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INTRODUCTION

Developments in biophysics, biology, epigenetics, neuroscience, psychology, mind-body therapies, and other fields suggest the existence of a subtle "biofield" system intimately involved in the regulation of basic biological processes. Relatedly, advances in mind-body research, psychoneuroimmunology, and psychosocial genomics, have shown that psychosocial factors, emotional states, intention, and stress levels can significantly affect biological function and health outcomes [1–7]. Thus, biofield interactions may involve the flow of information from molecular to psychosocial levels, producing a web of dynamic activity, wherein consciousness, emotional expression, and social behavior are interwoven with cellular, molecular, and organismic regulation and function. To more clearly understand the depth and breadth of these relationships, a unifying theory of biofield interactions needs to be developed. For the purposes of this inquiry, we provide a working definition of biofield interactions:

Biofield—An organizing principle for the dynamic information flow that regulates biological function and homeostasis. Biofield interactions can organize spatiotemporal biological processes across hierarchical levels: from the subatomic, atomic, molecular, cellular, organismic, to the interpersonal and cosmic levels. As such, biofield interactions can influence a variety of biological pathways, including biochemical, neurological, and cellular processes related to electromagnetism, correlated quantum information flow, and perhaps other means for modulating activity and information flow across hierarchical levels of biology.

A multitude of devices have been designed and developed to measure or manipulate biofield interactions. The primary goal of this chapter is to provide an overview of the many types of devices that have been created and to provide a synopsis of some of the key studies that have been carried out related to devices and biofield research. Descriptions of devices and the discussion of the manner in which these devices operate may also help illustrate some of the concepts required to grasp the notion of biofield interactions, and to clarify some of the challenges inherent in defining how biofield interactions act to coordinate biological activity.

Biofield devices may be thought of as any physical apparatus that operates through principles that can be most clearly understood in terms of a biofield paradigm. The gamut of biofield devices thus includes a wide variety of physical instruments that can be used to measure biofield emanations (i.e., biofield diagnostic devices) and/or to manipulate biofield interactions (i.e., biofield therapeutic devices) either directly or indirectly. Here, we review devices operating through novel or partially understood mechanisms as well as those with better understood substrates, and devices as simple as an acupuncture needle or as complex as magnetoencephalography equipment.

The biofield devices considered here operate through a variety of mechanisms such as electric currents, electromagnetic fields (EMFs), including heat, light, and nonthermal EMF, physical or mechanical interactions, gasses and plasmas, sound, music, mechanostimulation, bioacoustics, energy patterning, correlated quantum information flow, human intentionality effects, and nonlocal consciousness interactions, and occasionally via mechanisms which are not well understood at this time. Biofield devices have generally been developed to enable the detection and manipulation of biofield interactions. Thus, the study of these devices may also improve our understanding of the properties of biofield interactions, and how to best use them for the purpose of enhancing health and wellness.

Although the range of possible mechanisms is vast, these devices generally share a common property in that they do not operate in a mechanical, chemistry-centered manner. Rather, biofield devices are best understood from an information-based or consciousness-based viewpoint. Such a viewpoint emphasizes and presupposes the importance of the informational content of biological processes, and allows for the possibility that consciousness itself and low-energy or "subtle" processes may play fundamental roles in biological functions, including healing and the set-point maintenance of health. Also, many biofield devices use the body's natural rhythms and properties as diagnostic or therapeutic markers, for example, devices that analyze brain and heart rhythms and those meant to couple with or entrain natural rhythms using EMFs or sound.

DEVICE MODALITIES

Due to the large number and variety of devices that exist, and for the sake of clarity within this chapter, we summarize biofield devices here by modality (i.e., mode of operation). The modalities covered include EMF-light, EMF-heat, EMF-nonthermal, electrical current, vibration and sound, physical and mechanical, intentionality and nonlocality, gas and plasma, and other. Although EMF therapy devices are certainly the most widely studied type of biofield devices, there is substantial evidence suggesting efficacy for devices operating according to other mechanisms, and perhaps according to mechanisms that are not yet understood within the framework of Western biomedical science. Here, whenever possible, we refer to peer-reviewed scientific reports, rather than conference proceedings and manufacturer's whitepapers. However, when a device appears to have sufficient promise and relevance, but peer-reviewed reports are lacking, we present whatever evidence is available.

MODALITIES USING EMFS: LIGHT

Light has long been known to have therapeutic effects. Many ancient cultures practiced various forms of heliotherapy, including the people of Ancient Greece, Ancient Egypt, and Ancient Rome. The Inca, Assyrian, and early Germanic settlers also worshipped the sun as a health-bringing deity [8]. More recently, biological rhythms that repeat approximately every 24 hours have been studied in the field of circadian biology. Light is the main stimulus that helps the circadian clock entrain to the solar day in human beings [9]. If lack of synchrony or circadian disruption occurs, people may experience decrements in physiological functions and health, neurobehavioral performance, and sleep [9]. In northern countries a syndrome has been noted where people develop depression toward the end of a long winter. This depressive state has now been recognized as a condition caused by lack of sunlight and has been termed seasonal affective disorder (SAD). Exposure to full spectrum artificial light is commonly used to treat SAD in these countries [10]. We also know that human beings need sufficient exposure to sunlight in order to produce vitamin D, which is essential to prevent some diseases such as rickets and osteomalacia. Recently, it was found that lack of vitamin D has been associated with many acute and chronic illnesses, including disorders of calcium metabolism, autoimmune diseases, some cancers, type 2 diabetes mellitus, cardiovascular disease, and infectious diseases [11]. In addition to helping people suffering from SAD, artificial light has proven to be very useful in many other ways, such as the treatment of skin conditions such as psoriasis, eczema, and acne [12–16].

In addition to these health-promoting aspects of exposing the body to light, here we will focus on biophoton emission (BE), or the natural emission of light produced by all living organisms. The existence of BE raises the possibility that our bodies also use light for homeostatic processes. This in turn has generated an interest in using very sensitive instruments to determine whether our bodies give off measurable amounts of light and what the significance of those emissions might be.

Biophoton Emission

BE, a term coined by Fritz-Albert Popp [17], also called ultra-weak photon emission, is the spontaneous emission of light emanating from all living organisms, including humans. BE refers to weak photon emission with an intensity of 10–1000 photons/s·cm² at 37°C and in the spectrum of 300–800 nm [18]. The detection and characterization of human BE has led to suggestions that it may have applications in medicine [19]. BE is different from bioluminescence, which is a form of chemiluminescence in which light energy is released by a specialized chemical reaction: fireflies, anglerfish, and other organisms produce the chemicals luciferase (an enzyme), and luciferin (a pigment) [20] which react with oxygen to create light. Also, BE should not be confused with phosphorescence, which is a specific type of photoluminescence related to fluorescence (the emission of light by a substance that has absorbed light or other electromagnetic radiation).

In the 1960s, when detectors sensitive enough to detect BE were developed, plants were first examined and it was discovered that a severed plant emits more biophotons than an intact plant [21]. In humans, the hand has been the most studied body part with respect to BE. A number of researchers showed that BE varies depending on the part of the hand that is imaged [22,23]. Further, activity such as vigorous exercise generates a significant increase in BE [24]. Van Wijk measured BE from different parts of the body and found that BE differs greatly depending on the location chosen [23]. He also demonstrated that emission from the left hand can be different from the right hand even in similar experimental conditions and during simultaneous measurements [23]. Also, cell–cell signaling via BE has been reported in several studies [25], and Popp's work suggests that coherent biophoton signaling could explain many regulatory functions [26], including cell–cell orientation detection [27], biophoton-mediated secretion of neurotransmitters [28], respiratory activity in white blood cells [29], and accelerated seed germination [30].

There is ongoing controversy within the field of BE research regarding the theoretical source of detected biophotons. A majority of researchers have come to the conclusion that BEs originate as a product of electron excitation states formed during oxidative metabolic processes in microbial, plant, and animal cells [31]. Still, other groups maintain that there are other contributions due to a coherence field in the body, a kind of quantum field, that is the main source of BE [17]. Popp maintained that the cell nucleus was an important source of BE [17].

A systematic review was conducted to address whether BE from humans may be useful as a noninvasive health assessment [32]. This report demonstrates that the peer reviewed literature on human BE measurement is surprisingly large and that most of the human BE literature is of good to high quality [32]. Publications in the peer-reviewed literature over the last 50 years demonstrate that the use of "off-the-shelf" technologies and well-described methodologies for the detection of human photon emissions are being used on a regular basis in medical and research settings. The review concluded that the overall quality of this literature is good and the use of this approach for determining inflammatory and oxidative states supports the use of BE measurement as both a medical and research tool.

Laser Therapy

Laser therapy (LT) takes many forms, and is employed for a wide variety of pathologies [33]. While a comprehensive review is out of the scope of this chapter, the relevance of phototherapies to the biofield paradigm warrants a brief overview: Lasers used for therapeutic purposes are generally classified according to their power output: Class I, II, and III lasers, often referred to as "cold lasers," operate without ablating tissue, and are only nominally hazardous, while Class IV lasers can burn the skin, cause permanent eye damage, and may ignite combustible materials [34]. Because of the relevance to biofield science, we shall focus on low-power LT (i.e., devices that act without ablating tissues). Often termed low-level laser therapy (LLLT), bioeffects

induced by Class I–III lasers have been linked with photochemical reactions in cells and tissues [35]. A review of the basic mechanisms of nonthermal LLLT suggests cytochrome c oxidase as the photoacceptor, and elucidates some of the biochemical pathways involved in the stimulation of wound healing, cellular proliferation, production of transcription factors, and other reported stimulatory effects [36].

