on seeds and water in terms of the rate and percentage of germination of rice (*Oryza sativa* L.) and on the length and weight of germinating barley (*Hordeum vulgare* L.) and wheat (*Triticum aestivum* L.) have been carried out (Carbonell et al., 2000; Martinez et al., 2000, 2002). The field strength ranged from 125 to 250 mT depending on the research strategies. Results by Carbonell et al. showed that the rate and percentage of germination increased after chronic exposure to 150-mT fields. Magnetically treated water was found to improve the germination of rice seeds. Martinez et al. (2000) showed that the magnetic field increased the length and weight of barley seed, and the degree of this effect depended on the duration of exposure. Effects of magnetic biostimulation on the initial growth stages of wheat, with an exposure duration of 0, 1, 10, 20 min, 1 h, 24 h, and chronic exposure were investigated (Martinez et al., 2002). In the report, they defined the magnetic doses in terms of magnetic field energy density (J/m^3). An increase in plant height had been observed as the magnetic dose increased; thus, it was suggested that the stimulatory effects might be related to the amount of magnetic field energy. Florez et al. (2004) investigated the effects of 125- and 250-mT static magnetic fields on the germination and the initial growth stages of rice seeds (*O. sativa* L.). The seeds were exposed to the magnetic fields for various time durations, and the germination time was found to be shortened when the seeds were exposed to these fields. The seeds' maximum length and weight were obtained for the chronic exposure. It was shown that magnetic treatments, when applied under specific conditions, affected germination and the first stage of growth.

Piatti et al. (2002) investigated the effects of inhomogenous static magnetic fields ranging between 6 and 10 mT on the growth and viability of the plant-growing bacteria *Serratia marcescens*, barley callus cells (*Hordeum vulgare*), and blackberry (*Rubus fructiosus*). While there was no field effect observed on blackberry cells, it was found that the exposure reduced the number of bacterial cells and lowered both the number and the viability of barley cells. Diamagnetic susceptibility and root growth response to magnetic field exposure on three plant species, *Lens culinaris*, *Glycine soja*, and *T. aestivum* were investigated (Penuelas et al., 2004). Magnetic fields of 17.6 mT reduced root growth in all three plants. The field strength of 2.1 mT had no significant effect on reduction in the cereal *T. aestivum*.

Among the many studies that examined gradient magnetic field effects on various engineering, biological, and physicochemical phenomena, a study of effects of gradient magnetic fields of up to 10 T on the germination and growing process of cucumber (*Cucumis sativus* L.) was carried out (Hirota et al., 1999). It was found that the shoot germinated toward the field center, whereas the root grew in the opposite direction of the shoot. This observation seemed to be a result of the magnetic force influencing the geotaxis of the cucumber.

After calculating the magnetic field dependence of the ionic current density across the cellular membrane, Reina and colleagues examined the effects of 0–10 mT static magnetic fields on the amount and rate of water absorption in the lettuce seed cell membrane (*Lactuca sativa*) in order to compare the calculated and experimental results (Reina and Pascual, 2001; Reina et al., 2001). Theoretical calculations showed that the static magnetic field induced changes in the ionic concentration and in the osmotic pressure, which regulates the entrance of water into the seeds. The magnetic field exposure was 10 min in a Helmholtz coil, and this was carried out immediately before placing the seeds in water inside a climatized room. The investigators demonstrated a close correlation between their theoretical calculations and the actual experimental results. It was shown that exposure to the static magnetic fields altered the water absorption in seeds, which may possibly explain the change of germination rate. Adair (2002) discussed and questioned these results. Amyan and Ayrapetyan (2004) investigated changes in the wet and dry weight of barley seed after treatment by static magnetic field levels of 1.25, 2.50, and 3.75 mT. Seed treatment was carried out in cold (4°C) and warm (20°C) distilled water. After pretreatment by the fields, the seeds were incubated for 72 h. Results suggested that effects depend on not only the field strength but also the incubation time period.

Growth and sporulation of phytopathogenic microscopic fungi have been investigated under exposure to a static magnetic field that ranged from 0.1 to 1 mT (Nagy, 2004). It was shown that the growth was decreased by the magnetic field exposures. Increases in the number of developed conidia of *Alternaria alternata* and *Curvularia inaequalis* and a decrease in the number of *Fusarium oxysporum* conidia have been observed as well.

Effects of combined AC and DC magnetic fields on the germination of hornwort seed (*Cryptotaenia japonica* Hassk) have been reported by Kobayashi et al. (2004). They tested three directions of the AC magnetic field, which were vertical, parallel, and perpendicular to the direction of total geomagnetic field (DC). The frequency and strength of the AC magnetic fields ranged between 3.5 and 14 Hz and 500 and 750 μT. The total geomagnetic field was 50 μT. The seeds were exposed to the fields for 16 d at 24 h/d. The vertical AC magnetic field applied simultaneously with the DC field was found to promote the germination of seeds. Field level applications of 7 Hz, 750 μT and 14 Hz, 500 μT showed the maximum effects.

Effects of static magnetic fields ranging from 0 to 350 μT on gravitropic bending in the apical stem segments of flax seedlings (*Linum bienne*) have been investigated (Belova and Lednev, 2001). In comparison with the control group kept in a geomagnetic field of 46.5 μT, stimulation of the gravitropic bending was observed at $0 \leq B_{DC} \leq 2$ μT and $200 \leq B_{DC} \leq 350$ μT, and inhibition was observed at $100 \leq B_{DC} \leq 170$ μT.

Investigations of static magnetic field effects on the curvature of primary roots of radish seedling (*Raphanus sativus* L.) have been carried out (Yano et al., 2001). When radish roots were exposed to an inhomogenous static magnetic field, they responded to the south pole of the magnet. Trophic response was found at a field level of 13–68 mT with a gradient of 1.8–14.7 T/m. A small response to the north pole of the magnet was found as well.

Jovanic and Sarvan (2004) studied the effects of static magnetic fields on fluorescence spectra and leaf temperature in intact plant bean (*Phaseolus vulgaris* L.) The field strengths were as high as 160 mT, and the plant was grown for 3 weeks. It was reported that significant changes in fluorescence spectra and leaf temperature were induced after the field exposure. An increase of fluorescence intensity ratio and changes in leaf temperature ΔT were observed in parallel with increase in field intensity.

8.4.3 Magnetotaxis

There have been many studies reporting that magnetic fields affect the swimming behavior of *Paramecium*. A decrease in swimming velocity and an increase in the frequency of directional changes were observed after exposure to a magnetic field of 0.126 T during a motility study of *Paramecium* (Rosen and Rosen, 1990). Nakaoka et al. (2002) found that a typical ciliated protozoan, *Paramecium*, swam perpendicular to a static magnetic field of 0.68 T. It was suggested that the diamagnetic anisotropy of cellular components cilia and trichocysts was important for the magnetic orientation of their swimming.

Effects of horizontal magnetic fields on the movement of *Euglena gracilis* (ca. 50 μm in length) have been reported (Tanimoto et al., 2001). When the horizontal magnetic field with a gradient of ca. 400 T^2/m was applied, living *E. gracilis* moved to the higher field (positive magnetotaxis), whereas dead *E. gracilis* moved to the opposite, lower field. *E. gracilis* was found to be oriented perpendicularly to the magnetic field regardless of whether they were alive or dead. Thus, magnetotaxis of living *E. gracilis* may be explained by taking into account both the environmental inhomogenous magnetic forces and the magnetic orientation of *E. gracilis*. In contrast, magnetotaxis was not observed in a uniform magnetic field of 8 T. Effects of strong magnetic field gradient (max. 8 T, ca. 400 T^2/m) on the movement of *E. coli* have been investigated (Tanimoto et al., 2005). *E. coli* cells were placed in a 5 mm (diameter) × 150 mm (length) glass tube containing viscous media that flowed in the tube. The speed at zero field was 0.65 cm/h. The observed velocities of the movement from a high field (8 T) to a low field (1.5 T) and the movement in the opposite direction around were 1.35 and 0.49 cm/h, respectively. Diamagnetic *E. coli* experienced a repulsive behavior to magnetic forces of increased magnetic gradient. Therefore, it has been speculated that the velocity of *E. coli* would be accelerated toward the direction of the lower-strength field, while it would be decelerated in the direction of the stronger fields. Results suggested the magnetic force specifically, could be an important mechanism of magnetic field effects when a low-frequency high magnetic field was applied, since the microorganism might respond to mechanical stress due to alternating magnetic forces.

8.4.4 Others

As an initial study for investigating the relationship between magnetic fields and amoebae, Berk et al. (1997) examined the inhibitory effects of static magnetic fields on the population growth of amoebae. They tested three species, *Acanthamoeba hatcheii*, *Acanthamoeba castellanii*, and *Acanthamoeba polyphaga*. Amoebae were exposed to magnetic field strengths of 71 and 106.5 mT with an exposure duration up to 72 h. Results showed that magnetic fields decreased the growth of all three potentially pathogenic ameba populations significantly within 72 h. It was reported that the inhibitory effect did not depend on the field strength, and it was shown that this research would be important and advantageous in the development of disinfection strategies for surface material, such as the surface of contact lenses.

Rai et al. (1997) investigated the effects of a 0.1-T static magnetic field on the electrical parameters of goat eye lens. Under magnetic field application, the complex impedance between real and imaginary parts was obtained in the form of a Cole–Cole plot. It was reported that the static magnetic field altered the current flow in the tissue.

Iwasaka and Ueno (1998b) investigated the effects of a static magnetic field of up to 14 T on the near-infrared spectrum of water molecules and glucose solutions. They demonstrated the possibility that the static magnetic field affected the formation of hydrogen bonds of water molecules and the hydration of glucose molecules.

Morariu et al. (2000) exposed human blood samples to zero magnetic fields for 72 h in order to observe the aging process of erythrocytes. The control samples were kept in a normal geomagnetic field. In a zero magnetic field, increases in the rate of Na^+ and Ca^{2+} influx, in the rate of K^+ outflow, and in homolysis were observed. Reduction in Na^+-K^+-ATPase and Ca^{2+}-ATPase activities has been observed in a zero magnetic field; thus, zero fields significantly accelerated the aging of erythocytes. Effects of zero magnetic fields were further investigated on Zn and Cu concentrations in the human blood serum during *in vitro* aging of blood with a 48-h exposure (Ciortea et al., 2001). Blood samples were collected from both healthy donors and chronic bronchial asthma (BA) patients. While the Zn concentration was not found to be affected by the zero magnetic field exposure, Cu concentration was found to be sensitive to this field. It was also reported that the aging effect appeared to be decelerated for most BA types.

8.5 Medical Applications

8.5.1 Biomagnetic Phenomena

Biomagnetic phenomena for different intensities of magnetic fields and their frequency are shown in Figure 8.1. It is important to know the intensities and frequencies of magnetic fields involved in biomagnetic phenomena while discussing the relationship

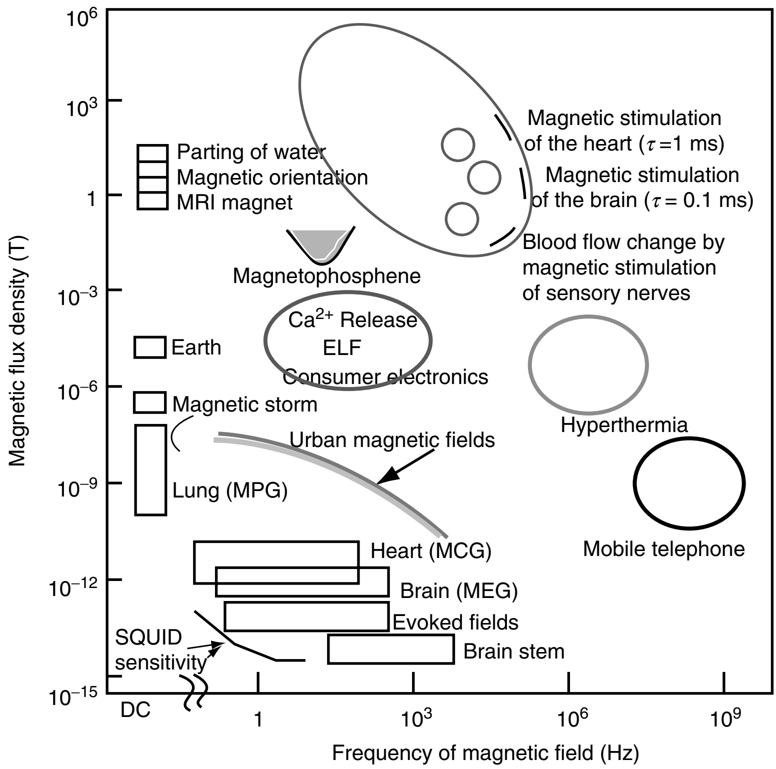

FIGURE 8.1
Biomagnetic phenomena for medical and therapeutic application.

between magnetism and living organisms. Regarding the effects of magnetism on living organisms, it should be realized that the actions of static and variable magnetic fields differ from each other in terms of the fundamental mechanism.

Studies on the biological effects of electromagnetic fields have resulted in significant developments in medical applications for electromagnetic fields, after the development of high-strength superconducting magnets. TMS, measurement of biomagnetic fields with the superconducting quantum interference device (SQUID), and MRI are the three mainstays of these medical applications. These techniques have also been leading the amazing progress in the understanding of the brain function. TMS locally stimulates the human cerebral cortex with millimeter-order spatial resolution from a figure-eight coil placed on the skull. A three-dimensional imaging of the brain neuron function has been enabled by utilization of SQUID in magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), and current-distribution MRI. Results from TMS and imaging studies indicate potential applications of biomagnetics in brain science and clinical neuropsychiatry.

In TMS, when a strong electric current is applied to a figure-eight coil positioned over the head for 0.1–0.2 ms, a pulsed magnetic field of 1 T is produced. This pulsed magnetic field generates eddy currents in the brain, which excite the targeted area of the nervous system.

Incidentally, unconscious and uncontrolled exposure of the brain to high-frequency electromagnetic waves has been increasing with the recent, rapid widespread use of cellular phones by the general public. Cellular phones in Japan are designed for operation with a frequency of 800 MHz and a microwave of 1.5 GHz (see Chapter 1 on environmental exposures by Mild and Greenebaum).

In biomagnetic measurements, MEG associated with auditory brain stem response is of the order of 10^{-15} T (1 fT), and it can be measured on the extremum of the sensitivity limitation of the SQUID gradiometer (Erne et al., 1988; Iramina and Ueno, 1995). In 10^{-12} T (1 pT)-order measurements, while α-wave spontaneous MEG can be detected without a signal-averaging technique, the technique is required to increase a signal-to-noise ratio (SNR) in order to detect various evoked responses and brain stem responses.

The recent development of noninvasive brain function measurement technologies, such as MEG and fMRI, has been contributing to the rapid progress in brain science research. Scientific discussions of mental problems such as thinking and psychomotor activities (e.g., joy, anger, sadness, and happiness) in terms of brain function became possible with the development of these new technologies.

In static magnetic fields of a few tesla, fibrin polymers, which are involved in blood coagulation, orient parallel to the magnetic fields in the course of polymerization (Yamagishi et al., 1989; Ueno et al., 1993). Furthermore, magnetic alteration of blood coagulation and dissolution processes by magnetic fields and magnetic orientation of biopolymers, such as fibrin and collagen, have been observed. These findings introduce a new aspect of biomagnetic applications in the regulation of living systems and biological materials.

8.5.2 Transcranial Magnetic Stimulation

TMS is the technique of locally applying magnetic stimulation by a strong pulsed magnetic field on the order of 1 T transcranially to the brain. When a strong electric current is applied to a figure-eight coil placed over the head for 150 μs, a pulsed magnetic field on the order of 1 T is produced that generates eddy currents in the brain, which excite the nervous system. The first study of magnetic stimulation in a human brain by Barker et al. (1985) utilized single coils; thus, localized magnetic stimulation of a targeted portion of the human brain was impossible. The localized vectorial magnetic stimulation of a human cortex using a figure-eight coil was developed by Ueno et al. (1978, 1986b, 1988, 1989, 1990a,b, 1991), which enabled stimulation of the motor cortex of a human brain at 5-mm resolution. Localized magnetic stimulation contributed to the creation of functional maps of the motor cortex related to hand and foot areas. An optimal direction of probe placement for the targeting of stimulating currents, which induce neural excitation in each functional area of the cortex, based on functional maps was observed, the so-called vectorial feature. Variations in the functional maps of the cortex with changes in orientation of the stimulating current were observed as well. It is proven that the vectorial feature allows for studies that reflect both functional and anatomical organizations of neural fibers in the brain. Localized magnetic nerve stimulation of the brain is suitable for investigations of brain function and construction without damaging any tissues.

