NIH - OAM
Electromagnetics

Panel Report

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NIH-OAM Panel Report:

Electromagnetic Applications In Medicine

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Submitted to:

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I. Introduction

A. Background

Medical practice has always been based on an evolving body of knowledge. Today there is increasing evidence that electromagnetic (EM) phenomena are more intimately involved in life processes than previously believed. Bioelectromagnetics (BEM) is the emerging science which studies how living organisms interact with EM fields. (See the Glossary in Appendix B for a more complete definition.)

Further development of the medical applications of BEM can serve the mission of the National Institutes of Health, in general, and the NIH Office of Alternative Medicine, in particular, as follows:

- In clinical practice, BEM offers the possibility of more economical and more effective diagnoses and new noninvasive therapies for medical problems, including those considered intractable or recalcitrant to conventional treatments. A sizeable body of recent work (cited in this report) has established the feasibility of treatments based on BEM, although presently the mainstream medical community is largely unaware of this work.

- In biomedical research, BEM can provide a better understanding of fundamental mechanisms of communication and regulation at levels ranging from intracellular to organismic. An improved knowledge of fundamental mechanisms of EM field interactions could lead directly to major advances in diagnostic and treatment methods.

- In the study of other alternative medical modalities, BEM offers a unified conceptual framework which can help explain how certain diagnostic and therapeutic techniques (e.g., acupuncture, homeopathy, ethnomedicine and healer effects) may produce results which are difficult to understand from a more conventional viewpoint. These areas of alternative medicine are based entirely on empirical and phenomenological approaches. Their future development could be accelerated if a scientific understanding of their mechanisms of action is attained.

This report addresses the following main topics:

- accomplishments of BEM research as reported in the literature (Section II)
- opportunities for future research on BEM applications (Sections III and IV)
- barriers to BEM research, and recommendations to overcome them (Section V)

B. Key Concepts in Bioelectromagnetics

Bioelectromagnetics essentially underlies biochemistry, in that chemical reactions of biological importance are mediated by the electromagnetic force. For instance, utilization of ATP, which provides the energy for life processes, can be viewed as a charge transfer process as well as a reaction (de-phosphorylation) among chemical species. However, BEM goes beyond biochemistry by emphasizing the fact that electromagnetic interactions are fundamentally important not just at the molecular level, but at all levels of biological organization, ranging from the sub-cellular to the whole organism. Consider, for example, that much of an organism's caloric intake is utilized to produce and maintain electrical activity, such as maintenance of membrane potential gradients, nerve activity, etc.

Figure 1 on the following page illustrates several types of EM fields of interest in BEM. Fields of *endogenous* origin (produced within the body) are to be distinguished from *exogenous* fields (produced by sources outside of the body). Exogenous EM fields can be classified as either natural, such as the earth's geomagnetic field, or artificial. Among the latter are those generated by electrical equipment (such as power lines, transformers, appliances, radio transmitters, etc.), as well as fields applied to the body intentionally by clinical devices. The term "electropollution" refers to man-made EM fields which may have harmful effects on humans.

There is increasing awareness of potential health hazards of certain man-made EM fields, as for example, power line fields at 60 Hz frequency [e.g., Nair et al., 1989; Wilson' et al., 1990; Bierbaum and Peters, 1991]. Recent epidemiological studies and other evidence indicates that problems may exist. However, this does not preclude the possibility that other natural or clinically applied EM fields, which have hardly been investigated, may have beneficial effects.

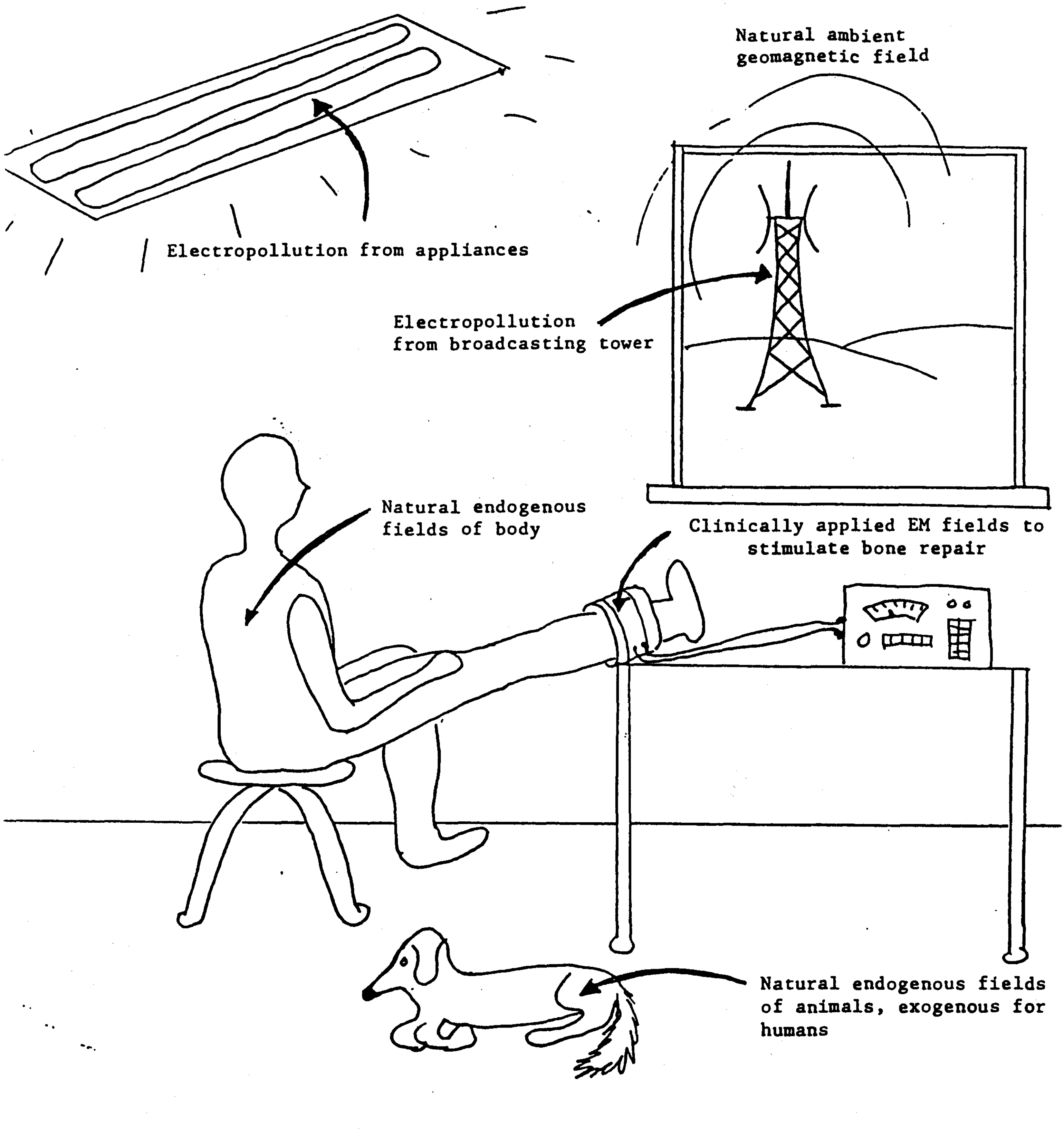

Figure 1. Examples of natural and man-made EM fields, exogenous and endogenous.

