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REVIEW

Life Rhythm as a Symphony of Oscillatory Patterns: Electromagnetic Energy and Sound Vibration Modulates Gene Expression for Biological Signaling and Healing

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INTRODUCTION—BIOLOGICAL RHYTHMS: MUSIC MEETING SCIENCE

All life exists within a sea of vibration, and rhythm is fundamental to all of life. Diurnal, seasonal, lunar, and solar cycles, and the resonant electromagnetic field (EMF) oscillations of our planet make up the symphony of rhythms in which life on Earth exists. As life evolved amidst these natural rhythms, they were integrated into many basic human biological responses, which coincide with diurnal and seasonal cycles[1] and the many aspects of human and animal behavior and physiology that are correlated with the phases of the moon.[2] From the basic activities of daily life to our relationship with the animals on Earth,[3] human society is structured around the moon's rhythm, and deeply rooted monthly circadian rhythms govern human sleep patterns, persisting even in isolation from our conscious awareness of the lunar phase.[4] Our lives contain a seeming infinity of rhythms, with vibrations at the atomic and molecular levels and within biochemical reaction rates. The physiological correlates of the rhythms of the breath, heartbeat, and brain have been extensively studied and shown to be intimately related to our emotions, thoughts, and psychospiritual state. For example, respiratory output is coupled to a complex interaction between the brainstem and higher centers connecting the limbic system and cortical structures, thus creating a basic link between breathing and the emotions.[5] A substantial body of research has demonstrated the fundamental interconnectedness of mind and emotion, brain and heart rhythms,[6] variations in circadian heart rhythms have been shown to correlate with psychiatric disorders,[7] an emerging language for interpreting brainwave electroencephalogram (EEG) rhythms is now allowing a deeper understanding of the relationships between EEG rhythms, cognition and neuropsychiatric disease,[8] and pulsatile dynamics in genetic circuits is essential for the temporal organization of cellular stress response, signaling, and development.[9] The thread that connects these various studies is the impact of rhythm and the notion that rhythms can communicate bioinformation that governs a wide variety of functions, including that of guiding living beings towards health and well-being.

Rhythm is the fundamental characteristic of music. In frequencies, timbres, and the passage of beats through time to form rhythms, music is an apt metaphor for this carrier of life-information. And the notion that music can touch the core of our being and is as old as human consciousness. Plato grappled with the powers of music in *The Republic*, stating that the various Greek modes convey specific qualities: "Then beauty of style and harmony and grace and good rhythm depend on simplicity—I mean the true simplicity of a rightly and nobly ordered mind and character."[10] And though Shakespeare has been famously quoted as referring to music as the "food of love," he went much further, writing that music has the power to create: "Orpheus with his lute made trees, And the mountain tops that freeze, Bow themselves, when he did sing," and the power to destroy life: "In sweet music is such art, Killing care and grief of heart, Fall asleep, or hearing, die."[11]

Music has been shown to modulate several cardiac and neurological functions and to trigger measurable stress-reducing pathways,[12] to modulate blood pressure, heart rate, respiration, EEG measurements, body temperature and galvanic skin response; alter immune and endocrine function; and ameliorate pain, anxiety, nausea, fatigue, and depression.[13] Significant correspondence has been found between specific musical tones played to the skin through speakers and traditional Chinese descriptions musical tones associated with the acupuncture meridians.[14] The notion that one "hears" sounds not only through the ears but rather through the whole body is echoed in the words of the Sufi musician, healer and mystic, Hazrat Inayat Khan:

> *A person does not hear sound only through the ears; he hears sound through every pore of his body. It permeates the entire being, and according to its particular influence either slows or quickens the rhythm of the blood circulation; it either wakens or soothes the nervous system. It arouses a person to greater passions or it calms him by bringing him peace. According to the sound and its influence a certain effect is produced. Sound becomes visible in the form of radiance. This shows that the same energy which goes into the form of sound before being visible is absorbed by the physical body. In that way the physical body recuperates and becomes charged with new magnetism.*[15]

Here, Khan reinforces the notion of a deep relationship between music and neurobiology, indicating that further understanding of how music can modify nervous system activity could have implications for developing mind-body-spirit therapies that are effective not only as adjuncts, but as central treatment modalities in rehabilitation and therapy.[16]

Rhythms show up in many aspects of life. They affect the way we feel day by day or throughout the seasons. They affect our moods and attitudes deeply, even on a personal basis, so that some activities and personal disciplines "click" with us while others don't. Even the language we use to communicate with each other is able to deliver multiple, between-the-lines, meanings according to the fine tuning of the sound of voice. In our daily activities, we may sometimes find deep satisfaction while at other times we are simply engaged in a boring routine, perhaps without realizing that at one time our activities are in tune with our natural life rhythm, and at another time we may be forced to adapt to a different rhythm for reasons that may not be fully natural.