Applications of TMS temporarily disturb brain function, which results in a virtual lesion in the brain. Zangaladze et al. (1999) showed that the disruption of the function of the occipital cortex with the use of focal TMS interferes with the tactile discrimination of grating orientation. Epstein et al. (2002) used TMS to investigate memory encoding and retrieval, particularly the role of the dorsolateral prefrontal cortex in associative memory for visual patterns. TMS disrupted associative learning of abstract patterns over the right frontal area, which suggests that the participating cortical networks may be lateralized in accordance with classic concepts of hemispheric specialization.

Traditionally, stimuli are applied at various scalp positions using a latitude- and longitude-based coordinate system referenced to Cz in the 10–20 international system at the vertex, while simultaneously, the amplitude of the motor evoked potentials generated in contralateral muscles is also measured (Ueno et al., 1989, 1990a). This gives a ''map'' of sites on the scalp from which responses can be obtained by each reference muscle.

Rothwell et al. (1987) revealed the enormous clinical importance of TMS, namely, for motor functional evaluation.

Recent developments in the navigated brain stimulation (NBS) stereotactic TMS devices allow noninvasive mapping of the spatial and temporal representation of any brain activity that reacts to magnetic stimuli (Krings et al., 2001), such as sensory, motor, language, and cognitive functions. Stereotactic TMS coil positioning and real-time visualization of the stimulating electromagnetic field effect using MRI allow precise replicability of stimulation parameters as well as accurate dose definition. Frameless NBS allows precise localization of a stimulation target in combination with other imaging modalities or by the use of anatomical landmarks. In a case where a brain tumor was resting adjacent to the precentral gyrus, the motor strip identified by TMS compared preoperative MRI and fMRI and revealed fine functional differences between results that were integrated on the navigation system. Distribution of the tumor margin and the motor cortex (both fMRI and TMS assisted) can be drawn on the patient's scalp using the navigation system. Skin incision, craniotomy, and operative approaches were considered from these results so as to avoid motor deterioration.

There has been no verification of which nerve cells are actually stimulated by TMS. There is one subject under discussion: whether a target neuron cell is directly stimulated by TMS (direct stimulation) or whether an interneuron is first stimulated and then a target neuron cell is stimulated indirectly (indirect stimulation). It is possible that alteration of eddy currents by heterogeneity of conductivity in the brain may affect the path of these currents and result in both neuronal excitation and excitatory directional changes at sites other than those targeted by the original intended direction of stimulation. Further investigation and analysis of TMS and construction of models using magnetic nerve stimulation are required to clarify how the relationship between a position of a coil and a site of stimulation can be affected by strength of stimulation, arrangement of neurons, heterogeneity of conductivity, and interneuronal participation. While a figure-eight coil is suitable for local stimulations at the surface of the cortex along the surface of the head, tridimensional localized stimulations are not possible with the coil at present.

Despite the problems described above related to TMS, there are high expectations for magnetic stimulation to contribute to a new era of brain science. A major and possibly very important future field of study is the application of TMS for obtaining therapeutic effects in neurological disorders. A number of animal studies testing the basic mechanisms of TMS-induced alterations of neurotrophic factors, gene expression, and changes in plasticity have been conducted (Fujiki and Stewart, 1997; Keck et al., 2000; Fujiki et al., 2003; Ogiue-Ikeda et al., 2003a).

There is strong evidence that the expression of certain genes such as the immediate early gene, astrocyte-specific glial fibrillary acidic protein mRNA (Fujiki and Stewart, 1997), and brain-derived neurotrophic factor is altered in response to repetitive TMS (rTMS). This indicates that the measurable effects of TMS reach the molecular and signaling levels. The most promising hypothesis is that magnetic field-induced neuroprotective or trophic factors may protect neurons from hypoxic insult (Fujiki et al., 2003). Long-duration rTMS modulates the monoamine neurotransmitter system in content and turnover and may also induce sprouting of mossy fibers in the hippocampus (Keck et al., 2000). Increased dopaminergic neurotransmission may contribute to the beneficial effects of rTMS in the treatment of affective disorders and Parkinson's disease.

The results of these studies provide strong evidence that noninvasive TMS can strongly modulate gene expression in neurons and astrocytes. Thus, TMS, originally used simply as a way to assess the function of descending motor tracts noninvasively, may in the end be used as a means to modulate gene expression and to induce restorative plasticity or tolerance against injury in the brain.

TMS does not cause any pain and requires no physical invasion of the body; therefore, it should become more important in functional, diagnostic, and therapeutic research of the brain. In brain functional research, application of magnetic stimulation for the temporary blockage or modification of the facultative information process and cognitive process of various sensory systems may be used to identify localization and connecting pathways of brain function. If a magnetic stimulation can effectively block and modify various sensory systems, it should be advantageous for pain treatment. Elucidation of the effects of magnetic stimulation on synaptic functions may lead to further research associated with brain plasticity. Further research for investigation of magnetic compensation and reconstruction of neuronal functions around damaged neurons may lead to the development of various magnetic field-based stimulation applications, including the treatment of depression, the prevention of dementia, and a safer and more effective magnetic pulse treatment, which may replace the current electroconvulsive therapy (ECT).

8.5.3 Magnetoencephalography

MEG measures the very weak magnetic fields of the order or 10^{-13} T (100 fT) generated by neuronal current flow, by the detection of magnetic signals measured by SQUID arrays. MEG can detect brain functions with high millisecond-order temporal resolution and high millimeter-order spatial resolution noninvasively; thus, it is useful for investigation of brain functions in humans, including higher brain functions such as memory and cognition. Since Cohen obtained a magnetoencephalogram for human α-waves with the use of a SQUID, a prototype developed by Zimmerman and Colleagues (1972), it was only until recently that the use of a whole-head MEG system that is able to carry out spontaneous measurement at multiple points has become practical (Squires, 1991; Ahonen et al., 1993; Vrva et al., 1993). In recent years, the whole-head MEG system has been incorporated into brain functional research all over the world and has accelerated progress in research.

Application of forward and inverse problems in MEG analysis is critical to estimate a localization of brain function. Ueno and Iramina (1991) measured MEG associated with short memory, cognition, and mental rotation in humans, constructed current-dipole and distributed intracerebral electrical source models, and carried out estimations for the localization of various brain functions during the processing of information. The electrical source of a visually evoked reaction with approximately 150 ms at latency localized in the primary visual cortex was described in a current-dipole model relatively well, while a distributed intracerebral electrical source model was more useful in estimation of the electrical source incident to a mental rotation with approximately 180 ms or higher at latency. In the distributed electrical source model, a chronological transition of electrical source groups from the occipital lobe area to the posterior temporal lobe area was captured. MEG is not only a tool for basic brain functional research, but is also applicable to medical research. Clinical applications of MEG include detection of epileptic spikes, measurements of slow waves associated with brain tumors and cerebrovascular diseases, and cerebroelectric activity of ELF induced by event-related potentials.

It is necessary to construct experimental paradigms that are able to perform more precise extraction of a specific brain function, allow understanding of brain function dynamics, and provide measuring techniques to assess the acquired information (Yoshida et al., 1995; Iwaki et al., 1999). It is also important to develop signal processing techniques for source determination of signals with very small SNRs and with distributed electrical sources, improve inverse problem approach methods, and construct suitable current source models (Ueno and Iramina, 1991; Iramina et al., 1994, 1995b). There are several factors to be taken into account in MEG inverse problem analysis: the shape of the head, heterogeneity of conductivity, alignment of neuron cells, interneurons, and thalamocortical specific projection system. An ideal electrical source model possesses electrophysiological features of complex cranial nerve systems with consideration of these factors.

In a study on language-related brain activities, Kuriki et al. (1995, 1998) used MEG imaging to examine the temporal and topographical characteristics of neural activities in the comprehension of Japanese complex sentences with a clause structure. The Korean language was also used as an experimental language (Kwon et al., 2005). The Korean language has a subject–object–verb order structure, ending with a verb. Semantic and syntactic violations, that is, errors introduced in a sentence, can be made by altering a single word, that is, a verb, in an inappropriate manner. Neural activities in response to such a violation are measured as the response elicited by the final verb in the verb-ending sentence. This study is aimed to identify neural activities in the cerebral cortex that occur during a latency course, processing syntactic and semantic aspects of spoken sentences.

In another MEG study on music, Kuriki and colleagues used melodies to measure the responses that are elicited by an out-of-key tone in musical phrases (Hirata et al., 1999; Kuriki et al., 2005). The musical context is established by the sense of a key and melodic pitch sequence. The responses would reflect the perception of these restricted aspects of melody. The results of the present study should provide an understanding of the spatiotemporal characteristics of cortical activities involved in melody perception. MEG measurements were also performed for musical tones and chord stimuli for well-experienced musicians and nonmusicians. The principal purpose of this study was to explore how the brain activity reflected in late auditory evoked responses would behave when exposed to the successively presented tones and chords stimuli and also how the activity would vary according to experience of musical training.

Although there is still ambiguity in the analytical technique, MEG still attracts medical researchers because it can reflect the chronological change of source signals to that of magnetic fields. It is obvious that MEG will become an essential technique in human brain function research, since there is only one technique that is noninvasive with millisecond-order high temporal resolution, electroencephalography, available at this time for estimation of brain function localization,. Development of MEG with higher sensitivity and operativity, construction of an intracerebral electric source model, and improvement of inverse problem analysis may become more important.

8.5.4 Magnetic Resonance Imaging

Since Lauterber suggested a linear magnetic field gradient in 1973, MRI has been rapidly developed (Lauterbur, 1973). MRI utilizes fusion techniques of spatially uniform direct current magnetic fields, spatially gradient direct current magnetic fields, and RF electromagnetic fields. A guideline of static magnetic field exposure to a human body by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) suggests 2 T as the ceiling value for body parts, except for arms and legs, in occupational exposure. In the application of clinical MRI, although the exposure is carried out under supervision of doctors, the current exposure level is confirmed to be 2 T or less. It is not feasible to obtain resonance images, except from hydrogen atoms, in static magnetic fields at this strength.

The use of MRI conducted at high static magnetic field levels is fast growing (Robitaille et al., 1998). With the advent of the 8-T/80-cm MRI scanner (Schenck et al., 1992; Kangarlu et al., 1999) the safety of the static magnetic field became a paramount issue for MRI researchers. While the primary concern in high magnetic field MRI has been excessive RF deposition in human subjects (Kangarlu et al., 2003, 2005), the static magnetic field could equally cause alarm for its potential for interaction with biological cells and molecules. One concern regarding human exposure to a high static magnetic field is the orientation of the molecules. Magnetohydrodynamics, which describes the interaction of moving charged particles with the magnetic field, has also raised concern with high magnetic field applications. Investigation of this effect with its possible consequences on human cognition has not received enough attention. As such, Chakeres et al. (2003) have recently conducted a series of studies on the effect of high static magnetic fields on human cognitive function. In spite of the availability and use of high magnetic field instrumentation for three decades, high magnetic field exposures of human subjects for extended periods of time have not been conducted. Such exposures did not pose a significant biological hazard at field strengths of up to 8 T as measured within the capability of their experimental design. In addition, human neuropsychological performance as a measure of any possible static magnetic field modification of cognition was not detected (Chakeres et al., 2003). To our knowledge, such a study has not been performed in the past at a field strength of 8 T for such an extended period of exposure time (Schenck et al., 1992; Kangarlu et al., 1999). In spite of the complex nature of an investigation of such effects, our present lack of observation of any detectable change in human cognition as related to high magnetic field exposure is an important reason for further research. In this regard, studies such as this could serve as a good starting point for *in vivo* characterization of static field effects in humans, in light of the rapidly expanding applications of high magnetic field MRI.

A time-varying magnetic field with sufficient intensity may be excitatory to peripheral nerve stimulation (PNS) (Ueno et al., 1986a; Barker, 1991; Sandrey et al., 2002; So et al., 2004). The physiologic mechanism is presumably due to interaction of neuronal structures with the induced electric field, rather than a direct physiologic effect of the magnetic field (Reilly, 1989).

Relatively early in the development of MRI, it was recognized that the pulsed gradient magnetic fields might induce PNS or cardiac stimulation (Reilly, 1991; Ueno et al., 1992). The pulsed gradients are of audio frequency, and they modulate the frequency and phase of the signal from the precessing magnetization as part of the MRI image reconstruction process. Reilly (1989) projected that a long-duration (>1 ms) pulse of induced electric field of 6.2 V would be sufficient to stimulate a 20-μm-diameter nerve fiber. The same amplitude of electric field was estimated to be the 1-percentile rank for stimulation of the human heart. Because of the much longer chronaxie for cardiac muscle, about 3 vs. 0.38 ms, the gradient field intensity, expressed in terms of the time derivative dB/dt of the magnetic field, required to achieve cardiac stimulation is far greater than that for PNS. The large projected values of dB/dt required for cardiac stimulation were confirmed in measurements in dogs by Mouchawar et al. (1992) and by Bourland et al. (1999), who reported that cardiac stimulation by pulsed gradient fields requires a dB/dt amplitude in excess of 2000 T/s for a 530-μs period. These values compare with representative dB/dt intensities of less than 100 T/s in an MRI system. For healthy patients, cardiac stimulation in MRI is avoided by a wide margin.

Mild PNS in MRI is not thought to be harmful, but painful stimulation should be avoided. To determine the population distribution for physiologic response to the time-varying gradient fields, the MRI safety group at Purdue University undertook a study with 84 human volunteers (Bourland et al., 1999; Nyenhuis et al., 2001). The volunteers were exposed to magnetic field patterns similar to those that would be experienced in a cylindrical bore MRI system. (Nyenhuis et al., 1997). The volunteers were asked to rate their responses to a gradient pulse sequence on a scale covering the range of 1 = onset of PNS, 5 = uncomfortable but acceptable for the duration of a scan, and 10 = intolerable. The duration of the dB/dt pulses ranged from 50 to 1000 μs, in order to determine parameters for the strength duration given by:

$$\frac{dB}{dt} = b\left(1 + \frac{c}{d}\right)$$

where b is rheobase for a long-duration pulse, c is chronaxie, and d is the pulse duration. The measured responses were well fit by a chronaxie of 380 μs. For onset of PNS (score = 1), the median rheobase b was found to be 18.8 T/s for the y-coil and 28.8 T/s for the z-coil. Median dB/dt intensities for scores of 5 and 10 were approximately 50% and 100% greater than the score = 1 values, respectively. From the population distribution, the lowest 1-percentile value for PNS (score = 1) was about half the median value, and the lowest 1-percentile for uncomfortable (score = 5) was approximately equal to the median of the PNS threshold.

den Boer et al. (2002) found good agreement among the Purdue and other studies for the PNS thresholds by the switched gradients. Accordingly, the results of these studies were used for determination of the allowable gradient field intensities in MRI, which were set to be 80% of the mean PNS threshold (IEC, 2002).

The values of chronaxie and rheobase in the Purdue study were determined for rectangular waveforms. Models based on the physiologic response to rectangular pulses can be used to predict the threshold intensities for nonrectangular waveforms (Havel et al., 1997; den Boer et al., 2002).

So et al. (2004) recently reported results of calculations incorporating a realistic human model of the rheobase electric field intensity for PNS in the Purdue study. The rheobase electric field intensities in subcutaneous fat ranged from 3.3 to 4.4 V/m for the different body models and coil configurations. These values are in reasonable agreement with a rheobase electric field of 5.36 V/m for PNS with a solenoidal coil enclosing the arm (Havel et al., 1997).

MRI of electrical phenomena in living bodies is potentially useful for quantitative evaluations of the biological effects of electromagnetic fields and for direct detection of neuronal electrical activities in the brain. Magnetic fields in an object cause a shift in the resonant frequency (Manassen et al., 1988; Sekino et al., 2004b) and a change in the phase of magnetic resonance signals (Joy et al., 1989). Spatial distributions of an externally applied magnetic field and electrical current can be estimated from these changes in magnetic resonance signals. These methods have use in certain medical applications, such as the imaging of current distributions in electrical defibrillation (Yoon et al., 2003).

The fMRI developed by Ogawa et al. (1992) utilizes a technology that reflects various magnetic features of hemoglobin in blood on magnetic resonance signal patterns. Tomograms of brain function can be obtained from information on localized blood flow in the brain. fMRI utilizes a blood oxygenation level dependent (BOLD) effect of localized blood flow on brain activation for indirect imaging of brain activities. However, no information on electrical conditions *in vivo* can be obtained with current MRI and fMRI systems.

Detection of electrical currents associated with neuronal or muscular electrical activities requires extremely high measurement sensitivity. The sensitivity for detecting weak magnetic fields in the human brain was estimated using numerical simulations (Hatada et al., 2005). The theoretical limit of sensitivity was approximately 10^{-8} T. The effect of neuronal electrical activities on magnetic resonance signals was investigated in several experimental studies (Kamei et al., 1999; Xiong et al., 2003). These studies potentially lead to a new method for visualizing brain function with a spatial resolution of millimeters and a temporal resolution of milliseconds.