A wide variety of clinically relevant effects have been reported for LLLT, and a growing body of systematic reviews supports its efficacy for a range of pathologies [33]. For example, a review of LLLT for skeletal muscle repair in animal models reported a reduction in the inflammatory process, modulation of growth factors and myogenic regulatory factors, and increased angiogenesis [37]. Another systematic review on clinical studies for LLLT treatment of tendinopathy concluded that the evidence lends strong support for efficacy [38], and a review on LLLT treatment of rheumatoid arthritis concluded that LLLT is an effective short-term treatment for pain and morning stiffness [35]. Reviews have also concluded that LT can promote nerve growth and repair and that broader clinical trials are needed [39,40]. Reviews on the use of LLLT for lateral elbow tendinopathy also support reports of efficacy for treating this pathology [41,42]. Other reviews suggest efficacy for osteoarthritis [43], neck pain [44], and chronic joint disorders [45].

The large number and wide variety of basic science and clinical studies reporting efficacy for LT suggests that light can play a central role in therapeutics. While much further work is required to establish optimal dosing and treatment parameters [35,42–46], LLLT has promise to deepen our understanding of how light interacts with biology. As our understanding of how the body responds to phototherapies improves in the years to come, it is likely that the efficacy of LT therapies will also improve. Some drawbacks to LT are that the nonspecific nature of exposure to light may make it difficult to target specific pathologies, and light attenuation by the body may make it difficult to treat regions deep within the body, although the directed manner of LT light propagation does make it possible to treat certain specific areas of the body.

The low, nonablative energy employed by LLLT suggests that therapeutic benefits can be gained from weak, often nonthermal interventions. While the lower limits of biodetectability and clinical efficacy have not been determined, observations that exposure to weak, nonthermal light sources has therapeutic benefits also suggests the role of light-signaling in the low-energy range wherein the informational content of an intervention may be more important than the energy of the input signal.

MODALITIES USING EMFS: HEAT

Infrared Thermography

IR light lies between the visible and microwave portions of the electromagnetic spectrum, in the region from approximately 700 nm to 300 μ m [47]. The IR light emitted or absorbed by molecules corresponds to their vibrational dynamics, making IR spectroscopy an important tool for studying chemical composition, protein structure [48], and a variety of other structure–function relationships in biology [49]. IR light emission is also used as a measure of the temperature of objects, and is especially convenient for measuring the temperature of warm-blooded organisms, which radiate most strongly at a wavelength of about 12 microns [50]. Thermal imaging using IR thermography (IRT) has a wide range of scientific, industrial, and military applications, and a variety of medical uses. Biological and metabolic activity generates small amounts of heat, and changes in muscular activity, subcutaneous blood flow, and perspiration patterns in specific body parts can be detected using IRT [51]. IRT is also commonly used in screening for fevers due to infectious diseases such as SARS and influenza.

Because of its versatility, lack of invasiveness, and high sensitivity, IRT lends itself to a large number of applications in biology [52]. IRT has been used to assess fever, inflammatory diseases, complex regional pain syndrome, and Raynaud's phenomenon, and has been shown to provide objective measurement of clinically significant temperature changes for a variety of syndromes [53], including breast cancer [54,55], vascular dysfunction [56], and tumor characterization [57] and has been used in angiology, allergology, rheumatology, plastic surgery [58], dermatology, orthopedics, diagnosis of circulatory abnormalities [59], and veterinary medicine [52].

An application of IRT with direct relevance to biofield science is the detection of psychophysiological activity, by assessing vital signs, physiological responses, and emotional states [60]. IRT has been developed as a method for gathering information about affective states in social situations [51,60]. A comparison of IRT results with established stress markers found mostly nonsignificant correlations, however IRT data were significantly correlated with stress-induced mood changes, suggesting a noninvasive method for the estimation of sympathetic activity [61].

Other interesting applications of IRT appear in the study of Traditional Chinese Medicine (TCM), for example, in the Zheng diagnosis system. Zheng works by detecting the relative temperature of viscera and bowels in patients and correlating this with states of illness and health. Clinical correlations with pulmonary disease suggest the utility of IRT as an adjunct to TCM-based diagnoses [62]. Observations of IR radiant tracks along human acupuncture meridians may have implications for the study of TCM, and suggest the possibility of developing new TCM-based diagnostic techniques [63]. Also, IRT-captured changes in finger temperature have been reported for "White Ball" TCM Qigong practice, which involves posture, breathing, mental focus [64], and changes in IR emissions in the $3-5 \,\mu$ m wavelength have been reported during "External Qi" practice by a "Qigong Master" [65].

IRT holds great promise as a technique allowing for the detection of small, localized changes in temperature that accompany a wide range of metabolic, disease, and psychophysiological states. The potential for detecting psychophysiological responses and emotional states, in particular, may provide new avenues of research. The large body of peer-reviewed IRT research also holds promise for the development of a deeper understanding of the connections

between mind, body, and emotions. Furthermore, IRT has some distinct advantages over other imaging techniques, as it is noninvasive, relatively inexpensive, and involves none of the ionizing radiation hazards associated with mammography, PET scanning, and others. However, the diagnostic use of IRT is somewhat limited, as it only detects changes in temperature and is thus unable to identify the etiology of a disease [52]. In addition, the use of IRT for early cancer detection is controversial; the U.S. FDA has stated that it is not sufficient as an alternative to other screening methods, and has issued several warning letters to manufacturers for making unsubstantiated claims [66]. Despite these objections, with the ongoing development of scanning and signal processing technologies, and the deepening understanding of psychophysiological correlates of IRT, this technique may grow into a body of approaches capable of diagnosing an array of biological states.

Therapeutic Applications Using IR Light

IR light therapy is beginning to be employed for the treatment of a variety of conditions. Although the biological effects of IR exposure remain poorly understood and some effects are hypothermic, enhanced wound healing has been reported in rats in the absence of changes in skin blood flow and skin temperature, suggesting the existence of nonthermal therapeutic mechanisms [67]. Also, IR-induced enhancement of bone healing in rabbits has been reported [68].

MODALITIES USING EMFs: NONTHERMAL

Endogenous EMFs and Biological Function

EMF interactions and endogenous fields produced within the body play essential roles in the regulation of ion transport, maintenance of the cell membrane electrical potential, formation of action potentials in the nervous system, regulation of transport pathways, coordination of cell migration, embryonic development, and wound healing [69,70]. In addition to these widely studied ion-driven interactions, recent evidence has shown that a variety of biological regulation processes occur via endogenous EMFs within the cytoskeleton. For example, it has been shown that electric fields generated by the intracellular network of microtubules, centrosomes, and chromosomes play a fundamental role in regulating the dynamics of mitosis, meiosis, and a variety of other processes [70-72]. It has also been shown that endogenous electric fields in nuclear DNA-containing chromatin play a key role in chromosome packing during mitosis [73], electric fields of physiological magnitude can orient cell division [74], and electrochemical rhythms in the cytoskeletal matrix can influence voltage-gated ion channel activity and the phosphorylation status of binding molecules such as MAP2 and CaMKII, which in turn affect cytoskeletal structure and connectivity [75]. Experimental evidence has demonstrated endogenous EMF signaling in microtubules, cytoskeletal structures that play a role in molecular signaling and transport. A recent review details substantial experimental evidence and theoretical support for the notion

that endogenous EMF signaling within the cytoskeletal network of neurons could be essential for the "very fast and complex changes of functional neuronal connectivity necessary for cognition" [72]. Theoretical models have predicted both classical and quantum information processing in microtubules [76,77], and these interactions have been suggested as a possible source of the observed EEG correlates of consciousness [78]. Also, a substantial body of research has demonstrated the fundamental interconnectedness of electrochemical and hormonal aspects of mind and emotion via analysis of frequency spectra of brain EEG and heart ECG rhythms [2]. Thus, more subtle forms of signaling related to consciousness, cognition, and emotion may point to an informational view of EMF biological interactions using rhythm, resonance, and synchronization to produce coordination across hierarchical levels [75].

Bioeffects Due to Exogenous EMFs

Biological effects have been reported in response to exposures to EMFs that nearly span the range of frequencies, field strengths, and amplitudes occurring in the natural and man-made environments, and a variety of mechanisms of action have now been suggested [69 [1], 2013, 70 Pall, 2013]. Although it is now clear that exogenous EMFs can influence biological function, controversy exists around potential dangers and therapeutic benefits of EMFs. Health concerns have led the International Agency for Research on Cancer to recently (31 May, 2011) classify radiofrequency radiation from mobile phone use as "possibly carcinogenic" to humans. Ongoing concerns regarding health risks of EMF exposure led to the release of the BioInitiative Report, A Rationale for a Biologically-Based Public Exposure Standard for Electromagnetic Fields (ELF and RF) [79], recommending dramatic revision of maximal exposure guidelines. However, in contrast to public alarm regarding long-term hazards, a large body of research suggests EMF exposures can yield clinically beneficial results [80-83], a wide range of therapeutic applications now exists, and the short-term use of EMFs is now cleared by the U.S. FDA and regulatory bodies worldwide for pathologies such as bone repair, pain, and edema [84].