In this review, we will provide evidence that, from the cellular level to the whole organism, every signaling event is fashioned by rhythms—as vibratory patterns—and that synchronization of coupled oscillators and dynamical systems is a crucial issue in the orchestration of essential processes of life. We will show that changes in the rhythms and modes of interaction of subcellular oscillators can result in remarkable modulation of gene expression and cellular dynamics, playing an essential role in states of wellness and disease. Within this context, we will discuss the use of EMFs and sound energy as tools for restoring healthy cellular dynamics, reprogramming DNA structure, and eliciting self-healing mechanisms. We will highlight how EMFs and sound energies can "sing" with stem cells, and even with non-stem-adult somatic cells to reprogram cell gene expression and fate, activate natural repairing abilities, and counteract cellular aging processes, paving the way toward unprecedented strategies of regenerative medicine. Particular emphasis will be placed on the large body of evidence demonstrating that cytoskeletal structures are dynamic modulators of subcellular, cellular, and intercellular information that coordinate biological regulation across the atomic/molecular to organismic levels, giving rise to the notion of a field of dynamic bio-information or "biofield." While molecular and gene expression rhythms affect the entire individual, it has been shown that the reverse also occurs. To this end, we will summarize how recent advances in neurobiology, psychosocial genomics, and research on yoga, meditation, and other mind-body disciplines have shown that emotional states, cognition, states of stress or relaxation and psychosocial factors can strongly affect genome function. This deep-seated bidirectional flow of information, branching between the atomic/molecular, organismic, and psychosocial levels, thus produces a dynamic, holistic biofield wherein our consciousness, emotional expression, and social behavior are intimately interwoven with our molecular and gene expression patterning.

BIOLOGICAL CLOCKS: SETTING LIFE'S RHYTHMS

The synchronization of multiple rhythms is an essential manifestation of living processes. While it is well known that biological clocks located in the central nervous system drive our circadian rhythms, there is now compelling evidence that the central nervous system also acts as a merging/integration point of biorhythms emerging from self-sustaining cellular and subcellular oscillators. For example, it has been shown that the regulation of metabolism and energy production of the entire organism across the daily cycles of fasting and feeding is orchestrated by subcellular transcriptional oscillations (clocks) controlling the basic dynamics of substrate biosynthesis and energy production (adenosine triphosphate, ATP) at the mitochondria.[17]

Another basic type of biological clock is made up of the mechanisms governing essential biological processes such as embryonic development, neuronal plasticity, cell memory, and differentiation of various types of stem cells. For these processes, calcium (Ca^{2+}) ions act as important messengers, for which intracellular sequestration of Ca^{2+} by specific agents has been shown to modulate the above pathways. It is striking that experimental evidence indicates that transient changes in intracellular Ca^{2+} homeostasis, rather than occurring in a manner corresponding to diffusion and passive transport (ie, increasing from a baseline to a stable long-lasting plateau and then declining again), is orchestrated in real-time by subcellular pacemaker sites producing Ca^{2+} waves and oscillations.[18] Accordingly, the rhythmic beating of stem cell–derived cardiac cells is governed by dynamic coupling of cellular electrophysiology and cytosolic Ca^{2+} oscillations.[19] Thus, Nature chose to create subcellular clocks to guarantee an exquisite regulation of the Ca^{2+} dynamics essential for many processes.

Cellular oscillators also play a crucial role in orchestrating embryogenesis and the patterning of differentiation in stem cells, which relies on the timely proliferation of progenitor cells and their subsequent differentiation into the multiple lineages that form different parts of the embryo. Modulation and orchestration of the timing of cell differentiation and cell fate choice are key issues for making organs of the right size, shape, and cell composition. To this end, both during embryogenesis and throughout adult life, the composition of secreted proteins that determine the overall rhythmicity of multiple-cell networks has been shown to be dependent upon cell crowding.[20] Starting from a single fertilized oocyte, up to the level of the entire organism, cell proliferation and differentiation are antagonistically regulated by multiple activator and repressor genes, whose activity is fash-

ioned according to specific oscillatory patterns in gene transcription.[21,22] There is compelling evidence that during embryonic development, during somite segmentation, for example, specific genes function as biological clocks, acting through both short and long lived oscillatory pathways often involving tonic feedforward and feedback mechanisms.[23-30] The biomedical implications of this are extremely important, as the impairment of these biological clocks leads to premature or aberrant stem cell differentiation, or depletion of certain stem cell pools, resulting in dysmorphic brain and heart structures incompatible with post-natal survival. [27,31-35]