Impedance-weighted magnetic resonance images were obtained during applications of external oscillating magnetic fields, which induce impedance-dependent eddy currents in a sample (Ueno and Iriguchi, 1998). In another study, spatial distribution of electrical impedance was obtained from the electrical current distributions by using an iterative algorithm (Khang et al., 2002). The apparent diffusion coefficient reflects electrical conductivity of a tissue, which enables an estimation of anisotropic conductivity of that tissue (Tuch et al., 2001; Sekino et al., 2004a). This method was applied to imaging of electrical conductivity in the human brain. Several regions in the white matter, such as the corpus callosum and the internal capsule, exhibited high anisotropy in conductivity. The magnitude and phase of magnetic resonance signals are affected by permittivity (Sekino et al., 2005). A distinctive signal inhomogeneity arises in images of objects whose dimension is comparable to the wavelength of the electromagnetic fields at the resonant frequency. This phenomenon, dielectric resonance, particularly appears in scanners with high static fields.

Once high-quality current distribution MRI of the detailed distribution of electric source incident to brain neural activities becomes available, comparison of results of MRI and fMRI will show the relationship between brain neural activities associated with BOLD effects and neural current distributions, which may lead to various new observations of dynamics in brain function localizations.

Impedance MRI may not be applied widely in brain function research; however, high-quality impedance MRI for impedance and admittance *in vivo* may lead to development of a new research field of impedance physiology. It is obvious that the information of impedance distributions is important for studying magnetic stimulation and MEG inverse problems.

8.5.5 Magnetic Orientation for Tissue Engineering

In the last decade, it has become possible to create static magnetic fields of 10 T and higher. With this development, studies regarding magnetic effects on macromolecules have increased. These studies include investigations into the magnetic effects on fibrin, collagen, erythocytes, and platelets (Higashi et al., 1993a,b; Iwasaka and Ueno, 1994; Iwasaka et al., 1998; Iino and Okuda, 2001). Recent research on effects of strong static magnetic fields includes their impact on morphogenesis, cell adhesion, and apoptosis (Tofani et al., 2001).

When technology for generation of stronger magnetic fields becomes available in the future, magnetic orientation research will be subdivided into several areas. Effects of magnetic orientation on cell functions such as morphogenesis, adhesion, motility, proliferation, differentiation, and apoptosis may become one of the important areas of research.

Macromolecules such as fibrin and collagen are oriented by static magnetic fields of several tesla. Fibrin polymers are diamagnetic materials that are oriented in a magnetic field. Collagen fibers orient perpendicular to the magnetic field orientation (Torbet and Ronziere, 1984). Polymerization and dissolution of fibrin in homogenous magnetic fields of up to 14 T have been investigated (Iwasaka et al., 1998). It was shown that the magnetic orientation of fibrin fibers accelerated both the polymerization and the dissolution of fibrin fibers.

Magnetic orientation of cells is associated with magnetic anisotropy of proteins and lipids. Erythrocytes orient the disk surface parallel to magnetic fields because of magnetic anisotropy of the biomembrane lipid bilayer. However, halophillic bacteria orient their membrane plane vertical to magnetic fields even though the purple membrane has a similar membrane structure as the erythrocyte membrane (Neugebauer et al., 1977). The purple membrane contains a membrane-bound protein (bacteriorhodopsin) that contributes 75% to the membrane weight. Since the magnetic anisotropy of bacteriorhodopsin is larger than that of the lipid bilayer, halophillic bacteria posses a different magnetic orientation from erythrocytes. Therefore, magnetic orientation is determined by the quantity and the alignment of cell components that possess magnetic anisotropy.

Higashi et al. (1996) found that an orientation of glutaraldehyde-fixed erythrocytes in strong static magnetic fields up to 8 T was perpendicular to the field. The effect was attributed to the paramagnetism of membrane-bound hemoglobin. The rates of sedimentation and aggregation of human erythrocytes in a homogenous magnetic field of 6.3 T have been studied (Iino, 1997; Iino and Okuda, 2001). It was reported that the cell aggregation accelerated the sedimentation rate. Results have suggested that the enhancement was especially significant in anisotropic erythocytes, and the increase in an intermembrane adhesive area might be due to the magnetic orientation of anisotropic erythrocytes.

DNA, which occupies most of the head portion in bovine sperm, may be involved in magnetic anisotropy and orientation determination of sperm. Cricket sperm with an acicular head part show the same magnetic orientation (vertical) as bovine sperm in magnetic fields of 0.09 T (Suzuki et al., 1995); this is because DNA, which is folded lengthwise, possesses large diamagnetic anisotropy. If DNA in the head part of bovine sperm is orderly aligned as in cricket sperm, the magnetic anisotropy may contribute to the magnetic orientation of sperm.

A significant feature of magnetic orientation of bovine sperm is the direction of orientation. Platelets orient parallel to magnetic fields because of the microtubules inside, which have a magnetic orientation parallel to the magnetic fields. Thus, bovine sperm without motility are assumed to orient parallel to magnetic fields as platelets do, since the tail (flagellum) consists of microtubules. On the contrary, the whole body of bovine sperm shows magnetic orientation vertical to magnetic fields, and the flat surface of the head also orients vertically to magnetic fields. A sperm with the tail removed shows the same orientation. Since it is impossible to obtain a tail without damaging flagellum, the magnetic orientation of a tail alone cannot be observed. In two separate experiments, Emura et al. (2001, 2003) studied the orientation of bull sperm cells and *Paramecium* cilia in static magnetic fields and measured their anisotropic diamagnetic susceptibility ($\Delta\chi$). Bovine sperm consists of a very flat head part (5 μm) and a long tail part (flagellum, 50 μm), which consists of microtubules. Compared to sperm of other species, the head, which contains DNA, is notably larger. The sperm showed an orientation perpendicular to the field of 1 T or lower. The diamagnetic cell components, such as cell membrane, DNA in the head, and microtubule in the tail, were thought to contribute to this orientation. It was observed that *Paramedium* cilia became oriented in parallel to the magnetic field at the strength of 8 T. The author suggested that $\Delta\chi$ for each was the quantitative index of the effect.

Iwasaka et al. (2003a) reported the effects of 14-T fields on assemblies of A7r5 smooth muscle cells. It was shown that the field affected the morphology of smooth muscle cell assemblies and the shapes of the cell colonies extended along the direction of the magnetic flux. They speculated that the mechanism was a diamagnetic torque force acting on cytoskeleton fibers, which are dynamically polymerizing and depolymerizing during cell division and cell migration. They also investigated the effects of the static magnetic field on the convection flow in a cell culture medium and on cell adhesion patterns (Iwasaka et al., 2003b). The mouse osteoblast cell line MC3T3-E1 and HeLa cell line were used in this study. The magnetic field of 6 T with a gradient of 60 T/m affected the convection of floating cell aggregations in a cell culture flask and reversibly changed the direction of convectional flow. After the exposure of MC3T3-E1 cells to the magnetic field of 8 T for 1 d, the thermal convectional flow in the medium was found to promote the cell orientation.

Iwasaka and Ueno (2003) examined the displacement of intracellular macromolecules under a static magnetic field of 14 T using linearly polarized light. The changes in polarized light intensity through the lamellar cell assembly under magnetic fields corresponded to the behavioral changes in cell components. They speculated that intracellular macromolecules rotated and showed a displacement due to diamagnetic torque forces during the exposure to the 14-T magnetic field for 2–3 h.

Matrix proteins provide a permissive environment for the orientation of cells, as demonstrated, for example, with the testing of smooth muscle cells and endothelial cells in collagen fibers under strong magnetic fields (Stefano and Tranquillo, 1993; Tranquillo et al., 1996).

Eguchi et al. (2003) observed the effect of a static magnetic field on orientation of Schwann cells. After a 60-h exposure, cultured Schwann cells from dissected sciatic nerves of neonatal rats oriented parallel to the field of 8 T, whereas Schwann cells suspended in a medium with collagen oriented perpendicular to the field after a 2-h exposure. It was suggested that magnetic field-oriented collagen fibers were the key factor in the orientation of Schwann cells.

Kotani et al. (2000) studied the effect of an 8-T magnetic field generated by a superconducting magnet on the orientation of osteoblasts alone and a mixture of osteoblasts and collagen. It was found that osteoblast cells oriented parallel to the magnetic field, but a mixture oriented perpendicular to the field.

Hirose et al. (2003a) investigated the preferred orientation of human glioblastoma cells A172 after exposure to a 10-T static magnetic field, in the presence or absence of collagen. It was found that A172 cells embedded in collagen gel oriented perpendicular to the direction of the static magnetic field.

By placing dorsal root ganglia (DRG) explants onto one end of magnetically aligned collagen gel formed into 4-mm-diameter rods, Dubey et al. (1999) developed an *in vitro* assay to study neurite elongation. The depth of neurite elongation from chick embryo DRG neurons into these aligned rods was found to be substantially greater than that under the control condition. The depth increased as the magnetic field strength increased, as did the collagen gel rod birefringence; collagen fibril aligned along the rod axis. These results may translate into an improved method of entubulation repair of transected peripheral nerves by directing and stimulating axonal growth through a tube filled with magnetically aligned collagen gel. The same research group later reported the improvement of peripheral nerve regeneration in mice after the treatment of magnetically aligned collagen gel filling of a collagen nerve guide (Ceballos et al., 1999). The hypothesis of this study was that contact guidance of regenerating axons or invading nonneuronal cells to the longitudinally aligned collagen fibrils would improve nerve regeneration. It was reported that mice exhibited regeneration with magnetically aligned collagen gel, including the appearance of nerve fascicle formation.

Application of magnetic orientation in the production of biologically functional materials and artificial organs has been started. By attaching aligned vascular smooth muscle cells and endothelial cells to artificial vascular walls in an orderly fashion, rheologically rational biological functions can be obtained. As techniques in bionics and biomaterials improve, application of magnetic orientation should expand.

8.5.6 Treatments of Pain, Cancer, and Other Diseases

Static magnetic fields or ELF-modulated static magnetic fields potentially have therapeutic effects on several diseases (see also Chapter 11 on medical applications of pulsed fields by Pilla). A static magnetic field in the 10-mT range blocks sensory neuron action potentials, which suggests that the magnetic field alleviates pain (Cavopol et al., 1995; McLean et al., 1995). To characterize the inhibitory effect of a static magnetic field, action potentials were elicited by intracellular application of 1-ms pulses of depolarizing current to the somata of mouse DRG neurons. During the control period, less than 5% of stimuli failed to elicit action potentials. During exposure to an approximate 11-mT static magnetic field produced by an array of four permanent center-charged magnets of alternating polarity, 66% of stimuli failed to elicit action potentials.

The efficacy of a nonpharmacologic, noninvasive static magnetic device was assessed for knee pain in patients with rheumatoid arthritis (Segal et al., 2001). Magnetic devices with four steep field gradients or one steep field gradient were taped to the knee of each subject for 1 week. Both devices demonstrated statistically significant pain reduction in comparison to baseline. Comparison between the two groups demonstrated a statistically insignificant difference.

Prato et al. (2005) reported effect of a magnetically shielded environment on opioid-induced analgesia. Mice were placed in a Mu-metal-lined box or an opaque Plexiglas box (sham condition) for 1 h/d for 10 consecutive days. Nociception was measured as the latency time to a foot lift/lick in response to an aversive thermal stimulus before and immediately after exposure. It was shown that mice can detect and will respond to the repeated absence of the ambient magnetic field, with the maximum analgesic response occurring over days 4–6 of exposure and returning to baseline thereafter. The effect was robust, independent of pre-exposure and intermittent testing, and seems to be opioid related, since the results obtained on day 5 were similar to those from a 5-mg/kg dose of morphine and were abolished with the opioid antagonist, naloxone.

Exposure to pulsed magnetic fields has been shown to have a therapeutic benefit in both animals (e.g., mice and snails) and humans. Shupak et al. (2004b) investigated the potential analgesic benefit of magnetic field exposure on sensory and pain thresholds following experimentally induced warm and hot sensations. Subjects were assigned to 30 min of magnetic field or sham exposure, between two sets of tests of sensory and pain thresholds and latencies at 1°C above and 2°C above pain thresholds. Results indicated that magnetic field exposure does not affect sensory thresholds. Pain thresholds were significantly increased following magnetic field exposure but not following sham exposure. A significant condition by gender interaction existed for postexposure pain thresholds. Taken together, these results indicate that magnetic field exposure does not affect basic human perception, but can increase pain thresholds in a manner indicative of an analgesic response.

Shupak et al. (2004a) showed an induction of analgesia in mice equivalent to a moderate dose of morphine (5 mg/kg) and the effect of both pulsed magnetic field (complex neuroelectromagnetic pulse, Cnp) exposure and morphine injection on some open-field activity. Cnp exposure was found to prolong the response latency to a nociceptive thermal stimulus (hot plate). Cnp plus morphine offset the increased movement activity found with morphine alone. These results suggest that pulsed magnetic fields can induce analgesic behavior in mice without the side effects often associated with opiates like morphine.

The effects of static and sinusoidal (AC) magnetic fields on myosin light chain phosphorylation were studied (Markov et al., 1993). In a cell-free preparation, exposure to DC (0–200 μT, vertically or horizontally controlled) or AC (16 Hz, 20.9 μT) magnetic fields significantly influenced myosin phosphorylation. Variations of the DC magnetic field (in the absence of AC components) were not only sufficient to alter the rate of phosphorylation but also gave the maximum effect.

The possibilities that magnetic fields cause antitumor activities *in vitro* (Tofani et al., 2001), *in vivo* (Tofani et al., 2002), and in human subjects (Ronchetto et al., 2004) have been investigated. *In vitro* experiments were carried out to study the role of magnetic field characteristics (intensity, frequency, and modulation) on two transformed cell lines (WiDr human colon adenocarcinoma and MCF-7 human breast adenocarcinoma) and one non-transformed cell line (MRC-5 embryonal lung fibroblast). Increase in cell death morphologically consistent with apoptosis was reported exclusively in the two transformed cell lines. Cell-death induction was observed with magnetic fields of more than 1 mT. Two different *in vivo* experiments were carried out on nude mice bearing a subcutaneous human colon adenocarcinoma (WiDr). In the first experiment, a significant increase in survival time (31%) was obtained in mice exposed daily to 70 min of modulated magnetic fields (static with a superimposition of 50 Hz) having a time average total intensity of 5.5 mT. In the second independent experiment, when mice bearing tumors were exposed to the same treatment for four consecutive weeks, significant inhibition of tumor growth (40%) was reported, together with a decrement in tumor cell mitotic index and proliferative activity. Human patients with heavily pretreated advanced cancer were enrolled in a pilot study, in which they were exposed to static magnetic fields that were amplitude modulated by ELF. Toxicity was assessed according to WHO criteria. ECG, chest x-ray, physical examination, blood cell count, and complete blood chemistry were performed before and at the end of the treatment. The results indicated that magnetic fields can be safely administrated according to the magnetic field exposure schedules.

Recently, several studies tested the application of pulsed magnetic stimulation as a form of cancer therapy. In one case, use of magnetizable beads and pulsed magnetic stimulation enabled targeted-cell destruction *in vitro* (Ogiue-Ikeda et al., 2003b). The cells were combined with the beads by an antigen–antibody reaction (cell–bead–antibody complex), aggregated by a magnet, and stimulated by a magnetic stimulator. The viability of the aggregated and stimulated cell–bead–antibody complexes was significantly decreased, and the cells were destroyed by the penetration of the beads into the cells or by rupturing of the cells by the beads. In another study, exposure to a pulsed magnetic stimulation caused a decrease of tumor weight in mice B16-BL6 melanoma models and induced the increase of cytokine (TNF-α and IL-2) production (Yamaguchi et al., 2006). These studies show the potential therapeutic possibilities of pulsed magnetic stimulation in cancer treatment.

Basic studies for magnetic stimulation treatment of depression, which has the potential to replace ECT, and also, magnetic treatment for a wide range of clinical problems, such as Parkinson's disease and various kinds of pain, are in progress. It is important to recognize the safety of magnetic stimulation and the limitations of its usefulness.

8.6 Conclusion

Over the last two decades, various studies have been carried out to examine the effects of static magnetic fields, including MRI fields, on biological systems. This chapter consisted of two parts. The first part focused on recent experiments covering behavior, cardiovascular system responses, reproduction and development, genotoxicity, molecular and cellular systems, cell-free systems, free radical and enzyme activity, etc. The second part concentrated on the recent development of medical and therapeutic applications of static magnetic fields.

There are many studies that have been mentioned in this chapter. With exposure to about 1 T and above, there are no adverse effects on reproduction and development, genotoxicity, and molecular and cellular systems, and no consistent evidence on behavioral effects. However, several studies suggest that static magnetic fields in millitesla ranges may affect microcirculation and blood pressure, and furthermore, higher-strength static magnetic fields at levels up to 10 T may reduce skin blood flow and lead to change in skin temperature. These findings need to be confirmed in further studies.