The large and rapidly growing body of research on nonthermal EMF bioeffects is of particular relevance to the study of biofield interactions. For these "weak" fields, no significant heating of cells or tissues occurs, and the apparent molecular interaction energies are less than the average thermal energy of the target [85]. The existence of such nonthermal effects has led to the establishment of guidelines for safe exposure levels by the International Commission on Non-Ionizing Radiation Protection (ICNIRP), for signals with frequencies below 100 kHz [86]. A number of theoretical models have been developed detailing thermal noise limits for such weak EMF interactions [85,87–93], and the mechanisms by which extremely low frequency (ELF), μ T-range, magnetic fields can directly influence biological processes have been more clearly elucidated [70,85,92–96].

The most common therapies use static magnetic fields (SMF) or pulsed EMFs (PEMF), that employ time-varying waveforms, and many of the therapeutic devices in use today involve interaction energies below the apparent

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thermal threshold. Broadly, nonthermal EMF devices consist of SMF and ELF <100 kHz [86] time-varying exposures. Many nonthermal EMF devices produce ambient-range EMF exposures (on the order of the 50 μ T geomagnetic field), and there are many reports of therapeutically relevant bioeffects for EMF signals of this strength [80,97 200]. In addition, a growing body of evidence has now reported bioeffects at much lower field strengths, on the order of nanoTesla (nT) [98,99–109]. A notable aspect of these extremely weak EMF bioeffects is that the energies of interaction are dramatically lower than the average energy due to random thermal motion [93 200, 95], suggesting the possibility of bioinformation flow at extremely low energies. The existence of this subtle information signaling, occurring well below the Brownian threshold, may suggest a fundamental shift in the biochemical paradigm, which had previously assumed that sub-thermal interactions are unable to affect biochemical processes.

SMF Therapies

In addition to a large and growing literature on SMF bioeffects, a wide variety of health claims have been made for SMF therapies [82,110], and a large number of manufacturers currently sell magnets intended for therapeutic purposes. The mechanisms of action of SMFs have been the subject of considerable speculation [85 2 90,95], and substantial experimental and theoretical support has been gathered for one mechanism of action based upon the dynamics of radical pair recombination (i.e., magnetic field modulation of free radical lifetimes) [111–115]. SMFs are nearly always applied with permanent ceramic or neodymium magnets placed on or very near to the body. Typical magnetic flux densities at the surface of therapeutic magnets range from less than 100 μ T to the mid-mT range, and field strengths within the body vary extremely widely, due to the magnet size and pattern of magnetization employed, that is, unipolar (same direction) versus bipolar (alternating North–South), for which substantial field cancellation occurs.

The published data on the effectiveness of SMF therapies is presently contradictory, and the quality of the studies varies greatly. For example, a critical review of randomized controlled trials of SMF therapies concluded that SMFs are able to induce analgesia [116], whereas a recent meta-analysis of randomized, double-blind, and placebo-controlled studies found SMF therapy to be ineffective for the treatment of pain [117]. Another review reported both enhancement and inhibition of microcirculation due to SMFs and PEMFs, and suggested that further research is required to determine more clearly the effects and mechanisms [118]. Also, although several recent trials have reported enhanced wound healing in animal models, a review of the literature showed conflicting evidence on the use of SMFs for healing bone, tendon, and skin, and suggested that more research is needed [119]. It has been suggested that some of this disparity could be understood by more careful assessment of the SMF field dosimetry within the body, as some studies neglected to clearly report the magnetic field exposure within the target tissue [110]. Nonetheless, several *in vivo*, blinded studies have reported beneficial effects Q2

for SMF exposures, including: reduction in discoloration, edema, and pain post suction lipectomy [120]; reduction in fibromyalgia pain and sleep disorders [121,122]; reduction in chronic pelvic pain [123]; relief from pain, numbness, and tingling due to diabetic peripheral neuropathy [124]; reduction in post-polio pain [125], and musculoskeletal pain [126]. Other blinded trials demonstrated both positive short-term and negative long-term results on osteoarthritis knee pain [127], no effects on foot [128,129] and chronic back pain [130], though it should be noted that the latter two trials employed magnets in bipolar configuration, resulting in lower amplitudes inside the target as compared to the unipolar configurations listed above.

Pulsed EMF Therapies

The majority of the nonthermal EMF devices presently available, often referred to as PEMF devices, use time-varying waveforms. PEMF devices generally employ current-carrying coil antennas to deliver a time-varying magnetic field to the target tissue. Treatment devices range in size from small coils intended to treat specific areas (such as recalcitrant fractures), to devices wherein patients sit or lie upon a pad or mattress-containing coils. A small number of devices place the patient inside large coils of sufficient size to treat the whole body. Signal generators may be portable and batteryoperated, or operate from a mains power source. The term PEMF has been used to describe nearly all time-varying waveforms used therapeutically, and devices in current use employ a range of amplitudes from the picoTesla (pT) and low microTesla (µT) to milliTesla (mT) range, and frequencies from several Hz to the MHz range [80]. There is now an extremely large, diverse, and rapidly growing literature on PEMF therapies, and we shall consider pathologies for which sufficient numbers of clinical studies have permitted literature reviews.

One of the most widely adopted PEMF therapies is bone repair, for which several devices are cleared by the U.S. FDA, and a clear benefit for nonunion fractures has been demonstrated [131]. However, the data also suggest that further research is needed: A review of blinded randomized placebo-controlled trials concluded that, while PEMF treatment may offer some benefit in the treatment of delayed union and nonunion of diaphyseal (long-bone shaft) fractures, the results are reported to be inconclusive, and insufficient to inform current clinical practice, due to the small overall effect size and substantial clinical and statistical heterogeneity in the studies reviewed [132]. Also, another recent review found no reduction in the incidence of nonunion fractures, but did find a reduction in time to radiological and clinical union in acute fractures [133]. Uncertainty regarding therapeutic efficacy is reflected in a recent multicenter, double blind, randomized trial concluding that PEMF treatment does not prevent secondary surgical interventions for delayed union or nonunion fractures, and does not improve radiographic union or patient-reported functional outcomes in acute tibial shaft fractures (TSF) [134], whereas an early double-blind study found positive results for TSF [135]. Thus, despite clear success in treating nonunion fractures, additional

studies are needed to determine the scope of efficacy of PEMF treatment for bone repair in general.

Pain and inflammation are other indications for which there is evidence of efficacy of PEMF treatment [83]. A substantial body of evidence has accumulated showing that exposure to EMFs can affect nociception and induce analgesia [136] and several devices are cleared in the United States by the FDA to reduce pain and edema, and enhance bone and wound repair [84]. Clinically, one of the most widely investigated examples of PEMF treatment for pain and inflammation is osteoarthritis, for which pain and clinical scores have been investigated in numerous studies. While statistically significant results for pain and improvement of physical function have been produced in some studies, several recent reviews have reported ambivalent conclusions, and have suggested that further research is needed to assess the clinical relevance [137–142].

While the above results hold great promise for PEMF therapeutics, the field is not without controversy. The term PEMF is commonly used to describe nearly all time-varying waveforms used therapeutically, and an extremely large variety of waveforms and signal strengths are currently in use [80]. This wide variation in signal parameters has contributed to contradictory data related to therapeutic efficacy, and has led to difficulties in comparing PEMF devices with one another, as the efficacy and mechanisms of action are likely to be different for various signals. Thus, in light of the evidence of nonthermal bioeffects summarized above, it is likely that different PEMF signals could yield different bioeffects and efficacy for different pathologies [143]. Further, heterogeneity of patients and patient health status may also be important experimental variables to monitor in future studies. These issues have yet to be systematically addressed.

While there is a large and growing body of research supporting the existence of beneficial effects for PEMF devices [80], and some devices have garnered enough merit to warrant FDA clearances, there is also considerable confusion as to which specific devices may yield intended benefits. Comprehensive studies comparing different devices have rarely been performed, and in many cases, manufacturers refer to reports of health benefits across the entire range of PEMF devices as lending support for the health claims for specific devices. Many devices lacking regulatory approval or solid scientific evidence are permitted for sale to the public. Also, many PEMF devices available for public purchase are manufactured by companies outside of the United States, where regulatory restrictions on health claims for such devices are not yet in place and health claims may be made in the absence of solid scientific proof. As a result, the claims made on websites and in promotional materials are often not backed by scientific support. Because of this obfuscation, it is often nearly impossible for scientists, physicians, or prospective patients to adequately assess the efficacy of many of the devices currently on the market. In addition, nearly all scientific studies today are funded by PEMF manufacturers, making it difficult to assess the number of negative results that have not been reported, and also resulting in a dearth of research

on possible deleterious effects. Thus, while there may indeed be significant therapeutic benefits from some devices, a fog of marketing bias and incomplete scientific evidence must be dispersed in order to obtain a clearer view.

Transcranial Magnetic Stimulation

Transcranial magnetic stimulation (TMS) employs rapidly changing magnetic fields to stimulate cerebral neurons and alter neuronal activity. TMS operates through electromagnetic induction, wherein a time-varying magnetic field gives rise to an electric field in the target tissue. Because magnetic pulses pass unattenuated through the body, TMS is able to induce small electrical currents that stimulate nerve cells in targeted brain regions. This induced electric field evokes changes in potential across neuronal membranes, and the resulting flow of ions can depolarize or hyperpolarize neurons.