In general, aberrant cellular oscillatory patterning is associated with severe disease. For example, genetic defects in the assembly or rhythmic function of primary cilia, which are oscillatory sensory organelles, give rise to developmental defects and diseases in mammals. One of these genetic disorders, known as *primary ciliary dyskinesia*, most commonly arises from loss of molecular motors that power ciliary beating.[36] The disease involves abnormal lung development and function, infertility, and in some cases a condition called situs inversus, in which the internal organs (for example, the heart, stomach, spleen, liver, and gallbladder) are in opposite positions from where they would normally be located. In mice, embryos bearing a mutation associated with lack of primary cilia develop a severe cardiac disease, including ventricular dilation, decreased myocardial trabeculation, and an abnormal outflow tract.[37] It is clear that impairment of the molecular mechanisms that govern the circadian clock at cellular level also play a central role in the so-called "metabolic syndrome" that represents a spectrum of disorders whose incidence continues to increase across the industrialized world. Comprised of several metabolic abnormalities, including central (intraabdominal) obesity, dyslipidemia, hyperglycemia, and hypertension,[38] this syndrome has become a major public health challenge worldwide, with an estimated 25% to 40% of the population between 25 and 64 years of age affected. An essential distinctive trait of the syndrome is the disruption of the fine tuning of cellular oscillators that compose the "mammalian circadian clock."[38] This clock consists of a series of interlocking transcription/translation feedback loops, involving the synchronization of the availability of transcription factors that activate the expression of downstream clock target genes. Recent evidence also indicates that disruption of circadian rhythms may play a pivotal role in cognitive disorders associated with schizophrenia.[39] In this disease, impairment may occur not only in the circadian master clock in the hypothalamic suprachiasmatic nuclei that is responsible for controlling circadian rhythms but also at the level of local semi-autonomous oscillators capable of generating self-sustained circadian oscillations in individual cells in a number of brain tissues, including the hippocampus, cerebral cortex, and cerebellum.[39]

Underlying all of the above reported findings one may see that the coupling of intrinsic oscillatory rhythms originating at the molecular and single cell level is intimately related to higher-level structure, function, and the generation of a wide range of biological rhythms. At the cellular and subcellular levels, oscillatory behaviors have been shown to emerge as a direct result of simple negative feedback loops and coupled positive and negative feedback loops,[40] and rhythms arise from stochastic, nonlinear biological mechanisms interacting with a fluctuating environment[41], indicating that oscillations are a natural outcome of a variety of essential cellular biochemical interactions. Another concept central to the study of biological rhythms is the existence of coupling between oscillators giving rise to collective behaviors such as phase synchronization.[41] An extremely large body of research has examined the conditions under which periodic behaviors, stochastic resonance (coherent entrainment due to noisy signals), and chaotic behaviors can occur in dynamical systems and systems of coupled oscillators, and the results have been applied to nearly every level of biological function, from the subcellular to the organismic.[41] For example, it has been clearly demonstrated that the generation of circadian rhythms at the suprachiasmatic nucleus is the result of the coupling of oscillators across the cellular and multicellular levels,[42] and a general framework for the emergence of synchronization in circadian cooperative systems employs non-linear coupled oscillators, resulting in phase-synchrony across large numbers of cells,[43] In neuronal networks, large scale simulations typically employ electrically phase-coupled systems that give rise to cooperative behaviors across large numbers of neurons.[44] Systems of genetic oscillators governing the synchronization of cells mediated by intercellular communication exhibit synchronous behaviors in spite of intrinsic parameter fluctuations and the presence of extrinsic noise.[45] Several novel behaviors have been noted, including phase synchronization within a system of weakly coupled self-sustained chaotic oscillators, suggesting that even under chaotic conditions, phases between individual oscillators can tend toward synchrony,[45] and there has recently been interest in the existence of "chimera states" in networks of coupled oscillators wherein a wide spectrum of complex states emerge from the underlying dynamics of a system of weakly coupled oscillators containing both synchronous and asynchronous elements.[46] Thus, the progression toward rhythmicity and complex behavior is a natural outcome of multipart, dynamically interlinked systems.

BIOLOGICAL EFFECTS OF ELECTROMAGNETIC FIELDS

All life exists in a sea of EMFs. In the modern world, we are constantly immersed in both natural and human-made fields, including the geomagnetic field, globally propagating waves in the earth-ionosphere cavity (Schumann resonances), the many EMFs pro-

duced by power transmission lines, microwave communication relays, and fields from a wide variety of commonly used devices, including mobile telephones and radiofrequency Wi-Fi stations. Because life on Earth evolved in the ambient geomagnetic environment, of particular interest to the question of possible coupling with natural geomagnetism are weak EMFs, ie, those with strength on the order of the Earth's 50 μT field. The existence of bioeffects for EMF signals of this strength has been firmly established, and the mechanisms by which constant and extremely low frequency (ELF) μT-range magnetic fields can directly influence biological processes have now been more clearly elucidated.[47-50] In addition to a significant amount of literature on bioeffects due to geomagnetic-range field strengths,[51] a growing body of evidence has shown that effects can also occur at much lower field strengths, on the order of nanoTesla, including effects on development in chick embryos,[52,53] in vitro breast cancer cell proliferation,[54] in vivo tumor growth,[55-57] planarian fission and regeneration[58,59]; allergic encephalomyelitis in rats[60]; gravitropism of plants,[61] MCF-7 breast cancer cell growth,[62] and an Alzheimer's model in mice.[63] A significant aspect of these extremely weak EMF bioeffects is that the energies of interaction are substantially lower than the average random thermal energy due to Brownian motion,[48] suggesting the existence of a more subtle level of bioinformation transduction operating at extremely low energies.