Although there are so many experiments to test the effects of static magnetic fields on the biology of living systems, using *in vivo* and *in vitro* techniques, the International Agency for Research on Cancer (IARC) has stated that static magnetic fields are *not* *classifiable as to their carcinogenicity to humans* by inconclusive carcinogenic evidence (IARC, 2002).

There are many experimental findings that suggest that animals use the static magnetic field, that is, the geomagnetic field for orientation, navigation, and migration. In order to establish the existence of a magnetoreception system in animals, Phillips argued that there are several key points that require further investigation: (1) establishing the lower limits of sensitivity to static magnetic, ELF, and RF fields in biological systems; (2) localizing specialized receptors responsible for sensing the geomagnetic field; (3) characterizing the underlying molecular and biophysical mechanisms; (4) identifying the regions of the brain involved in processing magnetic stimuli; and (5) understanding how the animal's perception of the magnetic field is physiologically processed for determining compass direction and spatial positioning (Phillips, 2005).

With the increasing exposure of humans to environmentally higher static magnetic fields generated from magnetic field equipment of higher capacity, it is necessary to investigate the possibilities of high static field effects on human biological and physiological processes.

There are an abundance of review papers and books published in recent years describing the possible physical and biological interactions of electromagnetic fields (Polk and Postow, 1986, 1997; Ueno, 1996; Andra and Nowak, 1998; Jin, 1999; Takebe et al., 1999; Lin, 2000; Shellock, 2001; Binhi, 2002; McLean et al., 2003a; Stavroulakis, 2003; Rosch and Markov, 2004). In addition, there have been many short reviews on the biological effects of static magnetic fields (Holden, 2005; Miyakoshi, 2005), since the physical interactions of static magnetic fields with living tissues were described (Schenck, 2005). In a report on the biological effects of exposure to MRI, an overview of the safety concerns regarding exposure to static magnetic fields, RF fields, and time-varying magnetic field gradients has been discussed (Formica and Silverstri, 2004). Application of novel high-throughput screening techniques for transcriptomics, proteomics, and metabolomics to determine *in vitro* effects of static magnetic fields have been suggested (Leszczynski, 2005). This report emphasized the research beyond screening that is required for the assessment of any possible health consequences. Possible physical mechanisms underlying the biological effects and interactions of zero-frequency (DC) and oscillating (AC) magnetic fields with biological matter have been reviewed (Binhi, 2001; Volpe, 2003). Effects of static and ELF electric and magnetic fields on human health have also been discussed (Repacholi and Greenebaum, 1999; McKinlay and Repacholi, 2005). Zhadin (2001) has introduced the Russian literature on the biological effects of DC and LF AC magnetic fields. These articles offer multidisciplinary information and knowledge for the understanding of magnetic field effects within living systems.

Acknowledgments

The authors wish to thank Drs. Ben Greenebaum and Frank Barnes for their suggestions and comments for organizing this chapter. The authors also wish to thank Drs. Minoru Fujiki, Yngve Hamnerius, Masateru Ikehata, Masakazu Iwasaka, Saeko Kanagawa, Alayar Kangarlu, Yohsuke Kinouchi, Shinya Kuriki, Tatsuki Matsumoto, Junji Miyakoshi, John Nyenhuis, Chiyoji Ohkubo, Hideyuki Okano, Frank Prato, Masaki Sekino, Masao Taki, Yoshifumi Tanimoto, Sotoshi Yamada, and Sachiko Yamaguchi for their valuable discussions.

References

Adair, R.K., Comments: influence of stationary magnetic fields on water relations in lettuce seeds, *Bioelectromagnetics*, 23, 550, 2002.

Ahonen, A.I., Hämäläinen, M.S., Knnutila, J.E.T., Kajola, M.J., Laine, P.P., Lounasmaa, O.V., Parkkonen, L.T., Simola, J.T., and Tesch, C.D., 122-Channel SQUID instrument for investigating the magnetic signals from the human brain, *Phys Scripta*, T49, 198, 1993.

Aldinucci, C., Garcia, J.B., Palmi, M., Sgaragli, G., Benocci, A., Meini, A., Pessina, F., Rossi, C., Bonechi, C., and Pessina, G.P., The effect of exposure to high flux density static and pulsed magnetic fields on lymphocyte function, *Bioelectromagnetics*, 24, 373, 2003a.

Aldinucci, C., Garcia, J.B., Palmi, M., Sgaragli, G., Benocci, A., Meini, A., Pessina, F., Rossi, C., Bonechi, C., and Pessina, G.P., The effect of strong static magnetic field on lymphocytes, *Bioelectromagnetics*, 24, 109, 2003b.

Amyan, A. and Ayrapetyan, S., On the modulation effect of pulsing and static magnetic field and mechanical vibrations on barley seed hydration, *Physiol Chem Phys Med NMR*, 36, 69, 2004.

Andra, W. and Nowak, H. (Eds.), *Magnetism in Medicine*, Wiley, New York, 1998.

Azanza, M.J. and del Moral, A., Isolated neuron amplitude spike decrease under static magnetic fields, *J Magn Magn Mater*, 157/158, 593, 1996.

Barker, A.T., An introduction to the basic principles of magnetic nerve stimulation, *J Clin Neurophysiol*, 8, 26, 1991.

Barker, A.T., Jalionus, R., and Freeston, I.L., Noninvasive magnetic stimulation of the human motor cortex, *Lancet*, 1, 1106, 1985.

Beason, R.C. and Semm, P., Does the avain ophthalmic nerve carry magnetic navigational information? *J Exp Biol*, 199, 1241, 1996.

Beaugnon, E. and Tournier, R., Levitation of organic materials, *Nature*, 349, 470, 1991.

Belova, N.A. and Lendnev, V.V., Activation and inhibition of gravitropic response in segments of flax stems exposed to static magnetic field with flux density ranging from 0 to 350 microtesla, *Biophysics*, 46, 117, 2001.

Belyaev, I.Y., Alipov, Y.D., and Harms-Ringdahl, M., Effects of zero magnetic field on the conformation of chromatin in human cells, *Biochim Biophys Acta*, 1336, 465, 1997.

Berk, S.G., Srikanth, S., Mahajan, S.M., and Ventrice, C.A., Static uniform magnetic fields and amoebae, *Bioelectromagnetics*, 18, 81, 1997.

Binhi, V.N., Theoretical concepts in magnetobiology, *Electr. Magnetobiol*, 20, 43, 2001.

Binhi, V.N., *Magnetobiology—Underlying Physical Problems*, Academic Press, New York, 2002.

Binhi, V.N., Alipov, Y.D., and Belyaev, I.Y., Effect of static field on *E. coli* cells and individual rotations of ion–protein complexes, *Bioelectromagnetics*, 22, 79, 2001.

Blackman, C.F., Blanchard, J.P., Benane, S.G., and House, D.E., Effect of AC and DC magnetic field orientation on nerve cells, *Biochem Biophys Res Commun*, 220, 807, 1996.

Blanchard, J.P. and Blackman, C.F., Clarification and application of an ion parametric resonance model for magnetic field interactions with biological systems, *Bioelectromagnetics*, 15, 217, 1994.

Blumenthal, N.C., Ricci, J., Breger, L., Zychlinsky, A., Solomon, H., Chen, G.G., Kuznetsov, D., and Dorfman, R., Effects of low-intensity AC and/or DC electromagnetic fields on cell attachment and induction of apoptosis, *Bioelectromagnetics*, 18, 264, 1997.

Bochert, R. and Zettler, M.L., Long-term exposure of several marine benthic animals to static magnetic fields, *Bioelectromagnetics*, 25, 498, 2004.

Bourland, J.D., Nyenhuis, J.A., and Schaefer, D.J., Physiologic effects of intense MRI gradient fields, *Neuroimaging Clin North Am* 9, 363, 1999.

Brocklehurst, B., Magnetic fields and radical reactions: recent development and their role in nature, *Chem Soc Rev*, 31, 301, 2002.

Brocklehurst, B. and McLauchlan, K.A., Free radical mechanism for the effects of environmental electromagnetic fields on biological systems, *Int J Radiat Biol*, 69(1), 3, 1996.

Buemi, M., Marino, D., Di Pasquale, G., Floccari, F., Senatore, M., Aloisi, C., Grasso, F., Mondio, G., Perillo, P., Frisina, N., and Corica, F., Cell proliferation/cell death balance in renal cell cultures after exposure to a static magnetic field, *Nephron*, 87, 269, 2001.

Carbonell, M.V., Martinez, E., and Amaya, J.M., Stimulation of germination in rice (*Oryza sativa* L.) by a static magnetic field, *Electr Magnetobiol*, 19, 121, 2000.
Carnes, K.I. and Magin, R.L., Effects of in utero exposure to 4.7 T MR imaging conditions on fetal growth and testicular development in the mouse, *Magn Reson Imaging*, 14, 263, 1996.
Cavopol, A.V., Wamil, A.W., Holcomb, R.R., and McLean, M.J., Measurement and analysis of static magnetic fields that block action potentials in cultured neurons, *Bioelectromagnetics*, 16, 197, 1995.
Ceballos, D., Navarro, X., Dubey, N., Wendelschafer-Crabb, G., Kennedy, W.R., and Tranquillo, R.T., Magnetically aligned collagen gel filling a collagen nerve guide improves peripheral nerve regeneration, *Exp Neurol*, 158, 290, 1999.
Chakeres, D.W. and de Vocht, F., Static magnetic field effects on human subjects related to magnetic resonance imaging systems, *Prog Biophys Mol Biol*, 87, 255, 2005.
Chakeres, D.W., Kangarlu, A., Boudoulas, H., and Young, D.C., Effect of static magnetic field exposure of up to 8 tesla on sequential human vital sign measurements, *J Magn Reson Imaging*, 18(3), 346, 2003.
Chignell, C.F. and Sik, R.H., The effect of static magnetic fields on the photohemolysis of human erythrocytes by ketoprofen, *Photochem Photobiol*, 67, 591, 1998.
Chionna, A., Tenuzzo, B., Panzarini, E., Dwikat, M.B., Abbro, L., and Dini, L., Time dependent modifications of Hep G2 cells during exposure to static magnetic fields, *Bioelectromagnetics*, 26, 275, 2005.
Ciortea, L.I., Morariu, V.V., Todoran, A., and Popescu, S., Life in zero magnetic field. 3. Effect on zinc and copper in human blood serum during *in vitro* aging, *Electr Magnetobiol*, 20, 127, 2001.
Cohen, D., Edelsack, E.A., and Zimmerman, J.E., Magnetocardiograms taken inside a shielded room with a superconducting point contact magnetometer, *Appl Phys Lett*, 16, 278, 1972.
Cohly, H.H.P., Abraham, G.E. III, Ndebele, K., Jenkins, J.J., Thompson, J., and Angel, M.F., Effects of static electromagnetic fields on characteristics of MG-63 osteoblasts grown in culture, *Biomed Sci Instrum*, 39, 454, 2003.
Coulton, L.A., Barker, A.T., Van Lierop, J.E., and Walsh, M.P., The effect of static magnetic fields on the rate of calcium/calmodulin-dependent phosphorylation of myosin light chain, *Bioelectromagnetics*, 21, 189, 2000.
Creanga, D.E., Morariu, V.V., and Isac, R.M., Life in zero magnetic field. IV. Investigation of developmental effects on fruit fly vision, *Electromagn Biol Med*, 21, 31, 2002.
Creim, J.A., Lovely, R.H., Miller, D.L., and Anderson, L.E., Rats can discriminate illuminance, but not magnetic fields, as a stimulus for learning a two-choice discrimination, *Bioelectromagnetics*, 23, 545, 2002.
Crozier, S. and Liu, F., Numerical evaluation of the fields induced by body motion in or near high-field MRI scanners, *Prog Biophys Mol Biol*, 87, 267, 2005.
Danielyan, A.A. and Ayrapetyan, S.N., Changes of hydration of rats' tissues after *in vivo* exposure to 0.2 tesla steady magnetic field, *Bioelectromagnetics*, 20, 123, 1999.
Danielyan, A.A., Mirakyan, M.M., Grigoryan, G.Y., and Ayrapetyan, S.N., The static magnetic field effects on quabain H3 binding by cancer tissue, *Physiol Chem Phys Med NMR*, 31, 139, 1999.
Del Seppia, C., Luschi, P., Ghione, S., Crosio, E., Choleris, E., and Papi, E., Exposure to hypogeomagnetic field or to oscillating magnetic fields similarly reduce stress-induced analgesia in C57 male mice, *Life Sci*, 66, 1299, 2000.
Del Seppia, C., Mezzasalma, L., Choleris, E., Luschi, P., and Ghione, S., Effects of magnetic field exposure on open field behaviour and nociceptive responses in mice, *Behav Brain Res*, 144, 1, 2003.
den Boer, J.A., Bourland, J.D., Nyenhuis, J.A., Ham, C.L.G., Engels, J.M.L., Hebrank, F.X., Frese, G., and Schaefer, D.J., Comparison of the threshold for peripheral nerve stimulation during gradient switching in whole body MR systems, *J Magn Reson Imaging*, 15, 520, 2002.
Denegre, J.M., Valles, J.M., Lin, K., Jordan, W.B., and Mowry, K.L., Cleavage planes in frog eggs are altered by strong magnetic fields, *Proc Natl Acad Sci USA*, 95, 14729, 1998.
Deutschlander, M.E., Borland, S.C., and Phillips, J.B., Extraocular magnetic compass in newts, *Nature*, 400, 324, 1999a.

Deutschlander, M.E., Phillips, J.B., and Borland, S.C., The case for light-dependent magnetic orientation in animals, *J Exp Biol*, 202, 891, 1999b.

Deutschlander, M.E., Freake, M.J., Borland, S.C., Phillips, J.B., Madden, R.C., Anderson, L.E., and Wilson, B.W., Learned magnetic compass orientation by the Siberian hamster, *Phodopus sungorus*, *Anim Behav*, 65, 779, 2003.

Diebel, C.E., Proksch, R., Green, C.R., Neilson, P., and Walker, M.M., Magnetite defines a vertebrate magnetoreceptor, *Nature*, 406, 299, 2000.

Dubey, N., Letourneau, P.C., and Tranquillo, R.T., Guided neurite elongation and Schwann cell invasion into magnetically aligned collagen in simulated peripheral nerve regeneration, *Exp Neurol*, 158, 338, 1999.

Edmond, D.T., A sensitive optically detected magnetic compass for animals, *Proc R Soc Lond B*, 263, 295, 1996.

Eguchi, Y., Ogiue-Ikeda, M., and Ueno, S., Control of orientation of rat Schwann cells using an 8-T static magnetic field, *Neurosci Lett*, 351, 130, 2003.

Eichwald, C. and Walleczek, J., Model for magnetic field effects on radical pair recombination in enzyme kinetics, *Biophys J*, 71, 623, 1996.

Emura, R., Ashida, N., Higashi, T., and Takeuchi, T., Orientation of bull sperms in static magnetic fields, *Bioelectromagnetics*, 22, 60, 2001.

Emura, R., Takeuchi, T., Nakaoka, Y., and Higashi, T., Analysis of anisotropic diamagnetic susceptibility of a bull sperm, *Bioelectromagnetics*, 24, 347, 2003.

Engstrom, S., Markov, M.S., McLean, M.J., Holcomb, R.R., and Markov, J.M., Effects of non-uniform static magnetic fields on the rate of myosin phosphorylation, *Bioelectromagnetics* 23, 475, 2002.

Epstein, C.M., Sekino, M., Yamaguchi, K., Kamiya, S., and Ueno, S., Asymmetries of prefrontal cortex in human episodic memory: effects of transcranial magnetic stimulation on learning abstract patterns, *Neurosci Lett*, 320, 5, 2002.

Eremenko, T., Esposito, C., Pasquarelli, A., Pasquali, E., and Volpe, P., Cell-cycle kinetics of friend erythroleukemia cells in a magnetically shielded room and in a low-frequency/low-intensity magnetic field, *Bioelectromagnetics*, 18, 58, 1996.

Erne, S.N., Hoke, M., Lutkenhoner, B., Pantev, C., and Scheer, H.J., Brainstem auditory evoked magnetic fields, in *Biomagnetism '87* (Atsumi, K., Kotani, M., Ueno, S., Katila, T., and Williamson, S.J., Eds.), Tokyo Denki University Press, Tokyo, 158–161, 1988.

Espinar, A., Piera, V., Carmona, A., and Guerrero, J.M., Histophysiological changes during development of the cerebellum in the chick embryo exposed a static magnetic field, *Bioelectromagnetics*, 18, 36, 1997.