TMS typically uses single- or multiple-coil antennas placed upon the scalp, producing magnetic fields in the range of 1.5–2.0 Tesla (T) at the face of the coil and to a depth of 2–6 cm [144,145]. Areas near the brain surface may be targeted with some accuracy, and multiple coils may be used to treat-related brain areas in a coordinated manner. Specialized coils can achieve greater depth of penetration, generally at the cost of less specifically targeted activity [144]. Safety considerations have been addressed, especially with regard to the possibility of inducing seizures, and the range of nonhazardous amplitudes and other treatment parameters have been defined [146,147]. One hazard identified in early studies is that rapid mechanical deformation of the TMS stimulating coil during magnetic pulse generation can produce an intense, broadband acoustic artifact that may exceed 140 dB of sound pressure level [148], exceeding the recommended safety levels for the auditory system [149].

TMS has been the topic of numerous clinical studies. Early reports of efficacy for depression [150–153] led to much further inquiry, and TMS has been used to investigate many aspects of cognitive neuroscience [154], including cognition, brain-behavior relationships, and the pathophysiology of a variety of neurologic and psychiatric disorders [147,155]. Therapeutic benefits have been reported for a very wide range of indications, including depression, acute mania, bipolar disorders, panic, hallucinations, obsessions/compulsions, schizophrenia, catatonia, posttraumatic stress disorder, drug craving, Parkinson disease, dystonia, tics, stuttering, tinnitus, spasticity, epilepsy, rehabilitation of aphasia or hand function after stroke, neuropathic pain, visceral pain, and migraine [146,147,155,156]. In recent years, repetitive TMS (rTMS), using magnetic pulses repeating at 1–20 Hz to entrain with neuronal activity, has been widely studied as a treatment tool for various neurological and psychiatric disorders including migraine, stroke, Parkinson disease, dystonia, tinnitus, and depression [147]. A meta-analysis of studies on the efficacy of rTMS in psychiatric disorders suggests its use for depression, auditory and verbal hallucinations, and possibly for negative symptoms of schizophrenia, but not for treatment of obsessive-compulsive disorder (OCD) [157]. A review of studies on the use of rTMS for pain concluded that efficacy is limited by the short duration of the induced analgesia, but prolonged pain relief can

be obtained through daily treatment for several weeks [156]. Although this broad range of therapeutic benefits has been reported, the mechanisms underlying TMS have yet to be fully elucidated. In particular, although lasting after effects of TMS have been found in healthy subjects, the neurophysiologic substrates remain unclear. Various mechanisms have been proposed, including synaptic changes resembling experimental long-term depression and long-term potentiation, as well as shifts in network excitability, activation of feedback loops, and activity-dependent metaplasticity [158,159].

TMS is now accepted as a clinically effective, noninvasive, low-cost means of stimulating the brain. Because magnetic fields pass unattenuated through the body, TMS is able to easily penetrate the scalp and skull and induce electric fields in the brain using relatively low power. TMS thus has a strong advantage over direct transcranial electric stimulation (TES) techniques which, due to the low conductivity of the skull, require that a large potential difference be applied between the electrodes on the scalp in order to stimulate neurons, thus requiring a much higher current density in the scalp [147]. TMS can thus stimulate cortical neurons without the pain associated with TES [147]. Also, recent advances in coil design and techniques for estimating field distributions inside the brain have resulted in greater ability to target specific brain areas [144]. However, due to the nature of EMF propagation through the body, TMS is unable to target specific neurons, and induced electric field distributions vary widely across brain structures. As such, further developments are needed in order to determine dosimetry for subject-specific anatomy, perhaps through use of high-resolution imaging modalities such as MRI [160].

PEMF "Resonance" Therapies

A variety of resonances for nonthermal PEMF waveforms have been reported, producing enhanced or inhibited bioeffects when the frequency and/or amplitude of the applied signal matches specific values. While the underlying mechanisms of action remain unclear [85], the conditions for which enhanced or diminished bioeffects occur are often referred to as "resonances," akin to sympathetic resonance behavior exhibited by harmonic oscillators. PEMF "bioresonance" therapies have been proposed both as therapeutic and diagnostic modalities intended to operate via such resonances with natural EMF frequencies or endogenous rhythms such as EEG or ECG frequencies. While the existence of these therapeutically relevant sympathetic resonances has not been clearly established, frequency- and amplitude-dependent EMF responses have been reported in a wide range of biological systems [95]. In addition to these reports of EMF resonances, sensitivity to specific EMF signal patterning has been demonstrated in human brainwayes [161] and pain perception in animals [162], further suggesting the existence of waveformdependence for some EMF effects.

While the underlying mechanisms remain unclear, a number of bioeffects from PEMF bioresonance devices have been reported in peer-reviewed journals [163–165]. In addition, devices for bone repair based upon the now-defunct ion cyclotron resonance model [166] have been shown to be effective [167]. However, it is unclear whether these bioeffects occur via a particular mechanism of resonance per se, or are due to less specific EMF interactions.

There are several grounds for criticism of PEMF resonance therapies. For example, many PEMF bioresonance devices employ low intensity, broad spectrum signals and some manufacturers cite the assumption that, through sympathetic resonance, each cell would "pick out exactly the proper frequency needed to reinforce its own internal vibration" [168]. Although this concept clearly has allure, to the authors' knowledge there have been no systematic results showing that cells indeed respond only to particular EMF frequencies for which only beneficial effects occur. Another mechanism of action described by several manufacturers is that frequencies are chosen to match EMF resonances described in the early papers of Adey and Bawin [169.170]. However, the resonances mentioned in these papers have not subsequently been confirmed, and it is likely that resonances at the cell membrane vary with transmembrane voltage [143]. Also, a double-blind study on bioresonance treatment for pediatric contact dermatitis found no effects, despite manufacturer's claims to the contrary [171], and a review of randomized, sham-controlled, double-blind trials on whole-body PEMF mats concluded that scientific evidence for therapeutic benefits is insufficient and therapeutic use cannot be recommended without further evidence from high-quality, double-blind trials [172]. Although these criticisms do not necessarily imply that bioresonance therapies are never efficacious, they have led to this branch of EMF therapeutics and the language used to describe bioresonance therapies to be described as "pseudoscientific" [173,174].

MODALITIES USING ELECTRIC CURRENTS, VOLTAGES, OR POTENTIALS

Electric Currents and Bioelectricity

Electrical potentials and currents that are produced by living organisms, known as bioelectricity, exist to varying extents in all species. In humans and other mammals, bioelectricity is a crucial substrate of biological function and transfer of information, allowing for membrane polarization, muscular contraction, and axonal conduction in neurons, among other biological processes vital to physiology [175]. Measurement and manipulation of bioelectricity in the body is increasingly of interest in scientific research and has already led to seminal advances in medicine [176]. This section will provide examples of devices that measure and manipulate the bioelectric properties of the body and could be considered for research tools in biofield studies. Electroencephalography (EEG) and electrocardiography (ECG) are included here as biofield devices. These approaches are sensitive measures of distributed information flow required for cellular regulation and function, and though well understood in terms of biophysical substrates, represent important examples of biofield interactions according to the above definition.

Electroencephalography

EEG is a noninvasive procedure in which electrodes are used to measure and record electrical activity along the scalp. Fluctuations in voltage detected at various points on the scalp are a result of ionic current flow into neurons and out into the extracellular space in the central nervous system. The charge, or polarization, that neurons maintain and require for communication, is dependent on ions (e.g., Na⁺, Ca²⁺, K⁺, Mg²⁺, Cl⁻), ion channels, and membrane transport proteins that maintain each neuron's membrane potential. While the electric potential of an individual neuron is too small to be detected by EEG, synchronous firing of groups of neurons can be measured and provides a rich source of quantitative information about the activity and functional state of the brain. More specifically, EEG data can be organized into "frequency bands" (i.e., delta, theta, alpha, beta, and gamma), each of which has unique features and associations with particular brain states, and can provide insight into how the brain is functioning on a cellular level. An interesting theory, proposed by Hameroff and Penrose, posits that consciousness is linked to quantum vibrations in microtubules, which are principal constituents of the neuronal cytoskeleton [177]. Within this framework, microtubule vibrations correlate with, and regulate, neuronal synaptic and membrane activity, therein, influencing state and behavior [177]. If correct, this theory suggests that consciousness would influence microtubule vibrations, which would, in turn, affect depolarization of neuronal networks, that latter being detectable by EEG.

Clinically, EEG is most commonly used to identify epileptic seizure activity. However, since EEG can provide detailed information on ion flux and cellular function, it has been used as a research tool to measure bioelectric changes related to biofield therapies [178]. A recent study reported that, when compared with placebo treatment, Okada Purifying Therapy (OPT), a biofield practice, generated a statistically significant increase in frontal and central alpha band (8.0–12.9 Hz) power in the OPT recipient [179]. This study corroborates previous work suggesting the relevance of alpha-band synchrony in biofield therapies [180]. A number of other studies have focused on practitioner EEG measurements during biofield therapy (see review) [178]. Some of these studies also identified changes in frontal alpha-band distribution and alpha synchrony in biofield practitioners, though none were properly controlled [181–184].

As a biofield research tool, some key advantages of EEG are inexpensive hardware, high temporal resolution (sampling rates over 20,000 Hz), tolerance to movement, silent operation, and noninvasiveness. The disadvantages are that EEG has low spatial resolution, poor sensitivity for signals originating below the cortex, a time-consuming setup, and generally poor signal to noise ratio. Overall, EEG has significant potential for further implementation and usefulness in biofield studies, particularly as higher quality, controlled studies are carried out and novel approaches to EEG data analysis are designed specifically for biofield research applications.