RESONANCES OBSERVED FOR WEAK EMF BIOEFFECTS

Resonance produces enhanced effects when the frequency and/or amplitude of an applied EMF matches specific values for which cells or tissues have increased or decreased sensitivity. In recent years, it has been firmly established that amplitude and frequency resonances can occur for μT-range EMF exposures in a variety of in vitro and in vivo systems, such as brainwaves and neuronal calcium efflux,[64] membrane transport,[65] 45Ca incorporation in human lymphocytes,[66] calcium flux in bone cells,[67] liposome permeability,[68] calcium signal transduction in the lymphocytes,[69] neurite outgrowth in PC-12 cells,[70,71] myosin phosphorylation,[72] calcium efflux though lipid vesicles,[73] glutamic acid currents in aqueous solution,[74-78] IGF-II expression for human osteosarcoma bone cells,[79] survival curve for mice infected with Ascites Ehrlich carcinoma,[80] and cytokine release from osteoblasts in response to different intensities of EMF stimulation.[81] In addition, recent experiments have shown that specific combinations and temporal sequences of weak subthreshold EMFs can alter neurological activity.[82-84] For these experiments, the EMF amplitudes and frequencies were below the thresholds required to evoke nerve firing, suggesting that the specific rhythms and patterning of weak EMFs are detectable by the nervous system at this more subtle subthreshold level. The above evidence for weak EMF resonances has been supported by theoretical modeling, with the results of current models corresponding well with experimental data.[49,50,68,85,86] Both theory and this experimental evidence show that resonances in this amplitude range often occur at frequencies at or near integral multiples of the Larmor and cyclotron frequencies,[49,50,85,86] which lie in the 5 Hz to 50 Hz range for the most common biological ions in μT-range fields.[50,86] Interestingly, the constant component of Earth's magnetic field averages approximately 50 μT worldwide, and the time varying components in the pT-nT range due to the Schumann resonances constitute the principal components of the natural background of the EMF spectrum in a similar frequency range from 6 Hz to 50 Hz.[87] Because of the ambient-range amplitudes employed, the above results suggest the possibility of functional interactions between living creatures and Earth's magnetic field. In addition to the substantial literature on animal navigation via Earth's magnetic field,[88] recent experiments report a functional role for the ambient geomagnetic field in a variety of biological processes. Bioeffects have been reported due to attenuation or shielding from the Earth's magnetic field, including modulation of neuronal spike frequencies,[89,90] reduction in stress-induced analgesia,[91,92] induction of amnesia in mice,[93,94] inhibition of tumor cell growth,[95] reduction in ability to survive ionizing radiation in drosophila,[96] and an increase in pain threshold in humans.[97]

SOLAR-GEOMAGNETIC RHYTHMS AND LIFE ON EARTH

The earth's magnetic field is also highly dependent upon solar activity, including changes due to solar storms and sunspot indices. Changes in solar radiation directly affect Earth's magnetic field, with effects that can be strong enough to disrupt communications and power distribution networks. Solar-induced fluctuations in the ambient geomagnetic field have been correlated with a wide range of biological effects, including changes in ultrastructure of cardiomyocytes, temporal changes in blood pressure and heart rate and heart rate variability,[98,99] changes in power in the gamma (>30 Hz) and theta (4-8 Hz) brain wave frequencies in humans,[100,101] coherence of human EEG oscillations,[102] pain perception in mice[103], and mortality due to limbic seizures in rats.[104] Importantly, changes in solar/geomagnetic activity have also been shown to impact human health in a clinically-relevant manner. Increased solar activity has been correlated with a substantially increased rate of myocardial infarctions,[105,106] decreased survival of acute coronary syndromes,[107] higher mortality from acute myocardial infarction, higher diastolic arterial pressure in healthy subjects and in treated hypertensive patients, higher prolactin and 17-corticosteroid levels in the peripheral blood, more severe migraine attacks and more admissions for cerebrovascular accident and cerebrovascular insufficiency in male

patients, changes in many blood coagulation cellular gradients (platelet count, basophils in the peripheral blood), a rise in platelet aggregation, fibrinogen level and a drop in leukocyte adhesiveness,[108] increased mortality due to a wide range of factors,[109] decreased human lifespan,[110] and increased rate of clinical admissions for convulsive seizures.[111] In addition, it has been reported by the US Federal Reserve Bank of Atlanta, Georgia that high geomagnetic activity has a negative, statistically and economically significant effect on the following week's stock returns for all US stock market indices.[112] Also, a correlation has been observed between both the US gross domestic product and Dow Jones Industrial Average and the number of sunspots,[113] and a majority (80%) of the most significant historical events from 1749 to 1926 occurred during solar maxima, which correlate with the highest periods of geomagnetic activity.[114] These results show that in addition to diurnal and seasonal solar rhythms, biological coupling with transient solar storm activity and the 11-year solar cycle also occurs, with clinically and socially significant effects.