Eveson, R.W., Timmel, C.R., Brocklehurst, B., Hore, P.J., and McLauchlan, K.A., The effects of weak magnetic fields on radical recombination reactions in micelles, *Int J Radiat Biol*, 76, 1509, 2000.

Fanelli, C., Coppola, S., Barone, R., Colussi, C., Gualandi, G., Volpe, P., and Ghibelli, L., Magnetic fields increase cell survival by inhibiting apoptosis via modulation of Ca2+ influx, *FASEB J*, 13, 95, 1999.

Flipo, D., Fournier, M., Benquet, C., Roux, P., Le Boulaire, C., Pinsky, C., Labella, F.S., and Krzystyniak, K., Increased apoptosis, changes in intracellular Ca^{2+}, and functional alterations in lymphocytes and macrophages after *in vitro* exposure to static magnetic field, *J Toxicol Environ Health A*, 54, 63, 1998.

Florez, M., Carbonell, M.V., and Martinez, E., Early sprouting and first stages of growth of rice seeds exposed to a magnetic field, *Electromagn Biol Med*, 23, 157, 2004.

Formica, D. and Silvestri, S., Biological effects of exposure to magnetic resonance imaging: an overview, *Biomed Eng Online*, 3, 11, 2004.

Formicki, K. and Perkowski, T., The effect of a magnetic field on the gas exchange in rainbow trout *Oncorhynchus mykiss* embryos (Salmonidae), *Ital J Zool*, 65 Suppl, 475, 1998.

Formicki, K., and Winnicki, A., Effects of constant magnetic field on cardiac muscle activity in fish, *Publ Espec Inst Esp Oceanogr*, 21, 287, 1996.

Formicki, K. and Winnicki, A., Reactions of fish embryos and larvae to constant magnetic fields, *Ital J Zool*, 65 Suppl, 479, 1998.

Formicki, K., Bonislawska, M., and Jasinski, M., Spatial orientation of trout (*Salmo trutta* L.) and rainbow trout (*Oncorhynchus mykiss* Walb.) embryos in natural and artificial magnetic fields, *Acta Ichtyol Piscat*, 27, 29, 1997.

Fujiki, M. and Steward, O., High frequency transcranial magnetic stimulation mimics the effects of ECS in upregulating astroglial gene expression in the murine CNS, *Brain Res Mol Brain Res*, 44, 301, 1997.
Fujiki, M., Kobayashi, H., Abe, T., and Kamida, T., Repetitive transcranial magnetic stimulation for protection against delayed neuronal death induced by transient ischemia, *J Neurosurg*, 99, 1063, 2003.
Fuller, M. and Dobson, J., On the significance of the time constants of magnetic field sensitivity in animals, *Bioelectromagnetics*, 26, 234, 2005.
Gmitrov, J. and Ohkubo, C., Geomagnetic field decreases cardiovascular variability, *Electr Magnetobiol*, 18, 291, 1999a.
Gmitrov, J. and Ohkubo, C., Static magnetic field and calcium channel blocking agent combined effect on baroreflex sensitivity in rabbits, *Electr Magnetobiol*, 18, 43, 1999b.
Gmitrov, J. and Ohkubo, C., Artificial static and geomagnetic field interrelated impact on cardiovascular regulation, *Bioelectromagnetics*, 23, 329, 2002.
Gmitrov, J., Ohkubo, C., and Okano, H., Effect of 0.25 static magnetic field on microcirculation in rabbits, *Bioelectromagnetics*, 23, 224, 2002.
Gray, J.R., Frith, C.H., and Parker, J.D., *In vivo* enhancement of chemotherapy with static electric or magnetic fields, *Bioelectromagnetics*, 21, 575, 2000.
Grissom, C.B., Magnetic field effects in biology: a survey of possible mechanisms with emphasis on radical-pair recombination, *Chem Rev*, 95, 3, 1995.
Grissom, C.B. and Natarajan, E., Use of magnetic field effects on study coenzyme B_{12}-dependent reactions, *Methods Enzymol*, 281, 235, 1997.
Guisasola, C., Desco, M., Millano, O., Villanueva, F.J., and Garcia-Barreno, P., Biological dosimetry of magnetic resonance imaging, *J Magn Reson Imaging*, 15, 584, 2002.
Hata, N., The effect of external magnetic field on the photochemical reaction of isoquinoline *N*-oxide, *Chem Lett*, 5, 547, 1976.
Hatada, T., Sekino, M., and Ueno, S., Finite element method-based calculation of the theoretical limit of sensitivity for detecting weak magnetic fields in the human brain using magnetic-resonance imaging, *J Appl Phys*, 97, 10E109, 2005.
Havel, W.J., Nyenhuis, J.A., Bourland, J.D., Foster, K.S., Geddes, L.A., Graber, G.P., Waninger, M.S., and Schaefer, D.J., Comparison of rectangular and damped sinusoidal dB/dt waveforms in magnetic stimulation, *IEEE Trans Magn*, 33, 4269, 1997.
Hayashi, H., *Introduction to Dynamic Spin Chemistry*, World Scientific Publishing Co, Singapore, 2004.
Higashi, T., Sagawa, S., Kawaguchi, N., and Yamagishi, A., Effects of a strong static magnetic field on blood platelets. *Platelet*, 4, 341, 1993a.
Higashi, T., Yamagishi, A., Takeuchi, T., Kawaguchi, N., Sagawa, S., Onishi, S., and Date, M., Orientation of erythrocytes in a strong static magnetic field, *Blood*, 82, 1328, 1993b.
Higashi, T., Sagawa, S., Ashida, N., and Takeuchi, T., Orientation of glutaraldehyde-fixed erythocytes in strong static magnetic fields, *Bioelectromagnetics*, 17, 335, 1996.
High, W.B., Sikora, J., Ugurbil, K., and Garwood, M., Subchronic *in vivo* effects of a high static magnetic field (9.4 T) in rats, *J Magn Reson Imaging*, 12, 122, 2000.
Hinch, R., Lindsay, K.A., Noble, D., and Rosenberg, J.R., The effects of static magnetic field on action potential propagation and excitation recovery in nerve, *Prog Biophys Mol Biol*, 87, 321, 2005.
Hirai, T., Nakamich, N., and Yoneda, Y., Activator protein-1 complex expressed by magnetism in cultured rat hippocampal neuron, *Biochem Biophys Res Commun*, 292, 200, 2002.
Hirata, Y., Kuriki, S., and Pantev, C., Musicians with absolute pitch show distinct neural activities in the auditory cortex, *NeuroReport*, 10, 999, 1999.
Hirose, H., Nakahara, T., and Miyakoshi, J., Orientation of human glioblastoma cells embedded in type I collagen, caused by exposure to a 10 T static magnetic field, *Neurosci Lett*, 338, 88, 2003a.
Hirose, H., Nakahara, T., Zhang, Q.-M., Yonei, S., and Miyakoshi, J., Static magnetic field with a strong magnetic field gradient (41.7 T/m) induces C-jun expression in HL-60 cells, *In Vitro Cell Dev Biol Anim*, 39, 348, 2003b.
Hirota, N., Nakagawa, J., and Kitazawa, K., Effects of magnetic field on the germination of plants, *J Appl Phys*, 85, 5717, 1999.

Hirota, N., Ikezoe, Y., Uetake, H., Nakagawa, J., and Kitazawa, K., Magnetic field effect on the kinetics of oxygen dissolution into water, materials transaction, *JIM*, 41, 976, 2000.

Holden, A.V., The sensitivity of the heart to static magnetic fields, *Prog Biophys Mol Biol*, 87, 289, 2005.

Horiuchi, S., Ishizaki, Y., Okuno, K., Ano, T., and Shoda, M., Drastic high magnetic field effect on suppression of *Escherichia coli* death, *Bioelectrochemistry*, 53, 149, 2001.

Horiuchi, S., Ishizaki, Y., Okuno, K., Ano, T., and Shoda, M., Change in broth culture is associated with significant suppression of *Escherichia coli* death under high magnetic field, *Bioelectrochemistry*, 57, 139, 2002.

Houpt, T.A., Pittman, D.W., Barranco, J.M., Brooks, E.H., and Smith, J.C., Behavioral effects of high-strength static magnetic fields on rats, *J Neurosci*, 23, 1498, 2003.

Ichioka, S., Iwasaka, M., Shibata, M., Harii, K., Kamiya, A., and Ueno, S., Biological effects of static magnetic fields on the microcirculatory blood flow *in vivo*: a preliminary report, *Med Biol Eng Comput*, 36, 91, 1998.

Ichioka, S., Minegishi, M., Iwasaka, M., Shibata, M., Nakatsuka, T., Harii, K., Kamiya, A., and Ueno, S., High-intensity static magnetic fields modulate skin microcirculation and temperature *in vivo*, *Bioelectromagnetics*, 21, 183, 2000.

Ichioka, S., Minegishi, M., Iwasawa, M., Shibata, M., Nakatsuka, T., Ando, J., and Ueno, S., Skin temperature changes induced static magnetic field exposure, *Bioelectromagnetics*, 24, 380, 2003.

Iino, M., Effects of a homogeneous field on erythrocyte sedimentation and aggregation, *Bioelectromagnetics*, 18, 215, 1997.

Iino, M. and Okuda, Y., Osmolality dependence of erythrocyte sedimentation and aggregation in a strong magnetic field, *Bioelectromagnetics*, 22, 46, 2001.

Ikehata, M., Koana, T., Suzuki, Y., Shimizu, H., and Nakagawa, M., Mutagenicity and co-mutagenicity of static fields detected by bacterial mutation assay, *Mutat Res*, 427, 147, 1999.

Ikehata, M., Iwasaka, M., Miyakoshi, J., Ueno, S., and Koana, T., Effects of intense magnetic fields on sedimentation pattern and gene expression profile in budding yeast. *J Appl Phys*, 93, 6724, 2003.

International Agency for Research on Cancer (IARC), *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Non-Ionising Radiation. Part I: Static and Extremely Low Frequency (ELF) Electric and Magnetic Fields*, vol. 80, IARC, Lyon, France, 2002.

International Electrotechnolgy Commission (IEC), *Particular Requirements for the Safety of Magnetic Resonance Equipment for Medical Diagnosis*, Standard 60601-2-33, 2nd ed., Geneva, Switzerland, 2002.

Iramina, K. and Ueno, S., Measurement of brainstem auditory evoked magnetic fields using a highly sensitive SQUID magnetometer with a variable base line, *IEEE Trans Magn*, 31, 4271, 1995.

Iramina, K., Ueno, K., and Ueno, S., Influence of spreading neuronal electric sources on spatio-temporal neuromagnetic fields, *J Appl Phys*, 75, 7168, 1994.

Iramina, K., Ueno, K., and Ueno, S., Spatio-temporal MEG pattern produced by spreading multiple dipoles, *IEEE Trans Magn*, 31, 4265, 1995.

Ishizaki, Y., Horiuchi, S., Okuno, K., Ano, T., and Shoda, M., Twelve hours exposure to inhomogeneous high magnetic field after logarithmic growth is sufficient for drastic suppression of *Escherichia coli* death, *Bioelectrochemistry*, 54, 101, 2001.

Iwaki, S., Ueno, S., Imada, T., and Tonoike, M., Dynamic cortical activation in mental image processing revealed by biomagnetic measurement, *Neuroreport*, 10, 1793, 1999.

Iwasaka, M. and Ueno, S., Effects of magnetic fields on fibrinolysis, *J Appl Phys*, 75, 7162, 1994.

Iwasaka, M. and Ueno, S., Bioluminescence under static magnetic fields, *J Appl Phys*, 83, 6456, 1998a.

Iwasaka, M. and Ueno, S., Structure of water molecules under 14 T magnetic field, *J Appl Phys*, 83, 6459, 1998b.

Iwasaka, M. and Ueno, S., Detection of intracellular macromolecule behavior under strong magnetic fields by linearly polarized light, *Bioelectromagnetics*, 24, 564, 2003.

Iwasaka, M., Takeuchi, M., Ueno, S., and Tsuda, H., Polymerization and dissolution of fibrin under homogeneous magnetic fields, *J Appl Phys*, 83, 6453, 1998.

Iwasaka, M., Miyakoshi, J., and Ueno, S., Magnetic field effects on assembly pattern of smooth muscle cells, *In Vitro Cell Biol Anim*, 39, 2003a.

Iwasaka, M., Yamamoto, K., Ando, J., and Ueno, S., Verification of magnetic field gradient effects on medium convection and cell adhesion, *J Appl Phys*, 93, 6715, 2003b.

Jajte, J., Grzegorczyk, J., Zmyslony, M., and Rajkowska, E., Effect of 7 mT static magnetic field and iron ions on rat lymphocytes: apoptosis, necrosis and free radical processes, *Bioelectrochemistry*, 57, 107, 2002.

Jin, J., *Electromagnetic Analysis and Design in Magnetic Resonance Imaging*, CRC Press, Boca Raton, FL, 1999.

Johnston, S.A., D'Andrea, J.A., Behavioral and cognitive effects of electromagnetic field exposures, in *Biological and Medical Aspects* (Barnes, F.S. and Greenebaum, B., Eds.), Taylor & Francis, Boca Raton, FL, 2006, Chapter 4.

Jovanic, B.R. and Sarvan, M.Z., Permanent magnetic field and plant leaf temperature, *Electromagn Biol Med*, 23, 1, 2004.

Jove, M., Torrente, M., Gilabert, R., Espinar, A., Cobos, P., and Piera, V., Effects of static electromagnetic fields on chick embryo pineal gland development, *Cell Tissues Organs*, 165, 74, 1999.

Joy, M., Scott, G., and Henkelman, M., *In vivo* detection of applied electric currents by magnetic resonance imaging, *Magn Reson Imaging*, 7, 89, 1989.

Kamei, H., Iramina, K., Yoshikawa, K., and Ueno, S., Neuronal current distribution imaging using magnetic resonance, *IEEE Trans Magn*, 35, 4109, 1999.

Kangarlu, A., Burgess, R.E., Zhu, H., Nakayama, T., Hamlin, R.L., Schenck, J.F., Abduljalil, A.M., and Robitaille, P.M.L., Cognitive, cardiac and physiological safety studies in ultra high field magnetic resonance imaging, *J Magn Reson Imaging*, 17, 1407, 1999.

Kangarlu, A., Shellock, F.G., and Chakeres, D.W., 8.0-Tesla human MR system: temperature changes associated with radiofrequency-induced heating of a head phantom, *J Magn Reson Imaging*, 17(2), 220, 2003.

Kangarlu, A., Ibrahim, T.S., and Shellock, F.G., Effects of coil dimensions and field polarization on RF heating inside a head phantom, *Magn Reson Imaging*, 23(1), 53, 2005.

Keck, M.E., Sillaber, I., Ebner, K., Welt, T., Toschi, N., Kaehler, S.T., Singewald, N., Philippu, A., Elbel, G.K., Wotjak, C.T., Holsboer, F., Landgraf, R., and Engelmann, M., Acute transcranial magnetic stimulation of frontal brain regions selectively modulates the release of vasopressin, biogenic amines and amino acids in the rat brain, *Eur J Neurosci*, 12, 3713, 2000.

Kefuss, J., M'Diaye, K., Bounias, M., Vanpoucke, J., and Ecochard, J., Biochemical effects of high intensity constant magnetic fields on worker honey bees, *Bioelectromagnetics*, 20, 117, 1999.

Khang, H.S., Lee, B.I., Oh, S.H., Woo, E.J., Lee, S.Y., Cho, M.H., Kwon, O., Yoon, J.R., and Seo, J.K., J-substitution algorithm in magnetic resonance electrical impedance tomography (MREIT): phantom experiments for static resistivity images, *IEEE Trans Med Imaging*, 21, 695, 2002.

Kimchi, T. and Terkel, J., Magnetic compass orientation in the blind mole rat *Spalax ehrenbergi*, *J Exp Biol*, 204, 751, 2001.

Kishioka, S., Yamada, A., and Aogaki, R., Analysis of gas dissociation rate into liquid phase under magnetic–field gradient, *Phys Chem Chem Phys*, 2, 4179, 2000.

Koana, T., Ikehata, M., and Nakagawa, M., Estimation of genetics effects of a static magnetic field by a somatic cell test using mutagen-sensitive mutants of *Drosophila melanogaster*, *Bioelectrochem Bioenerg*, 36, 95, 1995.

Koana, T., Okada, M.O., Ikehata, M., and Nakagawa, M., Increase in the mitotic recombination frequency in *Drosophila melanogaster* by magnetic field exposure and its suppression by vitamin E supplement, *Mutat Res*, 373, 55, 1997.

Kobayashi, M., Soda, N., Miyo, T., and Ueda, Y., Effects of combined DC and AC magnetic fields on germination of hornwort seeds, *Bioelectromagnetics*, 25, 552, 2004.