<Figure 1 goes on this page: picture of human w/ endogenous fields inside, natural exogenous fields outside, including the geomagnetic, and artificial exogenous field also outside (electropollution and those clinically applied). Person w/ arthritic leg w/ applied M-field coil; show microwave transmitter or radar antenna in environment.>

Table 1 below shows the usual classification of EM fields in terms of their frequency of oscillation, ranging from DC (direct current) through extremely low frequency, low frequency, radio frequency, microwave and radar, infrared, visible light, ultraviolet, X-rays, and gamma rays. For oscillating fields, the higher the frequency, the greater the energy content.

Table 1. Electromagnetic Spectrum

frequency range (Hz) - *note 1*	**classification**	
0	direct current (DC)	non-ionizing
0 – 300	extremely low frequency (ELF)	non-ionizing
300 – 10^4	low frequency (LF)	non-ionizing
10^4 – 10^9	radio frequency (RF) - *note 2*	non-ionizing
10^9 – 10^{12}	microwave and radar bands	non-ionizing
10^{12} – 4×10^{14}	infrared band (IR)	non-ionizing
4×10^{14} – 7×10^{14}	visible light	weakly ionizing
7×10^{14} – 10^{18}	ultraviolet band (UV)	weakly ionizing
10^{18} – 10^{20}	X-rays	strongly ionizing
over 10^{20}	gamma rays	strongly ionizing

note 1: Division of the EM spectrum into frequency bands is based on conventional but arbitrary usage in various disciplines.

note 2: Within the RF band, many sub-bands are often identified separately, including ultra-low frequency (ULF), very low frequency (VLF), ultra-high frequency (UHF), and very high frequency (VHF).

In radiation biophysics, an EM field is classified as *ionizing* if its quantum energy is enough (i.e., greater than approximately 10 eV) to dislodge electrons from an atom or molecule. High energy, high frequency forms of EM radiation (such as gamma rays and X-rays) are *strongly* ionizing in biological matter. Radiation in the middle portion of the frequency and energy spectrum (such as visible and especially ultraviolet light) is *weakly* ionizing, i.e., it can be ionizing or not, depending on the target molecules.

A very significant experimental discovery of BEM is that oscillating nonionizing EM fields in the very low ELF range can have profound bioeffects [e.g., Becker and Marino, 1982; Brighton and Pollack, 1991]. This discovery is a cornerstone in the foundation of BEM, and its full implications in medicine and biology are as yet unknown.

The frequency spectrum approach has known limitations because frequency is a meaningful parameter only for steady periodic waveforms. Transients (which have been implicated in health hazards of nearby power lines) and non-sinusoidal waveforms do not have a single well-defined frequency, and must be defined in terms of a range of frequencies, along with duration, intensity, phase, and possibly other factors.

It is unknown at present whether all EM field parameters relevant to biological interactions have been identified. Also, dosimetry of nonthermal EM fields (i.e., characterization and measurement of the relevant field parameters at the site of action) presents complex problems that are not fully resolved. An EM field in free space can be characterized in simple engineering terms such as field strength, directionality, frequency, duration and waveform. However, the human body's high conductivity (compared to air) at ELF frequencies can greatly modify an externally applied field. Local field strength near highly curved parts of the body, such as the head and fingertips, can be an order of magnitude greater than that of the free space field.

The actual mechanism by which exogenous EM fields produce biological effects is under intense study. Experimental evidence suggests that the cell membrane is one of the primary sites at which applied EM fields act on the cell. EM forces at the membrane's outer surface could modify ligand-receptor interactions (e.g., binding of hormones and growth factors), which in turn can alter the state of membrane macromolecules which help control the cell's internal processes [Tenforde and Kaune, 1987]. Experiments to establish the full details of a mechanistic chain of events such as this, however, are just beginnig.

Another line of study focuses on endogenous EM fields. The body's ubiquitous electrical activity at the level of tissues and organs is known to exhibit macroscopic patterns (or structures) which contain medically useful information. The diagnostic procedures of electroencephalography (EEG) and electrocardiography (EKG), for instance, are based on detection of endogenous EM fields produced in the central nervous system (CNS) and heart muscle, respectively. Current BEM research is exploring the possibility that weak EM fields associated with nerve activity in other tissues and organs might also carry information of diagnostic value. New technologies for constructing extremely sensitive EM transducers (e.g., magnetometers and electrometers) and for signal processing have made this line of research feasible.

A relatively new experimental discovery in BEM is that a form of highly coherent endogenous EM radiation (biophotons) is emitted by most living organisms, ranging from plant seeds to humans [Popp et al., 1984; Popp et al. 1988; Chwirot et al., 1987; Popp et al., 1992; Mathew and Rumar, in press]. There are indications that such endogenous EM fields are important in bioregulation, membrane transport, and gene expression, and that the effects (both beneficial and harmful) of exogenous fields are mediated by alterations in endogenous fields. For example, externally applied EM fields may act to correct abnormalities in endogenous EM fields characteristic of disease states. In research on alternative medicine, biophoton processes may prove to be involved in "energy medicine" modalities such as homeopathy, healer effects, and acupuncture.

A more detailed introduction to the field of BEM and an overview of research progress is available in the following monographs and conference proceedings: Liboff and Rinaldi, 1974; Brighton et al., 1979; Becker and Marino, 1982; Adey and Lawrence, 1984; Blank and Findl, 1987; Marino, 1988; O'Connor and Lovely, 1988; O'Connor et al., 1990; Brighton and Pollack, 1991; Ramel and Norden, 1991; Popp et al., 1992; Blank, 1993.

C. Controversial Issues

This Panel believes that several controversial issues surrounding BEM have inhibited progress in both science and medicine. These fall into roughly three distinct areas:

1. **Medical Controversy.** To conventional medical practitioners, BEM applications have a mixed reputation, ranging from obscure but possibly effective medical procedures to outright misuse. This can be resolved by bridging the gap between research and practice through certain steps including:

    - Conducting properly designed clinical trials to validate effects that have been reported or claimed for certain BEM-based treatments.