Electrocardiography: Heart Rate Variability

ECG, similar in principle to EEG, is a diagnostic tool in which electrical activity of the heart is measured and recorded. Typically, skin surface electrodes are placed in a number of locations across the chest, and sometimes the arms and legs. Small electrical fluctuations, driven by cardiac muscle depolarization, are amplified and recorded, providing detailed information about the rate and regularity of the heartbeat, the size and position of the cardiac chambers, and the presence of any damage to the heart. Clinical applications of ECG are numerous, including screening for myocardial infarction, syncope, and other heart-related conditions [185].

ECG can be used to measure heart rate variability (HRV), the variation of time interval between heart beats, for which greater HRV is generally considered to be favorable, and associated with improved health outcomes [186]. For example, lower HRV is associated with greater risk of mortality after myocardial infarction and has also been linked to congestive heart failure and diabetic neuropathy [187]. HRV has also emerged as an important noninvasive measure of emotional arousal, with reduced high-frequency HRV associated with increased state anxiety and emotional strain [188]. For example, individuals with major depression and posttraumatic stress disorder have been observed to have low HRV [189,190].

The sympathetic (SNS) and parasympathetic (PNS) arms of the autonomic nervous system (ANS) are the major inputs that influence HRV [187]. SNS activity can influence the heart via the production of epinephrine and norepinephrine, "fight-or-flight" hormones, whereas PNS activity is primarily mediated by vagus nerve-derived acetylcholine signaling. Respiratory sinus arrhythmia, a commonly used HRV metric, measures HRV associated with respiration, and under resting conditions, respiration-related changes to heart rate are effected primarily via vagal PNS activity. However, both SNS and PNS inputs are important, as HRV measures fluctuations in ANS activity, and therein, saturation or withdrawal of ANS input can lead to changes in HRV [187].

HRV has been used as an outcome measure in biofield studies that have focused on both practitioners and therapy recipients. Practitioners of a variety of biofield practices have been found to exhibit increased sympathetic and decreased parasympathetic tone or no difference from baseline, suggesting that further work is needed to shed light upon these findings [65,191,192]. HRV studies of biofield therapy recipients have included diverse clinical populations, some of which include professionals with burnout syndrome, patients with acute coronary syndrome, and patients with shoulder pain and immobility [193–196]. Increased HRV or no difference in HRV were reported in these populations, though, similarly, further research employing controlled study designs is needed to clarify these findings.

Of the limited number of objective physiological measures employed in biofield studies, HRV is one of the approaches most commonly used. HRV is an appealing outcome for biofield research because it is accepted in conventional

Western medicine, correlates with symptoms and clinical outcomes for a number of conditions, and reflects the functioning of underlying physiology on a number of levels (psychological, neurological, neuroendocrine, muscular, and cellular). Furthermore, the physical location of ECG HRV recording is nearby the putative location of the heart center, or the fourth chakra in some traditions, which is thought to be a key vital center in the body and one that may be manipulated during biofield therapy. As mentioned above, further controlled biofield studies need to be implemented in uniform clinical populations to demonstrate reproducibility of HRV findings, and consensus on methods of HRV analysis and data reporting need to be reached in order to allow for meaningful comparison across future studies.

Apparatus for Meridian Identification

The apparatus for meridian identification (AMI) is a device that is used to measure electrodermal conductance, capacitance, and polarization of the skin at specific acupuncture points called Jing-Well points (or Sei-points in Japanese), which are located near the base of finger and toe nails [197]. Jing-Well points are described as terminal points of meridian channels at which "Qi" exits or enters the meridians [198]. Measurements at the Jing-Well points are thought to reflect the "energy" or "strength" of their corresponding meridians [198].

Measurement procedures typically involve attaching conductive gel silverchloride electrodes to the left and right forearms as nonactive reference points [197]. Subsequently, 7 mm square gel silver foil electrodes are attached to the 28 Jing-Well points as active measurement electrodes. For each measurement, the AMI outputs a single square voltage pulse of 3 volts and 512 μ s between a Jing-Well point and the two reference electrodes. The waveform of the current response is digitally captured and transformed into three AMI output parameters: (1) before polarization (BP), initial peak current before ionic polarization, thought to be a measure of Qi energy in a particular meridian corresponding to the Jing-Well point; (2) after polarization, current after ionic polarization, interpreted as a measure of the state of the autonomic nervous system—similar to galvanic skin response; (3) integral electric charge, total electric charge of polarized ions, thought to be an index of immune function.

Publications detailing the use of the AMI in biofield research studies can be found in the literature, but are limited in number and are largely composed of uncontrolled studies or case reports. Lin et al. reported that 20 minutes of tai chi practice in expert practitioners generated an 17% increase in mean BP values across all Jing-Well points, ranging from +8% to +26% [199]. Similarly, they observed up to a 50% increase in mean BP values in expert Qi Gong practitioners, when comparing BP values before and after practice [200]. In a controlled study of subjects with claustrophobia, it was found that 30 minutes of an energy psychology intervention, involving percussion of acupuncture points during exposure therapy, resulted in a significant reduction in state anxiety and an increase in mean BP values at Jing-Well Points [201]. Relatedly, statistically significant differences between electric potential measurements obtained on and off acupoints and between external focus and healing states have been reported in "energy healing" practitioners [202].

The AMI is one of a number of devices designed to detect and/or measure electrical properties of acupuncture points on the skin. Other wellknown devices include: Dermatron (Electroacupuncture According to Voll), Neurometer, and the Prognos. To more definitively determine the utility of these devices for measuring the effects of biofield therapies, controlled studies with repeated measurements need to be implemented and replicated by independent laboratories. Further, there are a number of technical issues that need to be addressed when designing experiments and interpreting data generated by these devices, such as electrode polarizability, presence of sweat glands, electrode geometry, and other key issues. Ahn and Martinsen provide a thorough overview of these and other technical considerations [203].

Earthing, also known as grounding, a simple practice where people connect themselves electrostatically to the Earth, has been found to hold promise as a therapy for enhancing well-being. This can be accomplished using grounded conductive mats, bed sheets, or grounded body bands when indoors. Earthing is based upon the notion that a negative surface charge on the Earth provides a reservoir of free electrons [204,205]. The Earthing hypothesis states that this reservoir of charge is constantly replenished by the global atmospheric electric circuit, and the body uses these free electrons as antioxidants for neutralizing oxidative stress when direct electrical contact is made between the skin and the ground [206,207]. Studies published over the last decade indicate that such contact yields a broad array of health-related results, including effects on autonomic nervous system function, improved sleep, decreased pain, normalizing effects on cortisol, reduction and/or normalization of stress, diminished damage to muscles caused by delayed onset muscle soreness, reduction of primary indicators of osteoporosis, improved glucose regulation, and enhanced immune function [208-211].

Electrical Stimulation

Electrical stimulation is emerging as an important new paradigm in medicine, particularly for diseases and conditions that are otherwise nonresponsive to pharmacologic therapy. Both invasive stimulation (e.g., vagus nerve stimulation and deep brain stimulation) and noninvasive stimulation (e.g., transcranial direct current stimulation) approaches are currently practiced clinically and are under investigation for several new indications.

The vagus nerve, also referred to as cranial nerve 10, gives rise to efferent motor parasympathetic fibers that innervate nearly every organ in the body and also relays the majority of afferent sensory information about each organ to the brain [212,213]. Vagus nerve stimulation (VNS) requires implantation of a signal generator, similar to a pacemaker, in the chest cavity, placement of the stimulation electrode, and tuning of the stimulation parameters including current (0–4 mA), frequency (1–150 Hz), and pulse width (1–1000 μ s) [214]. VNS is currently cleared for the treatment of partial-onset epilepsy and

intractable depression, though it is being actively studied as a treatment for tinnitus, anxiety, Alzheimer disease, migraines, fibromyalgia, obesity, autism, and sepsis, among other diseases that lack adequate options for therapy. Seminal work by Tracey et al. has also shown that VNS can suppress inflammation by inhibiting inflammatory cytokine production, and has stimulated interest in using VNS to treat a variety of conditions associated with unresolved inflammation [215]. The mechanisms of action of VNS therapy as it relates to this broad array of pathologies are unclear, and are currently an active area of investigation [216].

Deep brain stimulation (DBS), similar in principle to VNS, involves implantation of a brain pacemaker, which transmits electrical impulses (1–200 Hz; 1–150 μ A) via an electrode to a targeted region of the brain [217]. DBS is currently FDA-cleared for the treatment of essential tremor, Parkinson disease, dystonia, and OCD and has been used in research contexts to treat patients with chronic pain, major depression, and Tourette syndrome, though the latter three indications have not received FDA clearance [218]. The clinical effects of DBS are dependent on which region of the brain is stimulated. For example, stimulation of the globus pallidus interna or the subthalamic nucleus has been reported to reduce the symptoms related to Parkinson disease, whereas stimulation of the nucleus accumbens has been associated with mitigation of symptoms of depression and OCD [219,220]. As with VNS, the mechanisms of action of DBS are unclear and remain fervently debated [221].

Transcranial direct current stimulation (tDCS) is an example of a noninvasive electrical stimulation technique, wherein electrodes are placed upon the scalp. The effects of tDCS are dependent on the placement of the electrodes, intensity (0.25–100 Hz; 0–250 μ A), and duration of stimulation, and whether anodal (generally excitatory) or cathodal (generally inhibitory) stimulation is applied [222]. tDCS is considered to be neuromodulatory and has been found to increase cognitive performance in tests of attention, memory, problem solving, and other executive functions [223]. Current understanding of the mechanisms of tDCS is, broadly, that stimulation either promotes neuronal hyperpolarization (decreasing excitability) or depolarization (increasing excitability). Interestingly, the neuromodulatory effects of tDCS can endure beyond the period of stimulation and this phenomenon is a function of current strength and duration of stimulation [222].