Kotani, H., Iwasaka, M., and Ueno, S., Magnetic orientation of collagen and bone mixture, *J Appl Phys*, 87, 6191, 2000.

Krings, T., Chiappa, K.H., Foltys, H., Reinges, M.H., Cosgrove, G.R., and Thron, A., Introducing navigated transcranial magnetic stimulation as a refined brain mapping methodology, *Neurosurg Rev*, 24, 171, 2001.

Kroeker, G., Parkinson, D., Vriend, J., and Peeling, J., Neurochemical effects of static magnetic field exposure, *Surg Neurol*, 45, 62, 1996.

Kula, B., A study of magnetic field effects on fibroblast cultures Part 3. The evaluation of the effects of static and extremely low frequency (ELF) magnetic fields on glycosaminoglycan metabolism in fibroblasts, cell coats and culture medium, *Bioelectrochem Bioenerg*, 39, 31, 1996.

Kula, B. and Drozbz, M., A study of magnetic field effects on fibroblast cultures Part 1. The evaluation of the effects of static and extremely low frequency (ELF) magnetic fields on vital functions of fibroblasts, *Bioelectrochem Bioenerg*, 39, 21, 1996a.
Kula, B. and Drozbz, M., A study on magnetic field on fibroblast cultures. Part 2. The evaluation of the effects of static and extremely low frequency (ELF) magnetic fields on free-radical processes in fibroblast cultures, *Bioelectrochem Bioenerg*, 39, 27, 1996b.
Kula, B., Sobczak, A., and Kuska, R., Effects of static and ELF magnetic fields on free-radical processes in rat liver and kidney, *Electr. Magnetobiol*, 19, 99, 2000.
Kula, B., Sobczak, A., and Kuska, R., A study of the effects of static and extremely low frequency magnetic fields on lipid peroxidant products in subcellular fibroblast fractions, *Electromagn Biol Med*, 21, 161, 2002.
Kuriki, S., Okita, Y., and Hirata, Y., Source analysis of magnetic field responses from the human auditory cortex elicited by short speech sounds, *Exp Brain Res*, 104, 144, 1995.
Kuriki, S., Takeuchi, F., and Hirata, Y., Neural processing of words in the human extrastriate visual cortex, *Cogn Brain Res*, 6, 193, 1998.
Kuriki, S., Isahai, N., and Otsuka, A., Spatiotemporal characteristics of the neural activities processing consonant/dissonant tones in melody, *Exp Brain Res*, 162, 46, 2005.
Kwon, H., Kuriki, S., Kim, J., Lee, Y., Kim, K., Park, Y., and Nam, K., MEG study on neural activities associated with syntactic and semantic violations in spoken Korean sentences, *Neurosci Res*, 51, 349, 2005.
Lauterbur, P.C., Image formation by induced local interactions: examples employing nuclear magnetic resonance, *Nature*, 242, 190, 1973.
Leszczynski, D., Rapporteur report: cellular, animal and epidemiological studies of the effects of static magnetic fields relevant to human health, *Prog Biophys Mol Biol*, 87, 247, 2005.
Levin, M. and Ernst, S.G., Applied DC magnetic fields cause alterations in the time of cell divisions and developmental abnormalities in early sea urchin embryos, *Bioelectromagnetics*, 18, 255, 1997.
Liboff, A.R., Geomagnetic cyclotron resonance in living cells, *J Biol Phys*, 13, 99, 1985.
Liboff, A.R., Cherng, S., Jenrow, K.A., and Bull, A., Calmodulin-dependent cyclic nucleotide phosphodiesterase activity is altered by 20 μT magnetostatic fields, *Bioelectromagnetics*, 24, 32, 2003.
Lin, J.C. (Ed.), *Advances in Electromagnetics Fields in Living Systems*, vol. 3, Kluwer Academic/Plenum Publishers, Hingham, MA, 2000.
Lockwood, D.R., Kwon, B., Smith, J.C., and Houpt, T.A., Behavioral effects of static high magnetic fields on unrestrained and restrained mice, *Physiol Behav*, 78, 635, 2003.
Lohmann, K.J. and Johnsen, S., The neurobiology of magnetoreception in vertebrate animals, *Trends Neurosci*, 23, 153, 2000.
Lohmann, K.J., Cain, S.D., Dodge, S.A., and Lohmann, C.M.F., Regional magnetic fields as navigational markers for sea turtles, *Science*, 294, 364, 2001.
Madec, F., Billaudel, B., Charlet de Sauvage, R., Sartor, P., and Veyret, B., Effects of ELF and static magnetic fields on calcium oscillations in islets of Langerhans, *Bioelectrochemistry*, 60, 73, 2003.
Magin, R.L., Lee, J.K., Klintsova, A., Carnes, K.I., and Dunn, F., Biological effects of long-duration, high-field (4 T) MRI on growth and development in the mouse, *J Magn Reson Imaging*, 12, 140, 2000.
Manassen, Y., Shalev, E., and Navon, G., Mapping of electrical circuits using chemical-shift imaging, *J Magn Reson*, 76, 371, 1988.
Markov, M.S., Myosin light chain modification depending on magnetic fields. II. Experimental, *Electromagn Biol Med*, 23, 125, 2004a.
Markov, M.S., Myosin light chain phosphorylation modification depending on magnetic fields. I. Theoretical, *Electromagn Biol Med*, 23, 55, 2004b.
Markov, M.S. and Pilla, A.A., Static field modulation of myosin phosphorylation: calcium dependence in two enzyme preparations, *Bioelectrochem Bioenerg*, 35, 57, 1994.
Markov, M.S. and Pilla, A.A., Weak static magnetic field modulation of myosin phosphorylation in a cell-free preparation: calcium dependence, *Bioelectrochem Bioenerg*, 43, 233, 1997.
Markov, M.S., Wang, S., and Pilla, A.A., Effects of weak low-frequency sinusoidal and DC magnetic-fields on myosin phosphorylation in a cell-free preparation, *Bioelectrochem Bioenerg*, 30, 119, 1993.

Martinez, E., Carbonell, M.V., and Amaya, J.M., A static magnetic field of 125 mT stimulates the initial growth stages of barley (*Hordeum vulgare* L.), *Electr. Magnetobiol*, 19, 271, 2000.

Martinez, E., Carbonell, M.V., and Florez, M., Magnetic biostimulation of initial growth stages of wheat, *Electromagn Biol Med*, 21, 43, 2002.

Mayrovitz, H.N., Groseclose, E.E., Markov, M., and Pilla, A.A., Effect of permanent magnets on resting skin blood perfusion in healthy persons assessed by laser Doppler flowmetry and imaging, *Bioelectromagnetics*, 22, 494, 2001.

Mayrovitz, H.N., Groseclose, E.E., and King, D., No effect of 85 mT permanent magnets on laser-Doppler measured blood flow response to inspiratory gasps, *Bioelectromagnetics*, 26, 331, 2005.

McKinlay, A.F. and Repacholi, M.H., More research is needed to determine the safety of static magnetic fields, *Prog Biophys Mol Biol*, 87, 173, 2005.

McLean, M.J., Holcomb, R.R., Wamil, A.W., Pickett, J.D., and Cavopol, A.V., Blockade of sensory neuron action potentials by a static magnetic field in the 10 mT range, *Bioelectromagnetics*, 16, 20, 1995.

McLean, M.J., Engstrom, S., and Holcomb, R.R., *Magnetotherapy: Potential Therapeutic Benefits and Adverse Effects*, TFG Press, New York, 2003a.

McLean, M.J., Engstrom, S., Holcomb, R.R., and Sanchez, D., A static magnetic field modulates severity of audiogenic seizures and anticonvulsant effects of phenytoin in DBA/2 mice, *Epilepsy Res*, 55, 105, 2003b.

Miyakoshi, J., Effects of static magnetic fields at the cellular level, *Prog Biophys Mol Biol*, 87, 213, 2005.

Miyamoto, H., Yamaguchi, H., Ikehara, T., and Kinouchi, Y., Effects of electromagnetic fields on K+ (Rb+) uptake by HeLa cell, in *Biological Effects of Magnetic and Electromagnetic Fields* (Ueno, S., Ed.), Plenum Press, New York, 101, 1996.

Mnaimneh, S., Bizri, M., and Veyret, B., No effect of exposure to static and sinusoidal magnetic fields on nitric oxide production by macrophages, *Bioelectromagnetics*, 17, 519, 1996.

Mohtat, N., Cozens, F.L., Hancock-Chen, T., Scaiano, J.C., McLean, J., and Kim, J., Magnetic field effects on the behavior of radicals in protein and DNA environments, *Photochem Photobiol*, 67, 111, 1998.

Morariu, V.V., Ciorba, D., and Neamtu, S., Life in zero magnetic field. I. *In vitro* human blood aging, *Electr. Magnetobiol*, 19, 289, 2000.

Morris, C. and Skalak, T., Static magnetic fields alter arteriolar tone *in vivo*, *Bioelectromagnetics*, 26, 1, 2005.

Mouchawar, G.A., Bourland, J.D., Nyenhuis, J.A., Geddes, L.A., Foster, K.S., Jones, J.T., and Graver, G.P., Closed-chest cardiac stimulation with a pulsed magnetic field, *Med Biol Eng Comput*, 30, 162, 1992.

Muehsam, D.J. and Pilla, A.A., Lorentz approach to static magnetic field effects on bound-ion dynamics and binding kinetics: thermal noise considerations, *Bioelectromagnetics*, 17, 89, 1996.

Munro, U., Munro, J.A., Phillips, J.B., Wiitschko, R., and Wiltschko, W., Evidence for a magnetite-based navigational ''map'' in birds, *Naturwissenschaften*, 84, 26, 1997.

Nagakura, S. and Molin, Y. (guest eds.), Magnetic field effects upon photophysical and photochemical phenomena, *Chem Phys*, 162(1), 1, 1992 (special issue).

Nagy, P. and Fischl, G., Effect of static magnetic field on growth and sporulation of some plant pathogenic fungi, *Bioelectromagnetics*, 25, 316, 2004.

Nakagawa, J., Hirota, N., Kitazawa, K., and Shoda, M., Magnetic field enhancement of water vaporization, *J Appl Phys*, 86, 2923, 1999.

Nakahara, T., Yaguchi, H., Yoshida, M., and Miyakoshi, J., Effects of exposure to CHO-K1 cells to a 10-T static magnetic field, *Radiology*, 224, 817, 2002.

Nakaoka, Y., Takeda, R., and Shimizu, K., Orientation of *Paramecium* swimming in a DC magnetic field, *Bioelectromagnetics*, 23, 607, 2002.

Narra, V.R., Howell, R.W., Goddu, S.M., and Rao, D.V., Effects of a 1.5-tesla static magnetic field on spermatogenesis and embryogenesis in mice, *Investig Radiol*, 31, 586, 1996.

Natarajan, E. and Grissom, C.B., The origin of magnetic field dependent recombination in alkylcobalamin radical pairs, *Photochem Photobiol*, 64, 286, 1996.

Nemec, P., Altmann, J., Marhold, S., Burda, H., and Oelschlaeger, H.H.A., Neuroanatomy of magntoreception: the superior colliculus involved in magnetic orientation in a mammal, *Science*, 294, 366, 2001.

Neugebauer, D.C., Blauruck, A., and Worcester, D.L., Magnetic orientation of purple membranes demonstrated by optical measurements and neutron scattering, *FEBS Lett*, 78, 31, 1977.

Nikolskaya, K. and Echenko, O., Alcohol addiction as the result of cognitive activity in altered natural magnetic field, *Electromagn Biol Med*, 21, 1, 2002.

Nikolskaya, K., Shtemler, V., Yeschenko, O., Savonenko, A., Osipov, A., and Nickolsky, S., The sensitivity of cognitive processes to the inhomogeneity of natural magnetic fields, *Electr Magnetobiol*, 15, 163, 1996.

Nikolskaya, K.A., Yeshchenko, O.V., and Pratusevich, V., The opioid system and magnetic field perception, *Electr. Magnetobiol*, 18, 277, 1999.

Nolte, C.M., Pittman, D.W., Kalevitch, B., Henderson, R., and Smith, J.C., Magnetic field conditioned taste aversion in rats, *Physiol Behav*, 63, 683, 1998.

Nyenhuis, J.A., Bourland, J.D., and Schaefer, D.J., Analysis from a stimulation perspective of the field patterns of magnetic resonance imaging coils, *J Appl Phys*, 81, 4314, 1997.

Nyenhuis, J.A., Bourland, J.D., Kildishev, A.V.D.J., and Schaefer, D.J., Health effects and safety of intense MRI gradient fields, in *Magnetic Resonance Procedures: Health Effects and Safety* (Shellock, F.G., Ed.), CRC Press, Boca Raton, FL, 31–54, 2001.

Ogawa, S., Tank, D.W., and Menon, R., Intrinsic signal changes accompanying stimulation: functional brain mapping with magnetic resonance imaging, *Proc Natl Acad Sci USA*, 89, 5951, 1992.

Ogiue-Ikeda, M., Kawato, S., and Ueno, S., The effect of repetitive transcranial magnetic stimulation on long-term potentiation in rat hippocampus depends on stimulus intensity, *Brain Res*, 993, 222, 2003a.

Ogiue-Ikeda, M., Sato, Y., and Ueno, S., A method to destruct targeted cells using magnetizable beads and pulsed magnetic force, *IEEE Trans Magn* 39, 3390, 2003b.

Ohkubo, C. and Xu, S., Acute effects of static magnetic fields on cutaneous microcirculation in rabbits, *In Vivo*, 11, 221, 1997.

Okano, H. and Ohkubo, C., Modulatory effects of static magnetic fields on blood pressure in rabbits, *Bioelectromagnetics*, 22, 408, 2001.

Okano, H. and Ohkubo, C., Anti-pressor effects of whole body exposure to static magnetic field on pharmacologically induced hypertension in conscious rabbit, *Bioelectromagnetics*, 24, 139, 2003a.

Okano, H. and Ohkubo, C., Effects of static magnetic fields on plasma levels of angiotensin II and aldosterone associated with arterial blood pressure in genetically hypertensive rats, *Bioelectromagnetics*, 24, 403, 2003b.

Okano, H., Gmitrov, J., and Ohkubo, C., Biphasic effects of static magnetic field on cutaneous microcirculation in rabbits, *Bioelectromagnetics*, 20, 161, 1999.

Okano, H., Masuda, H., and Ohkubo, C., Decreased plasma levels of nitric oxide metabolites, angiotensin II and aldosterone in spontaneously hypertensive rats exposed to 5 mT static magnetic field, *Bioelectromagnetics*, 26, 161, 2005a.

Okano, H., Masuda, H., and Ohkubo, C., Effects of 25 mT static magnetic field on blood pressure in reserpine-induced hypotensive Wistar–Kyoto rats, *Bioelectromagnetics*, 26, 36, 2005b.

Okazaki, R., Ootsuyama, A., Uchida, S., and Norimura, T., Effects of a 4.7 T static magnetic field on fetal development in ICR mice, *J Radiat Res*, 42, 273, 2001.

Okonogi, H., Nakagawa, M., and Tsuji, Y., The effects of a 4.7 tesla static magnetic field on the frequency of micronucleated cells induced by mitomycin C, *Tohoku J Exp Med*, 180, 209, 1996.

Okuda, T., Nishizawa, K., Ejima, Y., Nakatsugawa, S., Ishigaki, T., and Ishigaki, K., The effects of static magnetic fields and x-rays on instability of microsatellite repetitive sequences, *J Radiat Res*, 39, 279, 1998.

Okuno, K., Fujinami, R., Ano, T., and Shoda, M., Disappearance of growth advantage in stationary phase (GASP) phenomenon under a high magnetic field, *Bioelectromagnetics*, 53, 165, 2001.

Onodera, H., Jin, Z., Chida, S., Suzuki, Y., Tago, H., and Itoyama, Y., Effects of 10-T static magnetic field on human peripheral blood immune cells, *Radiat Res*, 159, 775, 2003.

Osuga, T. and Tatsuoka, H., Effect of 1.5 T steady magnetic field on neuroconduction of a bullfrog sciatic nerve in a partially active state within several hours after extraction, *Magn Reson Imaging*, 17, 791, 1999.

Pacini, S., Aterini, S., Pacini, P., Ruggiero, C., Gulisano, M., and Ruggiero, M., Influence of static magnetic field on the antiproliferative effects of vitamin D on human breast cancer cells, *Oncol Res*, 11, 265, 1999a.

Pacini, S., Vannelli, G.B., Barni, T., Ruggiero, M., Sardi, I., Pacini, P., and Gulisano, M., Effect of 0.2 T static magnetic field on human neurons: remodeling and inhibition of signal transduction without genome instability, *Neurosci Lett*, 267, 185, 1999b.