CELL-CELL COMMUNICATION AND ENDOGENOUS EMFS

From the above discussed findings, a picture emerges wherein, from the micro to macro levels, life is intimately connected to a wide variety of natural rhythms. As we described above, each biological cell is embedded within an interconnected environment of oscillatory patterns and widespread intercellular synchronization with resonating rhythms with large numbers of other cells that help determine the long-range functional assembly of tissues, organs, and the entire individual. Intercellular communication is critical for normal embryogenesis and development, neural activity, gamete production, endocrine function, immune function, cardiovascular function, and the regulation of cell proliferation, apoptosis, and differentiation,[115] and defects in cell-cell communication are associated with a wide variety of diseases, including diabetes, autoimmune disorders, atherosclerosis, cancer, neuropathy, and infertility, among others.[116] Also, activation of intercellular signaling mechanisms has been shown to be a key mechanism underlying the therapeutic effects of EMFs, and a review of electric field therapies concluded that "a study of many in vitro and in vivo reports revealed that the beneficial effects can be attributed to the activation of membrane proteins, and specifically proteins involved in signal-transduction mechanisms."[117] Of particular interest to cell-cell communication with regard to EMF sensitivity is the messenger molecule nitric oxide (NO). NO diffuses freely and rapidly across cell membranes, plays key roles in the rapid regulation of microcirculation, inflammation, and the cell growth and repair process,[118] and has been demonstrated to regulate chromatin folding dynamics, and thus gene expression, in human endothelial cells.[119] The importance of transient NO signaling is underscored by the observation that Nature has evolved a remarkable sensitivity to subcellular, subsecond (100 ms) NO transients in the low picomolar range, as demonstrated in human embryonic kidney HEK 293T cell lines.[120] A growing body of literature has demonstrated that NO signaling plays a significant role in biological EMF transduction, and effects on NO expression and NO-dependent pathways have been reported for a wide variety of nonthermal EMF amplitudes, frequencies, and signal shapes.[121-137] Thus, modulation of NO signaling has been established as one means by which cells and tissues can respond rapidly to changes in the EMF environment and could interact with nuclear DNA through modulation of chromosome folding dynamics.[119]

Because all biochemical reactions require the transfer of electrical charges, a wide variety of EMF sources exist within all biological systems, and observations that EMFs can be involved in intercellular communication also raise questions as to the role of those EMFs that occur naturally within the body. These endogenous EMFs and electrical currents are essential for a variety of activities, such as controlling ion transport and cell membrane electrical potential, coordinating cell migration and wound healing, and regulating ionic triggers modulating cellular activities.[138] In addition to these endogenous EMFs, arising mainly from ionic gradients and transport, there are other sources of endogenous EMFs. For example, microtubules are important, highly dynamic structures in the cytoskeleton that regulate cell shape and transport processes, and it has been demonstrated that the endogenous electric fields generated directly by the intracellular network of microtubules, centrosomes, and chromosomes play a fundamental role in regulating the dynamics of mitosis and meiosis,[139] and the high-frequency radiation characteristics of the microtubule network have been described mathematically.[140] Also, the recent characterization of the nearly ubiquitous network of telocyte cells (TCs) again suggests a fundamental role for intercellular communication played by networks of microtubular structures: TCs have very small cell bodies (consisting of a nucleus and a small amount of cytoplasm) and extremely long and thin tubular processes called telopodes (up to 100 micrometers long, yet only 20-200 nanometers wide), forming a dense convoluted network linking TCs with one another and with many other cell types.[141] TCs thus form an extensive, dynamic cytoskeletal network containing abundant microfilaments, microtubules, and the filament protein vimentin[41] and could play a fundamental role in EMF signaling at the cytoskeletal level. Of particular relevance, a recent, comprehensive review details substantial experimental evidence and theoretical support for the notion that electrical signaling activity within the cytoskeletal framework of neurons may carry information and could be essential in order to explain the "very fast and complex changes of functional neuronal connectivity

necessary for cognition."[142] Electrical activity in the cytoskeletal matrix could thus modulate a variety of behaviors, including voltage-gated ion channels and the phosphorylation status of binding molecules (eg, MAP2, CaMKII), which in turn affects cytoskeletal structure and connectivity.[41] These recent results regarding endogenous EMFs suggest that we may be in the nascent stages of a revolutionary development in the understanding of the role of EMF signaling through a bioinformation network essential to the real-time coordination of the astronomical numbers of biochemical activities necessary to maintain life.