Given our understanding of the bioelectric nature of cellular biology, development of technologies that pass targeted electrical current through tissues of the body represents a fundamental step forward in the evolution of medicine. These technologies should be viewed as cutting-edge examples of biofield therapies, as they work by introducing energy into a system that is experiencing dysfunction and generate systems-level effects that can alleviate symptomatology. While the above examples of invasive and noninvasive electrical stimulation are still in the nascent stages of refinement and understanding of the mechanisms of action, the potential for this class of devices to have a positive clinical impact is significant. However, devices that are presently used for electrical stimulation are not without safety issues or risks of side effects, and the long-term effects have largely not been studied. Thus, further work is needed to minimize risks and adverse effects and promote integration of electrotherapies into practice for a wider array of clinical indications.

MODALITIES USING VIBRATION/SOUND

Human beings have been using sound to access deeper states of consciousness, expand awareness, and heal the body for thousands of years. Chanting, toning, Tibetan singing bowls, Chinese meditation gongs, and mantras, are just a few examples of practices that use sound. Since vibration/sound as a modality has many different aspects, here we present a few device *modalities* that are closely related to biofield research.

Infrasound Therapy

Infrasound, sometimes referred to as low-frequency sound, is sound that is lower in frequency than 20 Hz, the "normal" limit of human hearing. One such form of infratonic therapy was developed from scientific research in Beijing China in which natural healers were studied. It was reported that some healers were able to emit a strong chaotic low-frequency sound signal from their hands. Testing in hospitals and research laboratories found that low frequency sound was effective at increasing vitality, accelerating healing, and strengthening immune function [224].

Transcranial Ultrasound Stimulation

Ultrasound (US), while best known for its uses in medical imaging, has also been used for several decades as a noninvasive means of modulating neuronal activity [226,227], and medical imaging studies have elucidated the manner in which US is able to propagate through bone and other tissues. More recently, interest has been directed toward applications of transcranial ultrasound (TUS) for treating mental health and neurological disorders [228,229]. For example, clinical studies have found improvement in subjective mood, suggesting TUS may be a promising noninvasive therapy for treating mental health conditions [230].

TUS works through the placement of US transducers directly upon the scalp. One significant advantage of TUS is its spatial resolution and depth of penetration, which are superior to those of TMS [231,232]. In early experiments, typical ultrasound frequencies and intensities ranged from 1 to 7 MHz, and 1 to 800 W/cm². These were found to be sufficient to destroy some nervous system tissues [229], leading to the development of low-intensity, low-frequency ultrasound (LILFU) techniques, using lower frequencies and intensities of approximately 0.5 MHz and 3 W/cm². Experiments on hippocampal slice cultures and *ex vivo* mouse brains reported that LILFU can stimulate electrical activity in neurons by activating voltage-gated ion channels and enhancing synaptic transmission in hippocampal circuits [229]. In a manner perhaps analogous to effects observed for weak EMFs, LILFU techniques may thus reveal a regime of neuronal sensitivity operating at energy levels below those

previously believed to yield bioeffects. In addition to effects on ion channels, it has been suggested that TUS may also act on intra-neuronal microtubules involved in synaptic plasticity, with relevance to learning, memory, and conscious experience [78,233]. Although TUS has recently been shown to acutely excite neural circuits in the brain, this neuromodulatory approach is still in its infancy, and further work is required to demonstrate the impact on cognitive function and potential therapeutic benefits [231,234].

Life Vessel Therapy

The life vessel is an FDA cleared, Class II medical device employing therapeutic modalities associated with vibration, sound, and light, for which five patents have been granted. Additionally, it utilizes an IR light source to facilitate an increase in both blood circulation and oxygen levels, while the simultaneous combination of vibration, light, and sound produces a profound relaxing effect. Relaxation provides benefits to the body that include: higher energy levels, improved sleep, stronger cognitive abilities, enhanced immune function, and the ability for an individual to reduce stress [235].

Music Therapy

Music therapy is the "clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program" [236]. Music therapy, comprising both creating, listening, and responding to music, has been shown to produce a variety of clinically beneficial results [237]. Music therapy functions along multiple neurological pathways, including those involved in cognitive, sensorimotor, and emotional processing [238], has been suggested to enhance neuroplasticity [239], and is thus included here as a device modality. Music therapy interventions have been designed to promote wellness, manage stress, alleviate pain, express feelings, enhance memory, improve communication, and promote physical rehabilitation. Research in music therapy supports its effectiveness in a wide variety of healthcare and educational settings [237]. Reviews of randomized controlled trials of music therapy concluded that music therapy improved global and social functioning in schizophrenia and other serious mental disorders, gait, and related activities in Parkinson disease, depressive symptoms, and sleep quality. MT may have the potential for improving other diseases [240], social interaction, verbal communication, initiating behavior, and social-emotional reciprocity in autism spectrum disorder [241]. Other reviews reported improved cognitive function and quality of life, and reduced anxiety, depression, and agitation in elderly people with dementia [242,243], reduced stress, anxiety, labor pain, and depression in childbearing women, and reduced number of days to discharge and pain response behaviors, increased weight gain, oxygen saturation, Brazelton scores, and formula intake in neonates [244], enhanced cognitive recovery and mood, improved gait in stroke patients [245,246], and improved emotional adjustment and decreased depression and anxiety following traumatic brain injury [247].

Bioacoustic Therapy

Bioacoustic therapy is distinguished from other sound therapy subcategories by the fact that it is based on human voice analysis. The basic hypothesis is that the human voice can portray a person's state of health. Bioacoustic analysis detects frequencies emitted by a patient's voice, referred to as a "signature sound," which is thought to represent vibrational energies of the body and its functions [248]. Many factors affect the frequencies of one's voice, and bioacoustic therapy claims to isolate and analyze those frequencies, which are related to the health of a patient [248].

Bioacoustics, as a therapeutic technique, originated with Sharry Edwards in 1982 [248]. According to Edwards, "BioAcoustics Voice Spectral Analysis can detect hidden or underlying stresses in the body that are expressed as disease." The vocal print is claimed to be able to identify toxins, pathogens, and depletion or excess of nutrients. In addition, it is claimed that the vocal print can be used to match the most compatible treatment remedy to each client. According to Edwards, bioacoustics has been shown to control: pain, body temperature, heart rhythm, and blood pressure. It has also been reported to regenerate body tissue, and alleviate the symptoms of many diseases [249].

Neuroacoustic Therapy

Dr. Jeffrey Thompson has been the most prominent pioneer of neuroacoustic therapy. His research has led to the development of protocols for using sound to modulate brain activity, affect sympathetic–parasympathetic balance, and synchronize the activity of the right and left brain hemispheres. He has applied these methods to promote stress reduction, cardiovascular disease prevention, management of depression, and a host of other conditions. His work with neuroacoustics is very different from other forms of music therapy. It is not about facilitating a patient's musical self-expression, nor does it use music as a palliative intervention. It involves direct application of specific sound combinations—unique to each patient to entrain beneficial physiologic responses [250].

Starting in the 1950s, another type of neuroacoustic device technology was developed by Robert Monroe and the Monroe Institute. Based upon early observations of binaural beat phenomena (BBP)—when two pure tones of slightly different frequencies are presented to each ear, the brain perceives the phase difference between these signals as a wavering sound—the Monroe Institute developed technology intended to induce particular neurological states using BBP [The Monroe Institute], 2010: The Monroe Institute Methodology. Retrieved September 22, 2010: The Monroe Institute Methodology. Retrieved September 22, 2010: The Monroe Institute Methodology]. Subsequent developments by the Monroe Institute were built upon observations that anomalous states of consciousness could be achieved through exposure to BBP [251], and that such changes had relevance to alterations in brain function and oxygen saturation during religious ceremonies [252]. BBP technology has also been found to alter theta-band EEG activity and hypnotic susceptibility [253], and affect vigilance and mood [254]. A summary of the history and

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present state of activities at the Monroe Institute may be found at http://www.monroeinstitute.org.

MODALITIES BASED UPON MECHANICAL/PHYSICAL INTERACTIONS

Acupuncture

TCM describes acupuncture as a technique for balancing the flow of "energy" or "Qi," believed to exist in channels in the body called meridians [255]. Within this framework, disruption of energy flow is a fundamental cause of disease. TCM posits that, in the human body, there are more than two thousand acupuncture points that are connected by 12 primary meridians and 8 secondary meridians [256]. After a diagnostic process, acupuncture practitioners often carefully select and stimulate a number of acupuncture points by inserting thin metal needles into the skin, and sometimes manipulating them manually (i.e., spinning, flicking), or in some cases, stimulating them electrically (electro-acupuncture). Acupuncture needles are most commonly made of stainless steel, ranging from a few centimeters in length to over 10 cm and between 0.16 and 0.46 mm in diameter [257].

