NIH-OAM Panel Report:

Electromagnetic Applications In Medicine

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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 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. >

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.

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.

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.

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

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.

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.

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.

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]

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].

<Table 2 from file BEMTBL2.WP goes here>

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

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

location or type of bioeffect	frequency range of EM fields				review articles and monographs
	DC	ELF, including sinusoidal, pulsed, and mixed	RF and microwave	IR, visible, and UV light	
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; Sherrard, 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			

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

location or type of bioeffect	frequency range of EM fields				review articles and monographs
	DC	ELF, including sinusoidal, pulsed, and mixed	RF and microwave	IR, visible, and UV light	
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, 1991; Walleczek, 1992			
arthritis treatments		Trock et al., in press	Devyatkov et al., 1991		
cellular and subcellular effects, including effects on cell membrane, genetic system and tumors	Estorly, 1982; Liburdy & Tenforde, 1986; Foxall 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; Marron 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 & Nordan, 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.

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.

- 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.

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:

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.

- 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

- 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.

- 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

- 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.

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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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.

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.