    - Increasing awareness within the medical community of well-documented, controlled clinical trials which already indicate the effectiveness of specific BEM applications (e.g., see Table 2).

2. **Scientific Controversy.** Some physicists claim that low intensity, nonionizing EM fields can have no bioeffects other than resistive (Joule) heating of tissue. Their argument is based on a physical model in which the only EM field parameter considered relevant to biological systems is power density [e.g., Adair, 1991]. They claim that measurable nonthermal bioeffects of EM fields are "impossible" because they contradict known physical laws or would require a "new physics" to explain them.

However, the BEM scientific community has addressed these questions both experimentally and theoretically. Numerous independent experiments reported in the refereed literature conclusively establish that nonthermal bioeffects of low intensity EM fields do indeed exist. Moreover, the experimental results lend support to certain new approaches in theoretical modelling of the interactions between EM fields and biological matter. Most researchers now feel that BEM bioeffects will become comprehensible, not by forsaking physics, but rather by developing more sophisticated (detailed) models based on known physical laws, in which additional parameters (such as frequency, intensity, waveform, field directionality, and others) are taken into account.

Above all, it must be recognized that this is a traditional scientific debate. It reflects only the difference of scientific opinions and typically occurs whenever a new scientific discipline is emerging. It can be resolved by applying the scientific method in the time-honored fashion; i.e., through experimentation, open publication of results, and unimpeded discussion.

3. **Social Controversy.** The use of electricity for both power and communication is woven into the very fabric of the U.S. economy. The safety of technologies such as electric power equipment and radio transmission is a legitimate matter of public concern and public policy. However, the policy debate on possible health hazards of EM fields from these sources has constrained research on the potential benefits of medically-applied EM fields of other types. In addition, a variety of economic, political, and social interest groups have attempted to influence in their own favor the medical and scientific debates in BEM.

   The role of BEM is not to advocate any particular position in the policy debate, but rather to document and quantify whatever hazardous and beneficial effects may be found to exist, and to communicate clearly these results to the public. A public information system without ties to vested interests is critical to progress in all fields of alternative medicine.

Controversial issues regarding alternative medicine in general, and BEM in particular, could be resolved most rapidly if university-based science were to play a larger role in future research, considering that academia is traditionally associated with fewer constraints and greater freedom to study frontier topics.

II. Applications of Bioelectromagnetics in Medicine

A. Overview

Medical applications of BEM have developed over a long period. As with other treatment modalities, certain BEM medical applications were seen as unconventional at first, only to become widely accepted later.

BEM medical applications may be classified according to whether the EM fields they employ are ionizing (capable of dislodging electrons) or nonionizing:

1. **Ionizing radiation**
   - X-rays
   - Therapies using gamma rays from radioactive isotopes (nuclear medicine)

2. **Nonionizing radiation**. These may be categorized as "thermal" or "nonthermal" (See Comment 3.b. below regarding the term "nonthermal.")

   a. **Thermal applications of nonionizing radiation** (i.e., application of heat).
   - Radiofrequency (RF) hyperthermia
   - Laser and RF surgery
   - RF diathermy

b. **Nonthermal applications of nonionizing radiation.** These are the most important BEM modalities. Section II.B. (below) discusses those in the following list that are considered new or unconventional.

i) **Diagnostic applications**

- Galvanic skin response (GSR) elicits a profile of psycho-physiological states by measuring changes in skin electrical conductivity.
- Electroencephalography (EEG), electrocardiography (EKG) and magnetic resonance imaging (MRI) are well-established diagnostic techniques.
- Diagnostic neuromagnetic stimulation assesses the patient's physiological response to a noninvasive, cerebrally-applied magnetic pulse.
- Magnetoencephalography (MEG) uses a SQUID (superconducting quantum interference device) to measure very weak endogenous magnetic fields associated with brain activity; i.e., MEG is the magnetic analogue of EEG.
- Other novel BEM devices are used to detect small electrical currents that may be associated with acupuncture meridians.

ii) Therapeutic applications

- Electromagnetic bone repair
- Electrostimulation therapies, including TENS (transcutaneous electrical nerve stimulation) and TCES (transcranial electrostimulation) used for chronic pain treatment and for soft-tissue healing and regeneration
- Electroacupuncture, magnetoacupuncture, and laser stimulation
- Microwave resonance therapy (MRT) and other exploratory methods pioneered outside the U.S. (see Comment 3.c. below).

3. **Comments.**

a. A large number of independent parameters characterize nonthermal nonionizing EM fields, including: pulsed vs. non-pulsed, sinusoidal vs. other waveforms, frequency, phase, intensity (as a function of spatial position), voltage, and current. If multiple fields are combined, these parameters must be specified for each component. Additional parameters needed to characterize the medical application of EM fields include the site of application and time-course of exposure. All of these can be experimentally varied, producing an enormous range of possibilities.

b. The term "nonthermal" is used with two different meanings in the medical and scientific literature:

- *Biologically* (or medically) nonthermal means "causes no significant gross tissue heating"; this is the most common usage.

- *Physically* nonthermal means "below the thermal noise limit at physiological temperatures." Thermal noise represents a much lower energy level than that required to cause heating of tissue; thus, any physically nonthermal application is automatically biologically nonthermal.

All of the "nonthermal applications of nonionizing radiation" listed above under item II.A.2.b. are nonthermal in the biological sense, i.e., they cause no significant heating of tissue. Some of the newer unconventional BEM applications are also physically nonthermal.

c. A variety of alternative medical practices developed outside the U.S. employ nonionizing EM fields at nonthermal intensities (i.e., below those known to cause tissue heating). For instance, microwave resonance therapy (MRT) in Russia uses low-intensity continuous or pulse-modulated sinusoidal microwave radiation at frequencies specified by the Russian Ministry of Health to treat conditions including arthritis, ulcers, esophagitis, hypertension, chronic pain, neurologic disorders, and side effects of cancer chemotherapy. The mechanism of action is thought to involve modifications in cell membrane transport and/or production of corticoids and other chemical mediators. Although a sizeable body of literature on this technique already exists in Russian [e.g., Devyatkov et al., 1991], investigators in the West will need to conduct independent validation studies. If such treatments prove to be effective, current views on the role of information and "thermal noise" (i.e., order and disorder) in living systems may need revision.

d. Some of the modalities listed above, although presently accepted medically or legally in the U.S., have not necessarily passed the most recent requirements of safety or efficacy. In relation to this, the Panel expresses the following concerns regarding the "grandfather clause."