Pagnac, C., Geneviere, A.-M., Moreau, J.-M., Picard, A., Joussot-Dubien, J., and Veyret, B., No effects of DC and 60-Hz AC magnetic fields on the first mitosis of two species of sea urchin embryos, *Bioelectromagnetics*, 19, 494, 1998.

Pan, H. and Liu, X., Apparent biological effect of strong magnetic field on mosquito egg hatching, *Bioelectromagnetics*, 25, 84, 2004.

Pate, K., Benghuzzi, H., Tucci, M., Puckett, A., and Cason, Z., Morphological evaluation of MRC-5 fibroblasts after stimulation with static magnetic field and pulsating electromagnetic field, *Biomed Sci Instrum*, 39, 460, 2003.

Penuelas, J., Llusia, J., Martinez, B., and Fontcuberta, J., Diamagnetic susceptibility and root growth responses to magnetic fields in *Les culinaris*, *Glycine soja*, and *Triticum aestivum*, *Electromagn Biol Med*, 23, 97, 2004.

Phillips, J.B., Magnetic navigation, *J Theor Biol*, 180, 309, 1996.

Phillips, J.B, Animal magnetoreception: future directions, *BioEM 2005*, 160, 2005.

Phillips, J.B., Deutschlander, M.E., Freake, M.J., and Borland, S.C., The role of extraocular photoreceptors in newt magnetic compass orientation: parallels between light-dependent magnetoreception and polarized light detection in vertebrates, *J Exp Biol*, 204, 2543, 2001.

Phillips, J.B., Borland, S.C., Freake, M.J., Brassart, J., and Kirschvink, J.L., 'Fixed-axis' magnetic orientation by an amphibian: non-shoreward-directed compass orientation, misdirected homing or positioning a magnetite-based map detector in a consistent alignment relative to the magnetic field, *J Exp Biol*, 205, 3903, 2002a.

Phillips, J.B., Freake, M.J., Fischer, J.H., and Vorland, S.C., Behavioral titration of a magnetic map coordinate, *J Comp Physiol A*, 188, 157, 2002b.

Phirke, P.S., Kubde, A.B., and Umbarkar, S.P., The influence of magnetic field on plant growth, *Seed Sci Technol*, 24, 375, 1996.

Piatti, E., Cristina, A.M., Baffone, W., Fraternale, D., Citterio, B., Piera, P.M., Dacha, M., Vetrano, F., and Accorsi, A., Antibacterial effect of a magnetic field on *Serratia marcescens* and related virulence to *Hordeum vulgare* and *Rubus fruticosus* callus cells, *Comp Biochem Physiol B Biochem Mol Biol*, 132, 359, 2002.

Pilla, A.A., Mechanisms and therapuetic applications of time-varing and static magnetic fields, in *Biological and Medical Aspects* (Barnes, F.S., and Greenebaum, B., Eds.), Taylor & Francis, Boca Raton, FL, 2006, Chapter 11.

Poiata, A., Creanga, D.E., and Morariu, V.V., Life in zero magnetic field. V. *E. coli* resistance to antibiotics, *Electromagn Biol Med*, 22, 171, 2003.

Polk, C. and Postow, E. (Eds.), *Handbook of Biological Effects of Electromagnetic Fields*, CRC Press, Boca Raton, FL, 1986.

Polk, C. and Postow, E. (Eds.), *Handbook of Biological Effects of Electromagnetic Fields*, 2nd ed., CRC Press, Boca Raton, FL, 1997.

Potenza, L., Cucchiarini, L., Piatti, E., Angelini, U., and Dacha, M., Effects of high static magnetic field exposure on different DNAs, *Bioelectromagnetics*, 25, 352, 2004a.

Potenza, L., Ubaldi, L., De Sanctis, R., De Bellis, R., Cucchiarini, L., and Dacha, M., Effects of a static magnetic field on cell growth and gene expression in *Escherichia coli*, *Mutat Res*, 561, 53, 2004b.

Prato, F.S., Kavaliers, M., and Carson, J.J.L., Behavioural evidence that magnetic field effects in the land snail, *Cepaea nemoralis*, might not depend on magnetite or induced electric currents, *Bioelectromagnetics*, 17, 123, 1996a.

Prato, F.S., Kavaliers, M., and Carson, J.J.L., Behavioural responses to magnetic fields by land snails are dependent on both magnetic field direction and light, *Proc R Soc Lond B*, 263, 1437, 1996b.

Prato, F.S., Robertson, J.A., Desjardins, D., Hensel, J., and Thomas, A.W., Daily repeated magnetic field shielding induces analgesia in CD-1 mice, *Bioelectromagnetics*, 26, 109, 2005.

Rai, D.V., Kohli, K.S., Goyal, N., and Jindal, V.K., The effect of static magnetic field on electrical properties of lens, *Electr. Magnetobiol*, 16, 293, 1997.
Raylman, R.R., Clavo, A.C., and Wahl, R.L., Exposure to strong static magnetic field slows the growth of human cancer cell *in vitro*, *Bioelectromagnetics*, 17, 358, 1996.
Reilly, J.P., Peripheral nerve stimulation in induced electric currents: exposure to time-varying magnetic fields, *Med Biol Eng Comput*, 27, 101, 1989.
Reilly, J.P., Magnetic field excitation of peripheral nerves and the heart: a comparison of thresholds, *Med Biol Eng Comp*, 29, 571, 1991.
Reina, F.G. and Pascual, L.A., Influence of a stationary magnetic field on water relations in lettuce seeds. Part 1: theoretical considerations, *Bioelectromagnetics*, 22, 589, 2001.
Reina, F.G., Pascual, L.A., and Fundora, I.A., Influence of a stationary magnetic field on water relations in lettuce seeds. Part 2: experimental results, *Bioelectromagnetics*, 22, 596, 2001.
Repacholi, M.H. and Greenebaum, B., Interaction of static and extremely low frequency electric and magnetic fields with living systems: health effects and research needs, *Bioelectromagnetics*, 20, 133, 1999.
Ritz, T., Adem, S., and Schulten, K., A model for photoreceptor-based magnetoreception in birds, *Biophys J*, 78, 707, 2000.
Ritz, T., Dommer, D.H., and Phillips, J.B., Shedding light on vertebrate magnetoreception, *Neuron*, 34, 503, 2002.
Ritz, T., Thalau, P., Phillips, J.B., Wiltschko, R., and Wiltschko, W., Resonance effects indicate a radical-pair mechanism for avian magnetic compass, *Nature*, 429, 177, 2004.
Robitaille, P.M.L., Abduljalil, A.M., Kangarlu, A., Zhang, X., Yu, Y., Burgess, R., Bair, E., Noa, P., Yang, L., Zhu, H., Palmer, B., Jiang, Z., Chakeres, D.W., and Spigos, D., Human magnetic resonance imaging at eight tesla, *NMR Biomed*, 11, 263, 1998.
Ronchetto, F., Barone, D., Cintorino, M., Berardelli, M., Lissola, S., Orlassino, R., Ossala, P., and Tofani, S., Extremely low frequency-modulated static magnetic fields to treat cancer: a pilot study on patients with advanced neoplasm to assess safety and acute toxicity, *Bioelectromagnetics*, 25, 563, 2004.
Rosch, P.J. and Markov, M.S., *Bioelectromagnetic Medicine*, Marcel Dekker, New York, 2004.
Rosen, A.D., Inhibition of calcium channel activation in GH3 cells by static magnetic fields, *Biochim Biophys Acta*, 1282, 149, 1996.
Rosen, A.D., Effect of a 125 mT static magnetic field on kinetics of voltage activated Na^+ channels in GH3 cells, *Bioelectromagnetics*, 24, 517, 2003.
Rosen, M. and Rosen, A., Magnetic influence on *Paramecium* motility, *Life Sci*, 46, 1509, 1990.
Rothwell, J.C., Day, B.L., Thompson, P.D., Dick, J.P.R., and Marsden, C.D., Some experiences of techniques for stimulation of the human cerebral motor cortex through the scalp, *Neurosurgery*, 20(1), 156, 1987.
Ruggiero, M., Bottaro, D.P., Liguri, G., Gulisano, M., Peruzzi, B., and Pacini, S., 0.2 T magnetic field inhibits angiogenesis in chick embryo chorioallantoic membrane, *Bioelectromagnetics*, 25, 390, 2004.
Ruiz-Gomez, M.J., Prieto-Barcia, M.I., Ristori-Bogajo, E., and Martinz-Morillo, M., Static and 50 Hz magnetic field of 0.35 and 2.45 mT have no effect on the growth of *Saccharomyces cerevisiae*, *Bioelectromagnetics*, 64, 151, 2004.
Sabo, J., Mirossay, L., Horovcak, L., Sarissky, M., Mirossay, A., and Mojzis, J., Effect of magnetic field on human leukemic cell line HL-60, *Bioelectrochemistry*, 56, 227, 2002.
Sakurai, H., Okuno, K., Kubo, A., Nakamura, K., and Shoda, M., Effect of 7-tesla homogeneous magnetic field on mammalian cells, *Bioelectrochem Bioenerg*, 49, 57, 1999.
Salerno, S., Lo Casto, A., Caccamo, N., D'Anna, C., de Maria, M., Lagalla, R., Scola, L., and Cardinale, A.E., Static magnetic fields generated by a 0.5 T MRI unit affects *in vitro* expression of activation markers and interleukin release in human peripheral blood mononuclear cells (PBMC), *Int J Radiat Biol*, 75, 457, 1999.
Sandrey, M.A., Vesper, D.N., Johnson, M.T., Nindl, G., Swez, J.A., and Chamberlain, J., Effect of short duration electromagnetic field exposure on rat mass, *Bioelectromagnetics*, 23, 37658, 2002.
Satow, Y., Matsunami, K., Kawashima, T., Satake, H., and Huda, K., A strong constant magnetic field affects muscle tension development in bullfrog neuromuscular preparations, *Bioelectromagnetics*, 22, 53, 2001.

Saunders, R., Static magnetic fields: animal studies, *Prog Biophys Mol Biol*, 87, 225, 2005.
Schenck, J.F., Physical interactions of static magnetic fields with living tissues, *Prog Biophys Mol Biol*, 87, 185, 2005.
Schenck, J.F., Dumoulin, C.L., Redington, R.W., Kressel, H.Y., Elliott, R.T., and McDougall, I.L., Human exposure to 4.0-tesla magnetic fields in a whole-body scanner, *Med Phys*, 19, 1089, 1992.
Schiffer, I.B., Schreiber, W.G., Graf, R., Schreiber, E.M., Jung, D., Rose, D.M., Hehn, M., Ebhard, S., Sagemuller, J., Spiess, H.W., Oesch, F., Thelen, M., and Hengstler, J.G., No influence of magnetic fields on cell cycle progression using conditions relevant for patients during MRI, *Bioelectromagnetics*, 24, 241, 2003.
Schulten, K., Staerk, H., Weller, A., Werner, H.J., and Nickel, B., Magnetic field dependence of the geminate recombination of radical ion pairs in polar solvents, *Z Phys Chem N F*, 101, 371, 1976.
Segal, N.A., Toda, Y., Huston, J., Saeki, Y., Shimizu, M., Fuchs, H., Shimaoka, Y., Holcomb, R., and McLean, M.J., Two configurations of static magnetic fields for treating rheumatoid arthritis of the knee: a double-blind clinical trial, *Arch Phys Med Rehabil*, 82, 1453, 2001.
Sekino, M., Inoue, Y., and Ueno, S., Magnetic resonance imaging of mean values and anisotropy of electrical conductivity in the human brain, *Neurol Clin Neurophysiol*, 55, 1, 2004a.
Sekino, M., Matsumoto, T., Yamaguchi, K., Iriguchi, N., and Ueno, S., A method for NMR imaging of a magnetic field generated by electric current, *IEEE Trans Magn*, 40, 2188, 2004b.
Sekino, M., Mihara, H., Iriguchi, N., and Ueno, S., Dielectric resonance in magnetic resonance imaging: signal inhomogeneities in samples of high permittivity, *J Appl Phys.*, 97, 10R303, 2005.
Shellock, F.G. (Ed.), *Magnetic Resonance Procedures: Health Effects and Safety*, CRC Press, Boca Raton, FL, 2001.
Shupak, N.M., Hensel, J.M., Cross-Mellor, S.K., Kavaliers, M., Prato, F.S., and Thomas, A.W., Analgesic and behavioral effects of a 100 microT specific pulsed extremely low frequency magnetic field on control and morphine treated CF-1 mice, *Neurosci Lett*, 354(1), 30, 2004a.
Shupak, N.M., Prato, F.S., and Thomas, A.W., Human exposure to a specific pulsed magnetic field: effects on thermal sensory and pain thresholds, *Neurosci Lett*, 363(2), 157, 2004b.
Slowik, T.J., Green, B.L., and Thorvilson, H.G., Detection of magnetism in the red imported fire ant (*Solenopsis invicta*) using magnetic resonance imaging, *Bioelectromagnetics*, 18, 396, 1997a.
Slowik, T.J., Green, B.L., and Thorvilson, H.G., Response of red imported fire ant to magnetic field in the nest environment, *South Entomol*, 22, 301, 1997b.
Snyder, D.J., Jahng, J.W., Smith, J.C., and Houpt, T.A., c-Fos induction in visceral and vestibular nuclei of the rat brain stem by a 9.4 T magnetic field, *Neuro Report*, 11, 2681, 2000.
So, P., Stuchly, M.A., and Nyenhuis, J.A., Peripheral nerve stimulation by gradient switching fields in MRI, *IEEE Trans BioMed Eng*, 51, 1907, 2004.
Sonnier, H., Kolomytkin, O., and Marino, A, Resting potential of excitable neuroblastoma cell in weak magnetic fields, *Cell Mol Life Sci*, 57, 514, 2000.
Sonnier, H., Kolomytkin, O., and Marino, A., Action potentials from human neuroblastoma cells in magnetic fields, *Neurosci Lett*, 337, 163, 2003.
Squires, K.C., Development of a 37-channel SQUID-based magnetometer for study of the brain and heart, *Med Biol Eng Comput*, 29(Suppl), 761, 1991.
Stamenkovic-Radak, M., Kitanovic, I., Prolic, Z., Tomisic, I., Stojkovic, B., and Andjelkovic, M., Effect of permanent magnetic field on wing size parameters in *Drosophila melanogaster*, *Bioelectromagnetics*, 22, 365, 2001.
Stansell, M.J., Winters, W.D., Doe, R.H., and Dart, B.K., Increased antibiotic resistance of *E. coli* exposed static magnetic fields, *Bioelectromagnetics*, 22, 129, 2001.
Stavroulakis, P. (ed.), *Biological Effects of Electromagnetic Fields*, Springer-Verlag, Berlin, 2003.
Stefano, G. and Tranquillo, R.T., A methodology for the systematic and quantitative study of cell contact guidance in orientated collagen gels, *J Cell Sci*, 105, 317, 1993.
Stern, S., Laties, V.G., Nguyen, Q.A., and Cox, C., Exposure to combined static and 60 Hz magnetic fields: failure to replicate a reported behavioral effect, *Bioelectromagnetics*, 17, 279, 1996.
Steyn, P.F., Ramey, D.W., Kirschvink, J., and Uhring, J., Effect of a static magnetic field on blood flow to the metacarpus in horses, *J Am Vet Med Assoc*, 217, 874, 2000.
Strickman, D., Timberlake, B., Estrada-Franco, J., Weissman, M., Fenimore, P.W., and Novak, R.J., Effects of magnetic fields on mosquitoes, *J Am Mosq Control Assoc*, 16, 131, 2000.

Suzuki, M., and Nakamura, H., Orientation of sperm DNA under a magnetic field, *Proc Jpn Acad*, 71(Ser B), 36, 1995.

Suzuki,Y., Ikehata, M., Nakamura, K., Nishioka, M., Asanuma, K., Koana, T., and Shimizu, H., Induction of micronuclei in mice exposed to static magnetic fields, *Mutagenesis*, 16, 499, 2001.

Tablado, L., Perez-Sanchez, F., and Soler, C., Is sperm motility maturation affected by static magnetic field? *Environ Health Perspect*, 104, 1212, 1996.

Tablado, L., Perez-Sanchez, F., Nunez, J., Nunez, M., and Soler, C., Effects of exposure to static magnetic fields on the morphology and morphometry of mouse epididymal sperm, *Bioelectromagnetics*, 19, 377, 1998.

Tablado, L., Soler, C., Nunez, M., Nunez, J., and Perez-Sanchez, F., Development of mouse testis and epididymis following intrauterine exposure to a static magnetic field, *Bioelectromagnetics*, 21, 19, 2000.

Takashima, Y., Miyakoshi, M., Ikehara, M., Iwasaka, M., Ueno, S., and Koana, T., Genotoxic effects of strong static magnetic fields in DNA-repair defective mutants of *Drosphila melanogaster*, *J Radiat Res*, 45, 393, 2004.