Also, in 1923, the Ukrainian histologist Alexander Gurwitsch made his famous discovery of ultraviolet (UV) light emission during cell division in onion roots.[143] Gurwitsch subsequently found that UV light could stimulate cell division, and posited the existence of "mitogenic rays" governing basic processes of growth and repair. In recent years, the body of research based upon the observations of Gurwitsch and others has led to contemporary biophoton research,[144,145] and cell-cell communication via coherent biophoton emissions has been demonstrated in several studies.[146] Further work reported that biophoton signaling can modulate many regulatory functions,[147] including cell-cell orientation detection,[148] secretion of regulatory neurotransmitters,[149] respiratory activity in white blood cells,[150] and acceleration of seed germination by biophoton exposure.[151] Thus, biophoton research has shown another means by which endogenous EMFs generated by living cells can play fundamental functional roles in cellular function and intercellular communication.

Finally, all of life occurs with the aqueous medium of highly electrically polar water molecules, themselves generating significant fields and creating charged aqueous coordination structures surrounding proteins. Functionally important protein molecular dynamics are slave to the thermal fluctuations of the aqueous medium,[152] and hydration has been shown to play a fundamental role in conformational dynamics controlling protein function,[153] suggesting that EMF interactions within the aqueous medium itself could modulate protein function. Along these lines, theoretical work has suggested that liquid water is an ensemble of phase-correlated molecules kept in tune by an endogenous EMF generated within the ensemble.[154] This endogenous EMF governs the interaction among biomolecules suspended in water and is in turn affected by the chemical interactions of molecules, suggesting a holistic framework for energetic/informational regulation of the complex dynamics of biochemical events. In a similar direction, in vivo observations of electric field absorption and emission suggest endogenous EMFs as an indicator of the physiological state of living organisms.[155] Taken as a whole, observations of the sensitivity of biological systems to weak EMFs summarized here, including the existence of amplitude/frequency resonances, and the demonstration of EMF-dependent endogenous regulatory mechanisms through microtubules and the cytoskeleton,[138,142] suggest a new paradigm wherein the concept of regulation via a biofield of dynamic information transfer may become central to biology.[156]

USING ELECTROMAGNETIC ENERGY AND SOUND VIBRATION TO MODULATE (STEM) CELL GENE EXPRESSION, POTENTIALITY, AND FATE

In the past several decades, a large number of experiments have reported EMF effects on cells in vitro, demonstrating conclusively that nonthermal field exposures can indeed produce clinically relevant bioeffects at the cellular level.[138] For these data, field strengths and frequencies were below the threshold for which heating could occur, indicating that cells themselves possess the ability to directly detect nonthermal EMFs. The rapidly growing body of literature regarding EMF effects on cellular gene expression is too large to summarize here, so we shall restrict our discussion to reports within the last decade of stem cell research yielding effects directly upon or immediately relevant to gene expression due to nonthermal EMFs. Even within this narrow category, a large number of effects have been observed over a wide range of nonthermal EMF amplitudes, frequencies and waveform shapes, and the current rate of progress is rapidly increasing. Recent reports of such effects are displayed in the following list.

- Decreased proliferation, upregulation of neuronal differentiation marker (MAP2)[157]
- A decrease in filament protein Nestin in bone marrow derived mesenchymal stem cells[157]
- Increased filament protein NF-L, MAP2 and NeuroD1 in human bone marrow derived mesenchymal stem cells[158,159]
- Induction of rat bone mesenchymal stromal cells to differentiate into functional neurons[160]
- Significant up-regulation of early and late neuronal differentiation markers and significant down-regulation of the transforming growth factor-α (TGF-α) and the fibroblast growth factor-4 (FGF-4) in NT2 pluripotent human testicular embryonal carcinoma cells[161]
- Increased osteogenic gene expression, alkaline phosphate activity in adipose-derived stem cells[162]
- Enhanced chondrogenic gene expression (SOX-9, collagen type II, and aggrecan) in adipose-derived stem cells[163]
- Modulation of early (such as Runx-2 and osterix) and late (specifically, osteopontin and osteocalcin) osteogenic genes in adult human mesenchymal stem cells[164]
- Up-regulation of insulin factor genes, peroxisome proliferative activity, calcium channel gene, genes for mitochondrial ribosomal protein S, and uncoupling protein 2, down-regulation of tumor necrosis factor alpha and interleukin 6 in human