FDA approval of a significant number of BEM-based devices, primarily those used in bone repair (see Section II.B.1 below). and neurostimulation (see Section II.B.2) was obtained under the grandfather clause. That is, medical devices sold in the U.S. prior to the Medical Device Law of the late 1970's automatically received FDA approval for use in the same manner and for the same medical conditions for which they were used prior to the law's enactment. Grandfathering by the FDA applies not only to BEM devices, but to all devices covered by the Medical Device Law.

This Panel cautions that the safety and/or efficacy of grandfathered devices is not established; i.e., they are approved on the basis of a "presumption" by the FDA, but are incompletely studied. Re-examination of devices in use, whether grandfathered or not, is recommended by this Panel.

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B. Important Clinical Applications

The major new (or "unconventional") applications of nonthermal nonionizing EM fields are described below. Table 2 provides an overview of selected citations to the refereed literature for these applications.

The first five applications listed below (bone repair, nerve stimulation, wound healing, osteoarthritis treatment, and electroacupuncture) have undergone clinical trials and are in limited clinical use.

Applications numbered 6 through 8 below offer the potential for developing new clinical treatments, based on existing animal and cellular studies, but clinical trials have not yet been conducted.

1. **Bone Repair.** Three different types of applied EM fields are known to promote healing of non-union bone fractures (i.e., those that fail to heal spontaneously):
   - pulsed (PEMF) and sinusoidal EM fields
   - direct current (DC)
   - combined AC/DC magnetic fields tuned to ion-resonant frequencies (these are extremely low intensity, physically nonthermal fields) [Weinstein et al., 1990]

FDA approval has been obtained on PEMF and DC applications and is pending for the AC/DC application. In PEMF and sinusoidal applications, the repitition frequencies used are in the

ELF range [Bassett, 1989]. In DC applications, magnetic field intensities range from 100 mG to 100 G, and electric currents range from less than 0.1 microampere to milliamperes [Baranowski, 1987]. FDA approval of these therapies covers only their use to promote healing of non-union bone fractures, not to accelerate routine healing of uncomplicated fractures.

Efficacy of EM bone repair treatment has been confirmed in double-blinded clinical trials [e.g., Barker et al., 1984; Sharrard, 1990]. A conservative estimate is that over 100,000 people have been treated with such devices [Lavine et al., 1972; Bassett et al., 1974; Brighton et al., 1979; Brighton et al., 1981; Bassett et al., 1982; Hinsenkamp et al., 1985].

2. **Stimulation and Measurement of Nerve Activity for Treatment and Diagnosis.** These applications fall into the following 5 categories:

   a. **TENS (transcutaneous electrical nerve stimulation).** Two electrodes are applied to the skin via wires attached to a portable device which may be clipped to the patient's belt [e.g., Hagfors and Hyme, 1975]. Over 100 types of FDA-approved devices in this category are presently available and used in physical therapy for pain relief.

b. **TCES (transcranial electrostimulation).** These devices are similar to the TENS units. They apply very low currents (below the nerve excitation threshold) to the brain via two electrodes applied to the head, and are used for behavior/psychological modification. A recent meta-analysis covering at least 12 clinical trials that were selected from over 100 published reports found that alleviation of anxiety is established [Klawansky, 1992]. With NIH support, TCES is under evaluation for alleviation of drug dependence.

c. **Neuromagnetic Stimulation.** In this application, which has both diagnostic and therapeutic uses, a magnetic pulse is applied noninvasively to a part of the patient's body to stimulate nerve activity via evoked current. In diagnostic use, a pulse is applied to the cerebral cortex and the patient's physiological responses are monitored to obtain a dynamic picture of the brain-body interface [e.g., Hallett, 1989]. As a treatment modality, it has replaced electro-shock therapy used to treat certain types of affective disorder (e.g., major depression)and seizures [Anninos and Tsagas, 1991]. It is also used in nerve conduction studies for conditions such as Carpal Tunnel Syndrome.

d. **Electromyography (EMG).** This diagnostic application detects electrical potentials associated with muscle contraction. Specific electrical patterns have been associated with specific abnormal states (e.g., denervated muscle), but the method has not yet been developed systematically beyond this.

e. **Electro-Retinography (ERG).** This diagnostic application monitors electrical potentials across the retina to assess eye movements. This is one of the only methods available for noninvasive monitoring of REM sleep.

3. **Soft-tissue Wound Healing.** Accelerated healing of soft-tissue wounds has been demonstrated in studies using DC, PEMF and electrochemical modalities, including the following:

- review of EM field applications to promote healing of chronic wounds [Vodovnik, 1992]
- double-blind studies of PEMF for healing of venous ulcers [Ieran et al., 1990; Stiller et al., 1992]
- application of ELF and RF fields to accelerate wound healing [O'Connor et al., 1990]
- electrochemical treatment that provides scarless regenerative wound healing [Becker, 1990]
- PEMF increases the rate of epithelialization in partial thickness wounds [Mertz et al., 1988]
- sinusoidal EM fields promotes vascular network repair [Herbst et al., 1988]
- human amniotic cells formed vascular tissue when exposed to magnetic fields [Yen-Patton et al., 1988]
- methods to treat atherosclerotic lesions and to control tissue growth have been patented [e.g., Gordon, 1986; Liboff et al., 1992b]

4. **Osteoarthritis.** In a recent clinical trial using a double-blind randomized protocol with placebo control, osteoarthritis (primarily of the knee) treated noninvasively by pulsed 30 Hz, 60 G magnetic fields (PEMF) showed an average 23 - 61% improvement of the treated group over that of placebo [Trock et al., in press]. It is believed that applied magnetic fields act to suppress inflammatory responses at the cell membrane level [O'Connor et al., 1990]

5. **Electroacupuncture.** Clinical benefits have been documented for the use of electrical stimulation in combination with acupuncture. Electrical stimulation via acupuncture needles is often used as a replacement or enhancement of manual needling. For example, a recent small-scale study showed electroacupuncture to be beneficial in the treatment of post-operative pain [Christensen and Noreng, 1989]. Other controlled studies have shown good success in using electro-acupuncture in the treatment of chemotherapy-induced sickness in cancer patients [Dundee and Ghaly, 1989]. Electrical stimulation was used recently to enhance the efficacy of manual acupuncture in a study showing benefit in the treatment of renal colic [Lee et al., 1992].