Acupuncture is used to treat a wide array of symptoms and diseases. Some of the most common applications of acupuncture treatment are for acute and chronic pain (elbow, knee, and back), osteoarthritis, chemotherapy side effects (nausea, fatigue), and fibromyalgia [258–261]. While many studies acknowledge the TCM basis of acupuncture theory, emphasis has been placed on identifying cellular and molecular signaling pathways that may be testable in an experimental design. For example, the latest findings suggest that some of the clinical effects of acupuncture may be related to local inflammatory responses, cytoskeletal remodeling, release of adenosine (anti-nociceptive effects), neuromodulation, endogenous opioid production, and autonomic nervous system tone [262-263]. That said, it is possible that a relationship exists between the reported biological cascades activated by acupupcture point stimulation and the movement and balancing of Qi in the boy The validity of this hypothesis, however, is yet to be established and will require further development of techniques to quantitatively measure Qi alongside the aforementioned Western biological outcome measures. Both the World Health Organization and the U.S. National Institutes for Health recommend acupuncture for a variety of health issues ranging from pain to otolaryngological, gastrointestinal, neurological, endocrinological, and dermatological conditions [266].

MODALITIES BASED UPON HUMAN INTENTION

Intention and Nonlocality Effects

Evidence of human intentionality interactions suggests that human consciousness may play a key role in experimental and health outcomes [268]. The role of human consciousness in biofield interactions has been extensively considered [269], and a summary of selected peer-reviewed publications may be found at http://deanradin.com/evidence/evidence.htm. The Global Consciousness Project may constitute the largest nonlocal intentionality-based biofield device to date, with reports of correlations between global events and statistics of continuously-operating random event generators around the world [270]. The Global Coherence Initiative is currently installing a global network of 12-14 ultrasensitive magnetic field detectors around the planet to examine the effects of external fields of solar and cosmic origin upon human activity and also to test the hypothesis that large numbers of people holding a shared intention might encode information on the earth's energetic and geomagnetic fields [271]. The motivation for this work is supported by a long history of research on intentionality effects and nonlocality [269], and recent reports of correlations with human intention that include: human intention and random event generators [272–274]; healing intention and cultured cells [275]; intention, music, and seed germination [276]; distant healing of surgical wounds [277]; and water crystal formation [278]. These reports are also bolstered by a growing number of experiments demonstrating EEG correlations between isolated human subjects [279-283], and corroboration using human neurons adhering to printed circuit boards [284]. Experiments performed with shielding suggest that some of these results are not mediated by EMFs [279,284] and it has been proposed that some form of quantum entanglement may be responsible for the observed correlations [285].

One example of a device methodology based upon intention and nonlocality is the intention host device (IHD) [286]. The general hypothesis is that quantum mechanical and thermodynamic concepts interact with biological systems via the influence of EMFs and electronic devices that have been exposed to human intention [287]. These devices are simple memory-containing electronic circuits, which are placed inside a laboratory, in close proximity to a target system that is hypothesized to be affected by the presence of the IHD. Intention is programmed into the IHD by the experimenter's conscious affirmation that the device will cause a change in the laboratory environment that will yield a particular change in the target system. In a series of IHD experiments it was found that these devices may broadcast intention in a manner that can alter, in a particular direction, time-series measurements of physicochemical quantities such as temperature, pH, drosophila fitness and energy metabolism, in vitro enzyme activity, and molecular concentration variability [286,287]. The results indicated that shielding from ambient EMFs via a Faraday cage made a significant difference relative to the unshielded control and that an intention effect yielded significant positive effects in the hypothesized direction in each target system [286,287]. Other trials showed effects on pH due to imprinting information onto IHD via passive exposure to Buddha relics and suggested that a verbal request from a deep meditative state by four humans appeared to be a necessary condition for this "imbedded loving kindness essence" to manifest itself in this way [288]. Additional experiments suggested that the observed phenomena are reproducible in different laboratories [289] and could occur across separation distances of

200–6000 miles [290,291] and that possible enhancement of the effects may occur in remote sites located underground [291]. A review of the results suggests a robust type of "subtle energy detector" and discusses the notion that such devices can "condition" laboratory spaces toward particular outcomes, based upon a gauge-field theory of EMF interactions [292]. Such results, if further confirmed, might have far-reaching implications not only for the study of consciousness, but also for biology in general and the reproducibility of experimental results.

MODALITIES USING GAS OR PLASMA

Gas and Plasma in Biology

Most of the known visible matter in the universe is in the form of ionized gas, which is by definition, plasma. All of the suns in all of the billions of galaxies are made of plasma. Most of the tenuous matter between solar systems and galaxies is also gas or plasma. Plasma is so pervasive that it receives a lot of attention from physicists and complex theories have been developed to explain the properties of plasma.

Plasma is a fascinating form of matter because it is so energetic and so dynamic. Thus it is no surprise that plasma attracted the attention of researchers such as Nicola Tesla and others who believed that there was more to understand of plasma, electricity, and magnetism, beyond what classical physics models posit. Using some of Tesla's ideas regarding plasma as a foundation, a group of engineers developed what is referred to as the "Tesla Energy Lights" [293]. These lights are tubes similar to neon tubes and emit light. The inventors of the Tesla Lights claim that these lights, which are made using noble gases, emit "subtle energies." They claim that these frequencies can empower the user to have clearer thinking, positive feelings, and higher awareness by directing and interacting with balanced energies [293].

Regarding gas, some researchers claim that an appropriate level of compression of noble gas immersed in a properly aligned magnetic field can generate "subtle" energies that can be used for healing [294]. Yury Kronn (formerly Yury Khronopulo), who was formerly a Soviet radio-physicist, and is now an American citizen, was quite famous in Russia. He developed a theory of resonant nonlinear interaction of light with matter, which was the basis for a physics text book [295]. Dr. Kronn has since developed machines based on his theories, which could be described as plasma machines capable of generating low-nonthermal energies under controlled conditions. He claims he can produce in water or creams the signature or resonance of any element or molecule, including the properties of that element or molecule, and has come up with a line of products based on his invention [296].

Electrophotonic Imaging/Gas Discharge Visualization

An important example of the use of plasma in energy medicine, the gas discharge visualization camera (GDV) is based on the Kirlian effect and utilizes modern optics, electronics, and computer processing for analyzing weak photon emission stimulated by a pulsed EMF. The Kirlian effect is based on photographic techniques used to capture the phenomenon of electrical glow, called coronal discharge. It is named after Semyon and Valentina Kirlian, who in the 1930s discovered that if an object placed on a photographic plate is submitted to a high intensity EMF, usually created by placing a high voltage metal plate under the photographic plate, an image of the glow around the object (a corona discharge) is captured on the photographic plate [297]. This technique has been called electrography [298], electrophotography [299], corona discharge photography (CDP) [300], bioelectrography [297], gas discharge visualization (GDV) [301], electrophotonic imaging (EPI) [302], and, in the Russian literature, Kirlianography [297]. The first GDV camera was made in 1995. Since that time, the Russian company Kirlionics Technologies International (KTI) has produced hundreds of such cameras and developed new designs. The latest design is an inexpensive, small camera called the BioWell. It functions under the same principle as the GDV/EPI (the Kirlian effect) but it is designed to be used in clinical settings while the GDV is a research device. These cameras are being used in 63 countries around the world. The EPI method can be viewed as an express method because it requires only about 5 minutes to take 10 images of the fingers, around 1 minute to calculate the parameters of the images, and about 15 minutes to display and provide a basic interpretation of the obtained results. These cameras have a Russian Certificate of Conformance as a medical device. The name EPI has appeared only recently, to describe the technique more directly [303]. This technique is becoming very popular in integrative medicine and in a wide range of scientific applications [304-306]. Simultaneously with these applications, the EPI technique has also been used in conventional medicine and in psychophysiologic applications [303].

The objective of the GDV is to identify the functional psycho-emotional and physiological state of a person using their fingertips [307]. The analysis of natural electrophotonic emission is mainly based on the intensity, fractal structure, and area of the gas discharge. The relationship of the captured image to organs and organ systems is determined by the acupuncture approach. Therefore, the image of each finger is divided into sectors corresponding to tissues, organs, and body systems [303]. Also, the GDV technique provides the integral parameters of entropy and autonomic tone, which are important components in the analysis of human functional state [297]. Entropy is a measure of disorder, and an increase in entropy has been postulated on the First International Congress of Systemic Medicine as a manifestation of sickness, negative impact of chemical, biological, physical, or emotional stress, and chronic degenerative disease [308].

There have been close to a thousand papers published involving research on the GDV (most papers in Russian) and a few hundred papers in the West, and a recent review of GDV medical and psychological applications has been published: "Electrophotonic Applications in Medicine: GDV Bioelectrography" [309]. One example of an application of the GDV in medicine is a study that focused on cancer [310]. The objective of the study was

to explore the potential of the GDV for oncology practice. All subjects were diagnosed via conventional techniques. GDV measures of the 10 fingers were taken before the beginning of an oncology treatment and 2 and 6 weeks after treatment. The complex treatment included surgery, chemotherapy, and irradiation. The results showed statistically significant differences in parameters between oncology patients and noncancerous patients, and a trend in which oncology patient parameters moved toward healthy values after 6 weeks of treatment. These data suggest that informatics based upon GDV measurements may be useful for gaining deeper understanding of the nature of disease states and guiding practitioners and their patients toward enhanced wellness.

OTHER DEVICE MODALITIES

In light of observations of nonlocal effects, which suggest that biofield interactions may involve means of information transfer that cannot be easily described via well-understood substrates (e.g., EMFs), this section briefly describes modalities that do not fit easily into the categories listed above. Although the list of devices that could fit in this section is quite extensive, we chose to focus on a few of the most popular or promising modalities, including torsion fields, orgone energy, and scalar waves because of their prominent positions amongst devices purported to act upon the biofield. The biophysical substrates of these modalities are either poorly understood and/or not generally accepted by the scientific community, and claims of effects and efficacy have not been verified.