embryonic stem cells[165]
- Enhanced expression of the collagen I gene in mouse bone marrow stromal cells[166]
- Increase in genetic markers for differentiation in human osteoprogenitor cells[167]
- Increased expression of Osterix and IGF-1 genes in rat bone marrow mesenchymal stem cells[168]
- Increased expression of osteogenic regulatory gene cbfa1 in human bone marrow mesenchymal stem cells[169]
- Up-regulation of cardiac markers such as troponin I and myosin heavy chain, decrease in angiogenic markers such as vascular endothelial growth factor and kinase domain receptor in cardiac stem cells[170]
- Up-regulation of expressions of Bmp1, Bmp7 mRNA and down-regulation of Egf, Egfr in murine bone marrow mesenchymal stem cells[171]
- Altered gene expression in human mesenchymal stem cells and chondrocytes[172]
- Alterations in transcript levels of the apoptosis-related bcl-2, bax, and cell cycle regulatory GADD45 genes in embryonic stem cell-derived neural progenitor cells[173]
- Up-regulation of c-jun, p21 and egr-1 mRNA gene expression levels in pluripotent embryonic stem cells[174]
- Alterations in gene expression through an EMF-activated free radical mechanism and[175]
- Increased expression of p21(WAF1/CIP1), cdk5 and cyp19 genes, involved in neuronal differentiation[176]
- Increased ALP gene expression and other osteogenic markers in bone marrow-derived human mesenchymal stem cells[175]
- Enhanced expression of ACTN2, alpha-actin and TNNT2 in rat bone marrow-derived mesenchymal stem cells[178]
- Induction of differentiation of mesenchymal stem cells into cardiomyocyte-like cells[179]
- Differentiation of rat bone marrow-derived mesenchymal stem cells into chondrocyte-like cells[180]
- Increased expression of GATA-4 and Nkx-2.5 cardiac lineage-promoting genes in embryonic stem cells[181]

Notably, in the past 2 years, several groups have reported that EMF exposure could coax mesenchymal stem cells toward cardiac myocite-like and chondrocyte-like gene expression,[179,180,182] suggesting the possibility of reprogramming stem cells toward specific destinies different than their native fates. Experiments from our group found similar results, using a 2.4 GHz electrode directly immersed in the cell culture medium. For these exposure conditions, we observed enhanced transcription of prodynorphin, GATA-4, Nkx-2.5, VEGF, HGF, vWF, neurogenin-1 and myoD, indicating commitment toward cardiac, vascular, neuronal and skeletal muscle lineages and alteration in expression of stemness-related genes, including Nanog, Sox-2, and Oct-4 in adipose-derived stem cells.[183] Recently, we have also observed direct reprogramming of human dermal skin fibroblasts into cardiac, neuronal and skeletal muscle lineages.[184] The effects occurred at the transcriptional level, enhancing gene expression of a set of cardiogenic/neurogenic genes, including Mef2c, Tbx5, Gata4, and prodynorphin, and also the transcription of neurogenin1 and myoD, essential for neuronal and skeletal muscle lineage specification respectively. Also, a biphasic action on pluripotency genes was observed, enhancing the expression of Nanog, Sox2, Oct4, and cMyc during the first 6 to 20 hours, while persistently downregulating this gene program after 24 hours.[184] These results suggest that human non-stem somatic adult cells can be reprogrammed to a pluripotent state without being "frozen" in such an intermediate condition but rather becoming rapidly committed to a high yield of fates that are crucial for the development of regenerative medicine. Our more recent studies have also shown a reduction in expression of senescence-associated beta-galactosidase, a persistence of fibroblast-like morphology typical of human adipose-derived stem cells,[185] and downregulation in beta-galactosidase expression and the senescence mediator genes p16INK4, ARF, p53, and p21(CIP1).[186] The results could suggest a new method to counteract in vivo aging of tissue-resident or transplanted stem cells playing an important role in clinical treatment of age-related processes.

While it is clear that EMFs can have significant effects on stem cell gene expression, the mechanisms of action remain unclear, and much further work is needed to identify the conditions for which specific genes might be expressed or inhibited. Importantly, the EMF effects on stem cell gene expression summarized here were observed for many different nonthermal EMF amplitudes, frequencies and waveform shapes, yet only two experiments sought to methodically study the effects of altering the EMF exposure conditions.[168,179] It should be noted that one such study reported optimal effects at a specific amplitude,[168] in accord with theoretical suggestions that resonance amplitudes and frequencies are likely to be interrelated.[49,50,85,86] One set of trials was able to optimize the ability for rat bone marrow mesenchymal stem cells to differentiate into cardiomyocyte-like cells by selecting the appropriate EMF treatment duration.[182] Related results reported that 6-hour EMF exposures yielded significant effects on gene expression, whereas 48-hour exposures produced no effects, suggesting "compensatory mechanisms at the translational and posttranslational level."[173] In light of the current state of knowledge of amplitude and frequency resonances/windows for nonthermal EMFs in general, these results collectively suggest the possibility of designing specific EMF signals and dosing regimens targeting specific gene expression. Clearly, much further work is required to determine if there is an EMF

"language" that would enable EMF signals to be configured to upregulate or downregulate specific genes. Notably, the majority of the reports summarized here were published in the last 3 years, reflecting the remarkably rapid progress currently being made in laboratories around the world. The ability to reprogram or determine cell fate using EMFs has several distinct advantages over conventional biological approaches. For example, cell reprogramming could be achieved without potentially risky viral vector-mediated gene delivery or protein transduction.[187] Moreover, this strategy avoids the persistence of stray cells that haven't fully differentiated and might have the ability to turn into an unwanted cell type, like a tumor or a cell that doesn't fulfill the desired requirement(s) for a targeted tissue repair.