Electrical stimulation applied to acupuncture points has also demonstrated clinical benefits. In a controlled study, stimulation applied by a TENS unit was effective in inducing uterine contractions in post-date pregnant women [Dunn and Rogers, 1989]. Further, research with rats has shown that electrical stimulation can enhance peripheral motor-nerve regeneration [McDevitt et al., 1987] and sensory-nerve sprouting [Pomeranz et al., 1984].

6. **Regeneration**. Animal research in this area indicates that the body's endogenous EM fields are involved in growth processes and that modifications of these can lead to modest regeneration of severed limbs. Russian research and clinical applications with replications now underway in the U.S. indicate that low intensity microwaves apparently stimulate bone marrow stem cell division and may be useful as an adjuvant (enhancement) to chemotherapy to maintain hematopoiesis [Devyatkov et al., 1991]. The following studies are also relevant:

   - PEMF applications promote peripheral nerve regeneration [Orgel et al., 1992; Siskin, 1992]
   - "Diapulse" method used for human wrist nerve regeneration [Wilson et al. 1974]
   - DC aplications promote rat spinal cord regeneration [Fehlings et al., 1992; Hurlbert and Tator, 1992]
   - Swedish work on rat sciatic nerve regeneration [Rusovan and Kanje, 1991; Kanje and Rusovan, 1992; Rusovan and Kanje, 1992; Rusovan et al., 1992].

7. **Immune-system applications.** Promising research with human lymphocytes shows that applied EM or magnetic fields alone produce changes in calcium transport [Walleczek, 1992] and cause mediation of the mitogenic response. Questions presently being addressed include the possible augmentation of natural killer-cell populations by applied EM fields [Cadossi and Torelli, 1988; Cadossi et al., 1988; Cossarizza, 1988a, b, c].

8. **Potential neuroendocrine modulations.** Changes in melatonin levels, typically suppressions, are among the best characterized biological responses to low-level pulsed EM fields [Lerchl et al., 1990; Wilson et al., 1990]. Melatonin as a hormone is oncostatic (stops cancer growth). If melatonin can be suppressed by magnetic fields, then it may also be possible to increase its output. Other applications may include use of EM fields to normalize circadian rhythms in jet lag and sleep cycle disturbances.

Table 2 (*continued*). **Selected Literature Citations on Biomedical Effects of Nonthermal EM Fields**

location or type of bioeffect	frequency range of EM fields: DC	ELF, including sinusoidal, pulsed, and mixed	RF and microwave	IR, visible, and UV light	review articles and monographs
neuroendocrine effects, including melatonin modifications	Feinendegen & Muhlensiepen, 1987;	Lerchl et al., 1990; Wilson et al., 1990			O'Connor & Lovely, 1988
immune-system effects		Cadossi & Torelli, 1988; Cadossi et al., 1988; Cossarizza et al., 1989a; Cossarizza et al., 1989b; Rosenthal & Obe, 1989; Philipps & McChesney, 1981; Welleczek, 1982			
arthritis treatments		Trock et al., in press	Devyatkov et al., 1991		
cellular and subcellular effects, including effects on cell membrane, genetic system and tumors	Esterly, 1982; Liburdy & Tenforde, 1986; Fexall et al., 1991; Miklavcic et al., 1991; Short et al. 1992	Cohen et al., 1986; De Loecker et al., 1987; Takahashi et al., 1987; Adey, 1988; Merron et al., 1988; Omura & Hui, 1988; Braymen & Miller, 1989; Cossarizza et al., 1989; Goodman et al., 1989; Rodeman et al., 1989; Brayman & Miller, 1990; Lerchl et al., 1990; Omote et al., 1990; Greene et al., 1991	Guy, 1987; Chen & Ghandi, 1989; Brown & Chattpadhyay, 1991; Devyatkov et al., 1991	Liboff et al., 1991	Adey & Lawrence, 1984; Marino, 1988; Blank & Findl,1987; Ramel & Norden, 1991; Grundler et al., in press
endogenous EM fields, including biophotons		Mathew & Rumar, in press	Mathew & Rumar, in press	Popp et al., 1984; Chwirot et al., 1987; Chwirot, 1988; Popp et al., 1988	Wijk & Schamhart, 1988; Popp et al., 1992

Note: Reports listed in Table 2 are selected from refereed medical and scientific journals, multi-author monographs, conference proceedings, and patents. See Appendix A for identification of sources. This is a representative selection from a very large body of relevant sources, and is not meant to be exhaustive or definitive.

Table 2. Selected Literature Citations on Biomedical Effects of Nonthermal EM Fields

location or type of bioeffect	frequency range of EM fields: DC	frequency range of EM fields: ELF, including sinusoidal, pulsed, and mixed	frequency range of EM fields: RF and microwave	frequency range of EM fields: IR, visible, and UV light	review articles and monographs
bone and cartilage, including treatments for bone repair and osteoporosis	Brighton et al., 1981; Baranowski & Black, 1987; Papatheofanis, 1989;	Levine et al., 1974; Bassett et al., 1982; Barker et al., 1984; Brighton et al., 1985; Hinsenkamp et al., 1985; Huraki et al., 1987; Bassett, 1989; Sharrard, 1990; Madroñero, 1990; Grange et al., 1991; Magee et al. 1991; Pollack et al., 1991; Skerry et al., 1991; Ryaby et al., 1992			Brighton et al., 1979
soft tissue, including wound healing, regeneration, and vascular-tissue effects	Vodovnik & Karba, 1992	Gordon, 1986; Herbst et al., 1988; Mertz et al., 1988; Yen-Patton et al., 1988; Albertini et al., 1990; Ieran et al., 1990; Im & Hoopes, 1991; Krause, 1992; Liboff et al., 1992b; Stiller et al., 1992; Vodovnik & Karba, 1992;	Devyatkov et al., 1991		Vodovnik & Karba, 1992
neural tissue, including nerve growth and regeneration		Wilson et al., 1974; Rusovan & Kanje, 1991; Subramanian et al., 1991; Horton et al., 1992; Rusovan & Kanje, 1992; Rusovan et al., 1992			
neural stimulation effects, including TENS and TCES		Hagfors & Hyme, 1975; Hallett & Cohen, 1989; Anninos & Tsagas, 1991; Klawansky et al., 1992			
psychophysiological and behavioral effects			Devyatkov et al., 1991	Thomas et al., 1986	O'Connor & Lovely, 1988
electroacupuncture	McDevitt et al., 1987	Pomeranz et al., 1984; Christensen & Noreng, 1989; Dundee & Ghaly, 1989; Lee et al., 1992			

(continued on next page)

C. Other Research Accomplishments

The following developments, along with the publications and medical applications cited in this report, serve to establish the status of BEM as an emerging scientific discipline:

1. The number of researchers investigating topics in BEM is growing.

2. Five international scientific societies focus on BEM:
    - Bioelectrical Repair and Growth Society (BRAGS)
    - International Society for Bioelectricity
    - Bioelectromagnetics Society (BEMS)
    - European Bioelectromagnetics Association (EBEA)
    - Japanese Bioelectrical Society

3. Three journals publish peer-reviewed scientific research reports:
    - **Bioelectromagnetics Journal**
    - **Electro- and Magnetobiology**
    - **Bioelectrochemistry and Bioenergetics** (a section of **Journal of Electroanalytical Chemistry**)

    Also, there is increasing discussion of fundamental BEM mechanisms in prestigious mainstream journals (e.g. **Science, Nature, Physical Review, Biophysical Journal, IEEE Transactions**, etc.)