Takebe, H., Shiga, T., Kato, M., and Masada, E., *Biological and Health Effects from Exposure to Power-Line Frequency Electromagnetic Fields—Confirmation of Absence of Any Effects at Environmental Field Strengths*, IOS Press, Amsterdam, 1999.

Tanimoto, Y., Hayashi, H., Nagakura, S., Sakurai, H., and Tokumaru, K. The external magnetic field effect on the singlet sensitized photolysis of dibenzoyl peroxide, *Chem Phys Lett*, 41, 267, 1976.

Tanimoto, Y., Izumi, S., Furuta, K., Suzuki, T., Fujiwara, Y., Fujiwara, M., Hirata, T., and Yamada, S., Effects of high magnetic field on *Euglena gracilis*, *Int J Appl Electromagn Mech*, 14, 311, 2001.

Tanimoto, Y., Ogawa, S., Fujitani, K., Fujiwara, Y., Izumi, S., and Hirata, T., Effects of a high magnetic field on *E. coli* movement, *Environ Sci*, 18, 53, 2005.

Tanioka, N., Sawada, S., and Hosokawa, T., Proliferative and metastatic activities of mouse tumor cells exposed to a strong static magnetic field, *Bioelectrochem Bioenerg*, 40, 29, 1996.

Taoka, S., Padmakumar, R., Grissom, C.B., and Banerjee, R., Magnetic field effects on coenzyme B12-dependent enzymes: validation of ethanolamine ammonia lyase results and extension to human methylmalonyl CoA mutase, *Bioelectromagnetics*, 18, 506, 1997.

Tenforde, T.S., Magnetcally induced electric fields and currents in the circulatory systems, *Prog Biophys Mol Biol*, 87, 279, 2005.

Teodori, L., Grabarek, J., Smolewski, P., Ghibelli, L., Bergamaschi, A., De Nocola, M., and Darzynkiewicz, Z., Exposure of cells to static magnetic field accelerated loss integrity of plasma membrane during apoptosis, *Cytometry*, 49, 113, 2002.

Testorf, M.F., Oberg, P.A., Iwasaka, M., and Ueno, S., Melanophore aggregation in strong static magnetic fields, *Bioelectromagnetics*, 23, 444, 2002.

Thomas, J.R., Schrot, J., and Liboff, A.R., Low-intensity magnetic fields alter operant behavior in rats, *Bioelectromagnetics*, 7, 349, 1986.

Till, U., Timmel, C.R., Brocklehurst, B., and Hore, P.J., The influence of very small magnetic field on radical recombination reactions in the limit of slow recombination, *Chem Phys Lett*, 298, 87, 1998.

Timmel, C.R., Till, U., Brocklehurst, B., McLauchlan, K.A., and Hore, P.J., Effects of weak magnetic fields on free radical recombination reactions, *Mol Phys*, 95, 71, 1998.

Tofani, S., Barone, D., Cintorino, M., de Santi, M.M., Ferrara, A., Orlassino, R., Ossola, P., Peroglio, F., Rolfo, K., and Ronchetto, F., Static and ELF magnetic fields induce tumor growth inhibition and apoptosis, *Bioelectromagnetics*, 22, 419, 2001.

Tofani, S., Cintorino, M. et al., Increased mouse survival, tumor growth inhibition and decreased immunoreactive p53 after exposure to magnetic fields, *Bioelectromagnetics*, 23, 230, 2002.

Tofani, S., Barone, D., Berardelli, M., Berno, E., Cintorino, M., Foglia, L., Ossola, P., Ronchetto, F., Toso, E., and Eandi, M., Static and ELF magnetic fields enhance the *in vivo* anti-tumor efficacy of cis-platin against Lewis lung carcinoma, but not of cyclophosphamie against B16 melanotic melanoma, *Pharmacol Res*, 48, 83, 2003.

Torbet, J. and Ronziere, M.C., Magnetic alignment of collagen during self-assembly, *Biochem J*, 219, 1057, 1984.

Torbet, J., Fryssinet, M., and Hudry-Clergeon, G., Oriented fibrin gels formed by polymerization in strong magnetic fields, *Nature*, 289, 91, 1981.

Trabulsi, R., Pawlowski, B., and Wieraszko, A., The influence of steady magnetic fields on the mouse hippocampal evoked potentials *in vitro*, *Brain Res*, 728, 135, 1996.
Tranquillo, R.T., Girton, T.S., Bromberek, B.A., Triebes, T.G., and Mooradian, D.L., Magnetically oriented tissue-equivalent tubes: application to a circumferentially oriented media-equivalent, *Biomaterials*, 17, 349, 1996.
Tsuchiya, K., Nakamura, K., Okuno, K., Ano, T., and Shoda, M., Effect of homogeneous and inhomogeneous high magnetic fields on the growth of *Escherichia coli*, *J Ferment Bioeng*, 81, 343, 1996.
Tsuchiya, K., Okuno, K., Ano, T., Tanaka, K., Takahashi, H., and Shoda, M., High magnetic field enhances stationary phase-specific transcription activity of *Escherichia coli*, *Bioelectrochem Bioenerg*, 48, 383, 1999.
Tsuji, Y., Nakagawa, M., and Suzuki, Y., Five-tesla static magnetic fields suppress food and water consumption and weight gain in mice, *Ind Health*, 34, 347, 1996.
Tuch, D.S., Wedeen, V.J., Dale, A.M., George, J.S., and Belliveau, J.W., Conductivity tensor mapping of the human brain using diffusion tensor MRI, *Proc Natl Acad Sci USA*, 98, 11697, 2001.
Ueno, S., Quenching of flames by magnetic fields, *J Appl Phys*, 65(3), 1243, 1989.
Ueno, S., *Biological Effects of Magnetic and Electromagnetic Fields*, Plenum Press, New York, 1996.
Ueno, S. and Harada, K., Redistribution of the dissolved oxygen concentration under strong DC magnetic field, *IEEE Trans Magn*, MAG-18, 1704, 1982.
Ueno, S. and Harada, K., Experimental difficulties in observing the effects of magnetic fields on biological and chemical processes, *IEEE Magn*, 22, 868, 1986.
Ueno, S. and Harada, K., Effects of magnetic fields on flames and gas flow, *IEEE Trans Magn*, MAG-23, 5, 2752, 1987.
Ueno, S. and Iramina, K., Modeling and source localization of MEG activities, *Brain Topogr*, 3, 151, 1991.
Ueno, S and Iriguchi, N., Impedance magnetic resonance imaging: a method for imaging of impedance distributions based on magnetic resonance imaging, *J Appl Phys*, 83, 6450, 1998.
Ueno, S. and Iwasaka, M., Parting of water by magnetic fields, *IEEE Trans Magn*, 30, 4698, 1994a.
Ueno, S. and Iwasaka, M., Properties of diamagnetic fluid in high gradient magnetic fields, *J Appl Phys*, 75, 7177, 1994b.
Ueno, S., Matsumoto, S., Harada, K., and Oomura, Y., Capacitative stimulatory effect in magnetic stimulation of nerve tissue, *IEEE Trans Magn*, MAG-14, 958, 1978.
Ueno, S., Lovsund, P., and Oberg, P.A., Effects of alternating magnetic fields and low-frequency electric currents on human skin blood flow, *Med Biol Eng Comput*, 24, 57, 1986a.
Ueno, S., Lovsund, P., and Oberg, P.A., Effects of time-varying magnetic fields on action potential in lobster giant axon, *Med Biol Eng Comput*, 24, 521, 1986b.
Ueno, S., Tashiro, T., and Harada, K., Localized stimulation of neural tissues in the brain by means of a paired configuration of time-varying magnetic fields, *J Appl Phys*, 64, 5862, 1988.
Ueno, S., Matsuda, T., and Fujiki, M., Localized stimulation of the human cortex by opposing magnetic fields, in *Advances in Biomagnetism* (Williamson, S.J., Hoke, M., Stroink, G., and Kotani, M., Eds.), Plenum Press, New York, 529, 1989.
Ueno, S., Matsuda, T., and Fujiki, M., Functional mapping of the human motor cortex obtained by focal and vectorial magnetic stimulation of the brain, *IEEE Trans Magn*, 26, 1539, 1990a.
Ueno, S., Matsuda, T., and Hiwaki, O., Estimation of structures of neural fibers in the human brain by vectorial magnetic stimulation, *IEEE Trans Magn*, 27, 5387, 1990b.
Ueno, S., Matsuda, T., and Hiwaki, O., Localized stimulation of the human brain and spinal cord by a pair of opposing pulsed magnetic fields, *J Appl Phys*, 66, 5838, 1991.
Ueno, S., Hiwaki, O., Matsuda, T. et al., Safety problems of dB/dt associated with echo planar imaging, *Ann NY Acad Sci*, 369, 96, 1992.
Ueno, S., Iwasaka, M., and Tsuda, H., Effects of magnetic fields on fibrin polymerization and fibrinolysis, *IEEE Trans Magn*, 29, 3352, 1993.
Valles, J.M. Jr., Model of magnetic field-induced mitotic apparatus reorientation in frog eggs, *Biophys J*, 82, 1260, 2002.
Valles, J.M. Jr., Lin, K., Denegre, J.M., and Mowry, K.L., Stable magnetic field gradient levitation of *Xenopus laevis*: toward low-gravity simulation, *Biophys J*, 73, 1130, 1997.

Valles, J.M. Jr., Wasserman, S.R.R.M., Schweidenback, C., Edwardson, J., Denegre, J.M., and Mowry, K.L., Processes that occur before second cleavage determine third cleavage orientation in *Xenopus*, *Exp Cell Res*, 274, 112, 2002.
van Rongen, E., International workshop ''effects of static magnetic fields relevant to human health'' Repporteurs report: dosimetry and volunteer studies, *Prog Biophys Mol Biol*, 87, 329, 2005.
Veliks, V., Ceihnere, E., Svikis, I., and Aivars, J., Static magnetic field influence on rat brain function detected by heart rate monitoring, *Bioelectromagnetics*, 25, 211, 2004.
Vink, C.B. and Woodward, J.R, Effect of a weak magnetic field on the reaction between neural free radicals in isotropic solution, *J Am Chem Soc*, 126, 16730, 2004.
Volpe, P., Interactions of zero-frequency and oscillating magnetic fields with biostructures and biosystems, *Photochem Photobiol Sci*, 2, 637, 2003.
Vrva, J., Bette, K., and Burband, M., Whole cortex 64 channel SQUID biomagnetometer system, *IEEE Trans*, AS 3, 1878, 1993.
Watanabe, Y., Nakagawa, M., and Miyakoshi, Y., Enhancement of lipid peroxidation in liver of mice exposed to magnetic fields, *Ind Health*, 35, 285, 1997.
Wieraszko, A., Dantrolene modulates the influence of steady magnetic fields on hippocampal evoked potentials *in vivo*, *Bioelectromagnetics*, 21, 175, 2000.
Wiltschko, R. and Wiltschko, W., *Magnetic Orientation in Animals*, *Zoophysiology*, vol. 33, Springer-Verlag, Berlin, 1995.
Wiltschko, R. and Wiltschko, W., Magnetoreception: why is conditioning so seldom successful? *Naturewissenschaften*, 83, 241, 1996.
Wiltschko, W. and Wiltschko, R., Light-dependent magnetoreception in birds: the behaviour of European robins, *Erithacus rubecula*, under monochromatic light of various wavelengths and intensities, *J Exp Biol*, 204, 3295, 2001.
Wiltschko, W. and Wiltschko, R., Magnetic compass orientation in birds and its physiological basis, *Naturwissenschaften*, 89, 445, 2002.
Winklhofer, M., Holtkamp-Roetzler, E., Hanzlik, M., Fleissner, G., and Petersen, N., Clusters of superparamagnetic magnetite particles in the upper-beak skin of homing pigeons: evidence of a magnetoreceptor? *Eur J Miner*, 13, 659, 2001.
Winnicki, A., Formicki, K., and Sobocinski, A., Application of constant magnetic field in transportation of gametes and fertilized eggs of salmonid fish, *Publ Espec Inst Esp Oceanogr*, 21, 301, 1996.
Wiskirchen, J., Groenwaeller, E.F., Kehlbach, R., Heinzelmann, F., Wittau, M., Rodemann, H.P., Claussen, C.D., and Duda, S.H., Long-term effects of repetitive exposure to a static magnetic field (1.5 T) on proliferation of human fetal lung fibroblasts, *Magn Reson Med*, 41, 464, 1999.
Wiskirchen, J., Groenwaller, E.F., Heinzelmann, F., Kehlbach, R., Rodegerdts, E., Wittau, M., Rodemann, H.P., Claussen, C.D., and Duda, S.H., Human fetal lung fibroblasts, *in vitro* study of repetitive magnetic field exposure at 0.2, 1.0, and 1.5 T, *Radiology*, 215, 858, 2000.
Xiong, J., Fox, P.T., and Gao, J.H., Directly mapping magnetic field effects of neuronal activity by magnetic resonance imaging, *Hum Brain Mapp*, 20, 41, 2003.
Xu, S., Okano, H., and Ohkubo, C., Subchronic effects of static magnetic fields on cutaneous microcirculation in rabbits, *In Vivo*, 12, 383, 1998.
Xu, S., Okano, H., and Ohkubo, C., Acute effects of whole-body exposure to static magnetic fields and 50-Hz electromagnetic fields on muscle microcirculation in anesthetized mice, *Bioelectromagnetics*, 53, 127, 2000.
Xu, S., Tomita, N., Ohata, R., Yan, Q., and Ikada, Y., Static magnetic field effects on bone formation of rats with an ischemic bone model, *BioMed Mater Eng*, 11, 257, 2001.
Yamagishi, A., Takeuchi, T., Higashi, T., and Date, M., Diamagnetic orientation of polymerized molecules under high magnetic field, *J Phys Soc Jpn*, 58, 2280, 1989.
Yamaguchi, S., Ogiue-Ikeda, M., Sekino, M., and Ueno, S., The effect of repetitive magnetic stimulation on the tumor development, *IEEE Trans Magn*, 40, 3021, 2004.
Yamaguchi, S., Ogiue-Ikeda, M., Sekino, M., and Ueno, S., Effects of pulsed magnetic stimulation on tumor development and immune functions in mice, *Bioelectromagnetics*, 27, 64, 2006.
Yan, Q.C., Tomita, N., and Ikada, Y., Effects of static magnetic field on bone formation of rat femurs, *Med Eng Phys*, 20, 397, 1998.

Yano, A., Ogura, M., Sato, A., Sakaki, Y., Shimizu, Y., Baba, N., and Nagasawa, K., Effect of modified magnetic field on the ocean migration of maturing chum salmon, *Oncorhynchus keta*, *Mar Biol*, 129, 523, 1997.

Yano, A., Hidaka, E., Fujiwara, K., and Iimoto, M., Induction of primary root curvature in radish seedlings in a static magnetic field, *Bioelectromagnetics*, 22, 194, 2001.

Yoon, R.S., DeMonte, T.P., Hasanov, K.F., Jorgenson, D.B., and Joy, M.L.G., Measurement of thoracic current flow in pigs for the study of defibrillation and cardioversion, *IEEE Trans Biomed Eng*, 50, 1167, 2003.

Yoshida, H., Ueno, S., Cheyne, D., and Weinberg, H., Measurements of low frequency brain magnetic fields associated with four-tone memory processes, *IEEE Trans Magn*, 31, 4268, 1995.

Zangaladze, A., Epstein, C.M., Grafton, S.T., and Sathian, K., Involvement of visual cortex in tactile discrimination of orientation, *Nature*, 401, 587, 1999.

Zhadin, M.N., Review of Russian literature on biological action of DC and low-frequency AC magnetic fields, *Bioelectromagnetics*, 22, 27, 2001.

Zhadin, M.N., Novikov, V.V., Barnes, F.S., and Pergola, N.F., Combined action of static and alternating magnetic fields on ionic current in aqueous glutamic acid solution, *Bioelectromagentics*, 19, 41, 1998.

Zhadin, M.N., Deryugina, O.N., and Pisachenko, T.M., Influence of combined DC and AC magnetic fields on rat behavior, *Bioelectromagnetics*, 20, 378, 1999.

Zhang, Q.-M., Tokiwa, M., Doi, T., Nakahara, T., Chang, P.-Q., Nakamura, N., Hori, M., Miyakoshi, J., and Yonei, S., Strong static magnetic field and the induction of mutations through elevated production of reactive oxygen species in *Escherichia coli* soxR, *Int J Radiat Biol*, 79, 281, 2003.

Zmyslony, M., Palus, J., Jajte, J., Dziubaltowska, E., and Rajkowska, E., DNA damage in rat lymphocytes treated *in vivo* with iron cations and exposed to 7 mT magnetic fields (static or 50 Hz), *Mutat Res*, 453, 89, 2000.