Torsion Field Devices

Torsions fields (also called axion fields, spin fields, spinor fields, and microlepton fields) have primarily been studied in Russia. The first research generally credited with the discovery of torsion fields was that done in the late 1800s by Russian professor N.P. Myshkin [311]. Einstein's colleague Dr. Eli Cartan first termed this force "torsion" in 1913 in reference to its twisting movement through the fabric of space time.

In the 1950s pioneering Russian astrophysicist Dr. N.A. Kozyrev (1908– 1983) was studying how binary stars, or stars that revolve around each other, evolve. He discovered that they evolve to resemble each other much faster than allowed by current accepted laws of physics. He suggested an explanation for this phenomenon by assuming that the burning interior of a star changes its degree of entropy, an irreversible process, which, in turns, affects the flow of time. From observations such as this one, Kozyrev arrived at his theory of "torsion" and "time density," which stipulates that if entropy decreases in one place it must increase at another place, and vice versa. Kozyrev also realized that time density variations would imply that space must have a twisting property. It is well known that all subatomic particles (electrons, protons, neutrons, etc.) have a spin. So, all of these particles must twist space around them because of their spin. Consequently, when a charged particle produces an EMF, it must produce a torsion field also. This results in a variety of phenomena that cannot be explained by current scientific models [254].

Many experiments in support of the existence of torsion fields are presented in a volume written by Swanson [312]. These include experiments with torsion pendulums, experiments showing a 50% reflection by aluminum, changes in mass density, astronomical observations, and other phenomena. Torsion fields are of interest here in that they could provide a theoretical framework for explaining some "subtle" low-energy nonthermal biofield interactions.

Orgone Energy

Orgone energy is a purported universal life force originally proposed in the 1930s by the Austrian psychoanalyst Wilhelm Reich (1897–1957) [313–315]. In its final conception, developed by Reich's student Charles Kelly after Reich's death, orgone energy was conceived as the anti-entropic principle of the universe, a creative substratum in all of nature comparable to Mesmer's animal magnetism, the Odic force of Carl Von Reichenbach, and Henri Bergson's *élan vital* [316]. Orgone was seen as a massless, omnipresent substance, similar to luminiferous a more closely associated with living energy than inert matter. It cound coalesce to create organization on all scales, from the smallest microscopic units, called bions in orgone theory, to macroscopic structures like organisms, clouds, or even galaxies [313].

Reich's theories held that deficits or constrictions in bodily orgone were at the root of many diseases, including cancer, much as deficits or constrictions in the libido could produce neuroses in Freudian theory. He created the Orgone Institute to pursue research into orgone energy after he immigrated to the United States, and used it to publish literature and distribute material relating to the topic for more than a decade. Reich designed special "orgone accumulators;" devices purported to collect and store orgone energy from the environment, for improvement of general health [313].

Scalar Waves

Scalar waves are said to be produced when two electromagnetic waves of the same frequency are exactly out of phase (opposite to each other) and the amplitudes subtract and cancel each other [317]. The result is said to be not exactly an annihilation of the magnetic fields but a transformation of energy back into a "scalar wave," which continues to convey information [317]. Scalar waves have been purported to be created by wrapping electrical wires around a figure of eight in the shape of a möbius coil. When an electric current flows through the wires in opposite directions, the opposing EMFs from the two wires cancel each other and create a scalar wave [317]. Scalar waves are purported to explain homeopathy, achieve lymph detoxification, treat diabetes, myopia, kidney stones, Parkinson disease, strokes, arthritis and cancer, and reverse the aging process [324].

DISCUSSION

The biofield devices described here span a wide range of diagnostic and therapeutic functions, yet share the common property of acting in a manner that might be best understood in terms of biofield interactions. Notably, many of the biofield devices described have been shown to be effective and have been adopted by the biomedical community, including ultrasound, thermal imaging, ECG, EEG, and other electrophysiological techniques, some EMF therapies, and techniques using light, such as LT. This indicates that a biofield viewpoint is already an integral part of the Western biomedical canon, and that substantial progress has been made in laying the foundations for further progress.

In contrast with the devices for which the mode of operation is well understood, several biofield devices appear to function in a manner that currently lacks complete explanation from a conventional Western scientific perspective. For example, weak nonthermal EMF bioeffects are beginning to be more clearly understood, yet the complexity of the biological targets and the spatially distributed nature of EMFs themselves, make it difficult to describe specifically the myriad biochemical interactions involved, suggesting that a "systems biology" approach to these topics may be needed [326]. A number of other device technologies also appear to employ mechanisms that are currently not clearly understood. Notably, acupuncture and other therapies based upon TCM are in widespread use, but from a Western scientific viewpoint their mechanisms of action have not yet been explained. Also, devices operating via consciousness or intention may act via nonlocal quantum correlations, yet further work is needed to understand the specific properties of these interactions, let alone the general significance of such quantum phenomena. There is strong experimental evidence for several of these modalities, for example, BE, consciousness and nonlocal interactions, GDV, and TCM, suggesting that further study in these areas may substantially advance our understanding of biofield interactions.

Relatedly, several device modalities suggest the existence of very low energy, or "subtle," interactions. For example, the existence of bioeffects due to extremely weak EMFs with energies of interaction many orders of magnitude below the average Brownian thermal energy, may provide a promising direction for future research. Also, recent evidence that a wide variety of biological regulatory processes occur via endogenous EMF and possibly quantum information processing via the cytoskeleton [70–73,76–78] may point toward a deeper understanding of how low-energy signaling is related to consciousness, cognition, and emotion, perhaps by coordinating events across the molecular, cellular, and organismic levels [75]. An added challenge is that some devices and interactions may require the identification of other low-energy interactions for which we currently have no knowledge or understanding.

Further research under carefully controlled conditions may shed light upon those aspects of biology which most clearly exhibit these remarkable sensitivities to low-energy influences. This would require the development of more sensitive instruments and experimental protocols designed to filter or clarify the effects of interfering factors. Methodological and logistical aspects, for example, would include: the development of instruments sensitive enough to measure biofields or low-energy interactions; specialized equipment and laboratories, including the use of Faraday cages, µ-metal enclosures, completely dark rooms, anechoic chambers, noiseproofing, etc. One step with relevance to a significant portion of cellular biology research is the careful assessment of all EMF exposure conditions, accounting for the fact that nearly all cell culture incubators produce a nonuniform EMF of a strength that has been clearly shown to produce cellular effects [85,327]. The picoTesla (pT) to nanoTesla (nT) EMF effects summarized above may be more difficult to control completely, as shielding for these extremely low field strengths may be technically difficult or impossible in some situations. These difficulties could indeed suggest that a new paradigm of research may be required wherein the naturally occurring extremely weak EMFs due to solar/geomagnetic and other ambient sources are considered as an integral part of the experimental environment. Along these lines, considering the potential for effects due to circadian and other natural rhythms may also be necessary.

A more comprehensive understanding of the nature of biofield interactions is likely to also require an evolving scientific paradigm. First, biofield interactions often involve exceedingly complex systems that cannot be meaningfully broken down into their constituent parts. Attempts at reducing biofield interactions to reductionist substrates may thus be misguided, suggesting that a more holistic "systems biology" approach would be fruitful [326]. Also, interactions involving consciousness and nonlocality suggest that the subjective nature of bioenergetic phenomena such as experimenter expectancy effects could play a role in research outcomes. This is especially important in the light of results described above suggesting that consciousness can influence sensitive devices. In order to more clearly asses this, systematic inquiry is needed to determine the extent to which intention and low-energy interactions might "condition" laboratory spaces toward particular outcomes [291]. The crossing of this boundary beyond objectivity, wherein experimenter expectancy and placebo effects play a measurable role in experimental outcomes, presents a major new challenge to the conventional biomedical research paradigm, which is based fundamentally on the assumption of objectivity. While caution is needed in the application of these results to conventional biology, some modern biochemical protocols, assays, and measurement devices could be sensitive to these subjective factors, perhaps shedding light on the apparent difficulties and complexities often encountered in experimental replication and translational medicine [328-330].

Although private sources of funding have become increasingly common in science today, such funding often produces conflicts of interest. For an emerging field such as biofield studies, which proposes a major paradigm shift in science, such conflicts of interests could significantly hinder the interest and adoption by the mainstream scientific and nonscientific community. As

much of the funding for biofield device technologies and even basic research has come from device manufacturers, effort could be made for cooperation between such manufacturers, in order to study multiple similar devices or replicate each other's findings. The long-term benefits of such cooperation may profoundly outweigh individual short-term goals.

CONCLUSIONS

In our modern technological society, devices have broad cultural and scientific impact, and these biofield devices are likely to be highly influential in furthering research and the dissemination of biofield concepts. The significant contributions to the biomedical sciences of the devices described here demonstrate that substantial progress in biofield studies has been made. In order to continue to move biofield studies forward, further systematic study is needed, and this will require collaboration between a community of research groups and sufficient funding.

The biofield paradigm described here, wherein an organizing principle, or set of principles, acts across hierarchical levels, informs a holistic philosophy in which all things are interconnected: within the human body, within communities, the environment, our planet Earth, and the cosmos. This paradigm of connectedness holds promise for more humane and personalized forms and medicine, and for the sustainable use of human and natural resources. As science, biomedical practice, and device technologies based upon this viewpoint emerge, it is natural that our human viewpoint will also undergo a corresponding shift, with important implications for the forward progress and evolution of our species.

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