4. BEM achieved recognition at important general scientific meetings:
    - five symposia at 1992 FASEB Annual Meeting

- symposium at 1991 American Society of Cell Biology Annual Meeting
- symposium at the Nobel Institute
- 1st World Congress for Electricity and Magnetism in Biology and Medicine, in June 1992; co-sponsored by EBEA, BEMS, and BRAGS. A proceedings [Blank, 1993 in press] will be published in early 1993.

5. BEM is contributing to the scientific study of an important public health problem, the potential hazards of EM fields generated by electrical equipment (power lines, transformers, appliances, radio transmitters, etc.). This aspect of BEM is receiving substantial increases in funding as the general public becomes more concerned about electropollution, and questions of public policy seek resolution.

BEM researchers have shown that low intensity 60 Hz fields produced by certain electrical equipment produce bioeffects other than simple resistive heating of tissue [e.g., Nair et al., 1989; Wilson et al., 1990; Bierbaum and Peters, 1991]. It is also becoming apparent that radar and microwaves at intensities less than 10 milliWatt/cm^2 may pose hazards [U.S. EPA, 1991]. In addition, two recent Swedish studies on power line field effects show that the epidemiological approach provides valid evidence demonstrating a statistical correlation between cancer rates and exposures to magnetic fields at mG levels.

The implications for future research are that there are beneficial bioeffects of certain low intensity nonthermal EM fields, just as there are health hazards of other EM fields. The path is open for new research to develop beneficial applications of these bioeffects in medicine. The same analogy can be drawn with X-rays and chemotherapy drugs, which both have valuable therapeutic applications despite their unquestioned hazards.

6. The German government sponsored review meetings on EM mechanisms of interactions with cellular systems, resulting in the formulation of a 6-year national research program on this topic [e.g., Grundler et al., in press].

7. Private foundations, such as the Fetzer Institute, are showing increasing interest and support for long term research programs in BEM.

III. Research Opportunities

A. Overview

This Panel believes that an integrated program including *both clinical research and basic research* in BEM is necessary and proper, considering the mission of the NIH Office of Alternative Medicine. These two approaches should be pursued simultaneously along parallel tracks:

- **clinical research**, including pre-clinical assessments, with the aim of bringing the most promising BEM treatments and diagnoses from limited use into widespread use as quickly as possible, and

- **basic research**, with the aim of establishing the fundamental knowledge needed to improve and develop new BEM medical modalities.

Factors that were considered in making this recommendation include the following:

- Certain BEM-based modalities (e.g., TENS) that offer distinct benefits (e.g., noninvasive application) over current approaches are already in limited clinical use and can be transferred rapidly into mainstream medical practice.

- Elucidation of the physical mechanisms of BEM medical modalities is the single most powerful key to developing efficient and optimal clinical intervention. Even a relatively small advance beyond present knowledge of fundamental mechanisms would be of considerable practical value. In addition, progress in the development of a mechanistic explanation of the effects of alternative medicine could increase its acceptability in the eyes of mainstream medicine and science.

- Studies prepared for three federal agencies (OTA, NIOSH, and EPA) have recommended independently that research on fundamental mechanisms of EM field interactions in humans should receive high priority [Nair et al., 1989; Bierbaum and Peters, 1991; U.S. EPA, 1991].

- BEM offers a powerful, new approach to understanding the neuroendocrine and immunological bases of certain major medical problems (e.g., wound healing, cancer and AIDS). However, substantial funding and time are required to perform the basic research needed in developing this approach. Such is the case when any science is found to have significant medical applications.

- BEM provides a comprehensive theoretical framework, grounded in fundamental science, through which many alternative medical practices can be studied. BEM offers a promising starting point for exploring traditional alternative medical systems from a scientific viewpoint.

- An awareness exists within the alternative medical community that, in comparison to other sciences, BEM is willing to study unconventional treatments in a fairer, more open, and unprejudiced manner.

- Of all the areas in alternative medicine, basic research in BEM may have the greatest potential to interface with other NIH programs in the OAM's approach to "strategic partnerships" and leveraging of funding.

B. Clinical Research Opportunities

This Panel believes that clinical trials of BEM-based treatments for the following conditions would yield useful results within the short term (1 to 3 years):

- arthritis
- psychophysiological states (including drug dependence and epilepsy)
- wound healing and regeneration
- intractable pain
- Parkinson's disease
- spinal cord injury
- degenerative conditions associated with aging
- cancer
- AIDS

Among these, this Panel recommends that highest priority be given to the following three:

- arthritis
- psychophysiological states (including epilepsy)
- wound healing and regeneration

EM fields may be applied clinically as the primary therapy or as adjuvant therapy along with other treatments in the conditions listed above.

Efficacy can be measured via the following clinical markers:

- in arthritis, the usual clinical criteria including decrease of pain, less swelling, and greater mobility
- in psychophysiological problems, relief from symptoms of drug withdrawal, and alleviation of anxiety
- in epilepsy, return to greater normality in EEG, more normal sleep patterns, and reduction in drug dosages
- in wound healing and regeneration, soft tissue repair, reduction of collagenous tissue in scar formation; regrowth via blastemal (primitive cell) formation, increase in tensile strength of surgical wounds; alleviation of decubitus chronic ulcers (bedsores); increased angiogenesis (regrowth of vascular tissue such as blood vessels); and healing of recalcitrant chronic venous ulcers

For instance, a short-term double-blind clinical trial of magnetic-field therapy for osteoarthritis of the knee or elbow [Trock et al., in press] could be based on the following protocol:

- Suitable patient population is divided into treatment and control groups. Individual assignments are coded and remain unknown to patients, clinicians, and operators until treatment and assessment is complete.
- Pre-treatment clinical markers are assessed by clinicians and/or by patients themselves.
- Treatments consist of 3 to 5 half-hour sessions each week for total of 18 treatments over 5-6 weeks.
- During treatment, patient inserts the affected limb into annulus of a Helmholtz coil (a solenoid about 12" in diameter and 6" long), and rests while appropriate currents are applied to the coil via the apparatus' pre-set program.
- The treatment is noninvasive and painless; the patient feels nothing; there is no measurable transfer of heat to the patient.
- Control group follows same procedure except that, unknown to operator and patient, a sham apparatus (altered internally so that no current flows in the coil) is used.
- Patients' post-treatment clinical markers are assessed.
- Appropriate data reduction (scoring of assessments, un-coding of the treatment and control groups, and statistical analysis) is performed.

Clinical trials of BEM-based treatments for a variety of other conditions could follow a similar general outline.

C. Basic Research Opportunities

The current status of basic research in BEM may be summarized as follows:

- It is established that nonionizing nonthermal EM fields exert measurable bioeffects in living organisms. In general, the organism's response to applied EM fields is highly frequency-specific and the dose-response curve is nonlinear. Extremely weak EM fields, at the proper frequency and site of application, can produce large effects, either beneficial or harmful.

- It is suspected that the cell membrane is a primary site of transduction of EM field bioeffects, and that relevant mechanisms may include: changes in cell-membrane binding and transport processes, displacement or deformation of polarized molecules, modifications in the conformation or "structure" of biological water, and others.

- It is suspected that EM interactions with biomolecules may be described in terms of phenomena including: cyclotron resonance [Liboff, 1985; Liboff, 1991], radical pair recombination [Grundler et al., in press], triplet states, soliton oscillations, and other nonlinear cooperative dynamic phenomena.

- It is suspected that endogenous nonthermal EM fields, ranging from DC to the visible spectral region, are intimately involved in regulating physiological and biochemical processes.

This is the starting point for future research in BEM. This Panel believes that the most fruitful topics for future investigation include the following:

- Assay methods based on EM field interactions, e.g., for potassium transport, calcium transport, and cytotoxicity, should be developed. Existing studies of such phenomena in cellular systems should be applied to humans.

- EM-based treatments for osteoporosis should be developed, based on the large body of existing work on EM bone repair and other research [e.g., Cruess and Bassett, 1983; Brighton et al., 1985; Madroñero, 1990; Magee et al., 1991; Skerry et al., 1991; Liboff et al., 1992a]. NASA researchers have already expressed interest in collaborative work to develop EM treatments for weightlessness-induced osteoporosis.

- Mechanisms of EM field interactions in cells and tissues should be studied further, with emphasis on:
  - i) coherent or cooperative states and resonant phenomena in biomolecules
  - ii) coherent brainwave states and other long-range interactions in biological systems

- The role of water as a mediator in biological interactions should be studied, with emphasis on the quantum electromagnetic aspects of its conformation (or "structure," as implied in some forms of homeopathy). The response of biological water to EM fields should be studied experimentally. The novel informational capacity of water in relation to EM bioeffects may provide insights into homeopathy and healer effects (i.e., "laying on of hands").

- The role of the body's internally-generated (endogenous) EM fields (e.g., biophotons) and the body's natural electromagnetic parameters should be studied in detail. Knowledge of such processes should be applied to develop novel diagnostic methods, and to understand alternative treatments such as "energy medicine" and healer effects.

- A knowledge-base (an intelligent database) should be established to provide convenient access to all significant BEM work in both basic and clinical research.

- A meta-analysis of existing BEM studies should be performed to identify the most promising clinical endpoints for EM treatments in humans.

This Panel recommends that the following general principles should be applied to basic BEM research:

- Standardized dosimetry protocols for medically-applied EM fields should be established and followed uniformly in BEM research. Protocols are needed for characterizing (i.e., defining and measuring) EM field sources (both exogenous and endogenous) and EM parameters of biological subjects. Such variables must be characterized in greater detail than is commonly practiced in clinical research. Artifacts caused by ambient EM fields in the laboratory environment (e.g., from power lines) must be avoided.

- Initial studies should focus on systems in which both *in vitro* and *in vivo* results are available in both animals and humans, and at both cellular and organism levels,

- Great care is needed when extrapolating studies from cellular systems to whole organisms. Systemic effects, such as immune system response, may be dependent on whole-organism integrity, and may be absent or distorted in cell cultures.

- In general, a balanced approach to basic research – including studies in humans, animals and cells, along with theoretical modeling and close collaboration with other investigators in alternative medicine – will produce the most valuable results in the long run.

IV. Recommended Criteria for Research Priorities

A. Recommended Criteria for Clinical Research

To be considered suitable for funding, a proposed clinical study should have the following characteristics:

- addresses a significant clinical problem
- addresses questions of efficacy and/or safety
- offers benefits commensurate with patient risks involved
- is cost-effective
- employs double-blind protocol with use of appropriate controls (placebo)
- employs appropriate tests of statistical significance and power
- provides adequate characterization (i.e., measurement following a well defined protocol) of EM fields applied and in the experimental environment
- allows questions of efficacy to be decided within a predictable time frame
- when appropriate, includes comparisons to conventional medical modalities

B. Recommended Criteria for Basic Research

To be considered suitable for funding, a proposed basic research project should have the following characteristics:

- addresses a significant fundamental question
- has applications to significant clinical problems
- employs double-blind protocol with use of appropriate controls
- employs appropriate tests of statistical significance and power
- provides adequate characterization (i.e., measurement following a well defined protocol) of EM fields applied and in the experimental environment
- if non-human biological systems are used, presents evidence to indicate how the results would be applicable to humans
- is based on hypotheses that are plausible in light of current knowledge in the practice of alternative medicine and bioelectromagnetic science

V. Barriers to Research and Development

A. Identification of Barriers:

1. Members of NIH Review Panels in medical applications are not adequately knowledgeable about alternative medical practices or BEM. Also, an appeals system is lacking. These two are the most serious barriers.

2. Funding in BEM research is weighted heavily towards the study of hazards of EM fields, with very little funding for potential beneficial medical applications or the study of basic mechanisms of EM interactions with life processes. Also, the bulk of funding in BEM is administered by DOD and DOE, agencies whose missions are unrelated to medical research. The small amount of BEM work funded by NIH thus far has largely addressed only the hazards of EM fields.

3. Regulatory barriers to making new BEM devices available to practitioners are formidable. The approval process is slow and exorbitantly expensive even for conventional medical devices. The problem is compounded by the fact that existing FDA protocols do not take into account the principles and experimental findings of bioelectromagnetic science.

4. Barriers in education include:
   - Basic education in biological science is weak in physics.
   - Undergraduate or graduate level programs in BEM are virtually non-existent.

- There is a lack of multidisciplinary training in medicine and biology.

5. Conservatism within the mainstream scientific and medical communities responds to emerging disciplines, such as BEM, with reactions ranging from ignorance and apathy to open hostility. Consequently, accomplished senior researchers may simply not be aware of the opportunities for fruitful work in (or in collaboration with) BEM, while junior researchers may be reluctant to enter a field perceived by some as detrimental to career advancement.

B. Recommendations to Overcome Barriers

1. Whenever a research proposal submitted to NIH is approved but not funded due to lack of funds, the appropriate NIH office should issue a letter certifying the scientific merit of the proposal. This would help the investigator to obtain support from other sources.

2. Remove barriers within the NIH peer review system:

   - The preferable aproach would be to establish a regular study section in the NIH Division of Research Grants (DRG) (or other appropriate office) to deal with all BEM medical applications, not just those related to alternative medicine.

   - An alternative approach would be to establish a special NIH study section to deal with all aspects of alternative medicine (including BEM), the members of which would be drawn from a pool of appropriately qualified investigators and practitioners.

3. NIH should be made the lead agency to coordinate research on both the hazards of EM fields and the medical applications of BEM.

4. NIH-OAM should work closely with FDA to ensure that protocols for regulation of BEM devices are commensurate (i.e., neither unduly restrictive nor lenient) with the risks involved in their use, and are based on appropriate scientific principles, including the research cited in this report.

5. NIH should encourage the academic community to develop a curriculum which provides greater emphasis on physics and biophysics in the education of medical and biological researchers.

6. Additional NIH pre- and post-doctoral training grants programs in BEM should be funded.

7. NIH should provide support for an increased number of tutorials and symposia at mainstream scientific meetings.

8. Funds should be made available specifically for:
   - collaborative research between qualified BEM researchers and qualified alternative medical practitioners, and
   - interdisciplinary research between investigators in biology, medicine, physics, engineering, mathematics, and other relevant disciplines.

9. NIH should initiate RFAs (Requests for Applications) to perform selected clinical trials and certain critical experiments, with the aim of validating previously reported results and/or resolving apparent conflicts.

10. NIH-OAM should examine institutional models in other countries, especially in Europe, for the integration of alternative medicine with conventional medicine and mainstream science. Whatever success alternative medicine has achieved outside the U.S. may be due, in part, to the existence of a framework in which alternative and mainstream medical communities can cooperate, or at least coexist.

Appendix A - References

(Note: Reports listed in Appendix A are selected from refereed medical and scientific journals, multi-author monographs, conference proceedings, and patents. This is a representative selection from a very large body of relevant sources, and is not meant to be exhaustive or definitive.)

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Appendix B: Glossary

bioelectromagnetics (BEM): the scientific study of interactions between living organisms and electromagnetic fields, forces, energies, currents, and charges. The range of interactions studied ranges from atomic and molecular, through intracellular, to the whole organism.

Electromagnetic fields studied in BEM include those of *endogenous* origin (from within the organism) and *exogenous* origin (from outside the organism). Sources of exogenous fields include: the earth and sun, electrical equipment (powerlines, radio transmitters, etc.), clinical treatment devices (e.g., TENS), and other organisms. The electromagnetic fields of greatest interest in BEM are generally classified as *nonionizing* (i.e., lacking sufficient energy to dislodge electrons from molecules).

BEM is a scientific discipline emerging on the boundaries between physics and biology. As in other sciences, progress in BEM is made by testing falsifiable hypotheses against valid measured data obtained in repeatable experiments.

biophoton: a quantum of coherent EM field energy emitted by biomolecules in living organisms. Biophoton emission is associated with processes such as mitosis (cell division) and with mechanisms such as soliton vibrations of DNA and other alpha-helix proteins [Popp et. al., 1984; Popp et. al., 1992]. An organism's biophoton field may represent a highly-structured innate organizing field capable of encoding or transmitting information over macroscopic distances.

electropollution: EM fields that are produced by technologies such as electric power transmission and radio transmission and that may have harmful effects on humans.

ELF: extremely low frequency; used to describe electromagnetic fields whose frequency lies in the range from 0 Hz (direct current) to 300 Hz. This includes power line frequencies (60 Hz in U.S. and 50 Hz in Europe) and frequencies used by certain U.S. military communication systems.

EM field: electromagnetic field. In this report, "EM field" refers in a very broad way to any field, force or energy associated with electromagnetic interactions, charges and currents. Thus, the "EM field" includes electrostatic fields, magnetostatic fields, electromagnetic fields (including radiation and induction), vector-potential and scalar-potential fields, Hertz potentials, Fitzgerald potentials, etc.

The EM field is usually said to be comprised of two components: an "electric field" and a "magnetic field." However, these two components are not truly independent of each other , but rather are closely coupled according to apparently well-established physical laws (e.g., Maxwell's equations). In general, in situations where the EM field interacts with a highly-structured anisotropic medium (such as biological matter), which itself may be a source of EM fields, the interplay is quite complex and distinctions between "electric" and "magnetic" fields must be drawn very carefully.

Strictly speaking, the term "electromagnetic radiation" refers to only one type of EM field, namely, an oscillating EM field which propagates freely (i.e., its interaction with the underlying medium is negligible), at a spatial position which is distant (with respect to the wavelength) from the field's source. Thus, "EM field" is not synonymous with "EM radiation."

The ELF EM fields produced by the therapeutic devices mentioned in this report or employed in the studies cited in Appendix A generally have the physical characteristics of *force fields*. In these cases, the amount of energy being transmitted as *electromagnetic radiation* (i.e., propagating waves) is negligible [Tenforde and Kause, 1987].

This report avoids use of the letters "EMF" as an abbreviation for "electromagnetic field," to prevent confusion with the engineering usage in which "EMF" means electromagnetic force (or potential, or voltage).

Gauss (G): the cgs unit of magnetic flux density. In colloquial terms, the "strength" of a magnetic field is specified in terms of Gauss; for instance, the strength of a typical household magnet that holds papers on a refrigerator is about 200 G.

Hertz (Hz): cycles per second, the unit used to specify the frequency of oscillation of EM radiation. Table 1 in Section I.B. of this report shows the electromagnetic spectrum ranging from 0 Hz to over 10^{20} Hz.

PEMF: pulsed electromagnetic field; also used as the name of the clinical treatment modality in which pulsed EM fields are applied.

TCES: transcranial electrostimulation; a clinical treatment modality described in Section II.B.2.b. of this report.

TENS: transcutaneous electrical nerve stimulation; a clinical treatment modality described in Section II.B.2.a of this report.