CELL REPROGRAMMING WITH SOUND VIBRATION

The cytoskeleton plays an important role in defining the mechanical and functional features of cells, regulating transport and governing a variety of cellular processes, including mitosis and meiosis. The intrinsic dynamic properties of the cytoskeleton and the role it plays in cellular regulation through amplitude and frequency modulation of spontaneous oscillatory patterns (eg, by fluctuations in intracellular calcium homeostasis described above) also make cells exquisite detectors of mechanical vibrations.[188] For example, recent studies have reported that specific *in vitro* human mesenchymal stem cells form multicellular structures in response to applied cyclic strain mechanical signals,[189] and the mechanosensing apparatus of stem cells is different from that of differentiated cells,[188] suggesting that innovative strategies based on targeted modulation of stem cell mechanosensors could be selective for tissue repair. Importantly, there is now ample evidence that mechanical forces and audiofrequency stimulation can alter gene expression, determine cell fate, and promote the healing of injured tissues, as evidenced by reports of osteogenic differentiation in mesenchymal stem cells,[190] enhanced expression of osteoblastic genes involved in bone formation and remodeling in human periodontal ligament stem cells,[191] modulation of mesenchymal stem cell differentiation,[192] increased expression of extracellular matrix proteins type I collagen and decorin and enhanced myotube formation,[193] regulation of mesenchymal stem cell fate using treatment regimen to target rapid cellular adaptation,[194] differentiation of umbilical mesenchymal stem cells into neural cells,[195] differentiation of adipose tissue–derived mesenchymal stem cells into neural cells,[196] differentiation of human adipose–derived stem cells (hASCs) into osteoblasts,[197] and differentiation of adipose-derived stem cells toward bone-forming cells.[198] This suggests a rationale for using mechanical vibrations and sound as a tool to modulate the rhythm of cellular mechanics and affect cell growth and fate.

Just as EMF sensitivity in cells is coupled to the existence of endogenous EMF fields, mechano-sensitivity observed in cells might be tied to an endogenous cellular language of vibration wherein cells express nanovibrational signatures of their health and differentiating potential. The developing field of "sonocytology" refers to the use of atomic force microscopy (AFM) to record audiofrequency nanomolecular vibrations at the cell surface,[199] making it possible to gain information on the integrity and local nanomechanical properties of living cellular membranes under a variety of metabolic conditions.[199] This technique can image biological samples with sub-nanometer resolution in the natural aqueous environment, detecting and applying small forces with high sensitivity, and changes in vibrational frequencies observed using AFM have been shown to be dependent on cellular metabolism.[200] In yeast and bacterial cells, cellular activity, metabolism, growth, and morphogenetic changes are associated with specific nanomechanical patterns of vibration observable at the cell surface,[199,200] and differentiation in cardiac myocytes has been observed to correspond to changes in audio-range vibrations that may be detected using AFM.[199] Also, stem cells directed to cardiac myocyte differentiation begin to beat at a particular point in differentiation. This beating motion requires a major reorganization of the cell cytoskeleton and in turn a significant change in cellular nanomechanical properties. Other examples of cellular processes that can be measured with AFM include activation of platelets, exocytosis, movement of cells, and cell division, as a spectroscopic measuring tool for chromosomes, chromatin, and DNA,[201] and as "nanocytology," ie, employing AFM as a possible means of detecting cancer cells and other pathologies.[202]

Along these lines, we have demonstrated and patented the use of AFM to detect and interact with cells' audio-range nanomechanical signatures as an indication of their health and differentiating potential.[199] We are currently developing the hypothesis that application of information using nanoprobes or nanopatterned substrates may inhibit, enhance, or direct cellular differentiation via modulation of cellular nanomechanical activity. Previous suggestions of an intrinsic relationship between protein allosteric transitions and their low-frequency motions[203] could thus be expanded to include a wide range of bioinformation "sounds" from cells/tissues/organs, suggesting the possibility of applying such sounds or "biomusic" toward targeted outcomes from suitable cell populations.[199] These strategies may represent a new tool to allow selective tuning of cell/tissue/organ homeostasis, paving the way for the use of sound physics and music for optimization as a cell therapy in regenerative medicine. Also, it is interesting to note that parallels have been drawn between traditional Chinese medicine (TCM) and sonocytology, with the suggestion that nanotechnology may shed light upon the acupuncture

meridian system and contribute to the modernization of TCM techniques, including those that traditionally use musical tones for preventive treatment of disease.[204] Cumulatively, the results found using AFM techniques support the hypothesis that cell decisions are not restricted to biochemical effectors, but can be orchestrated though nanomechanical regulators, and exposure to specific acoustic-range vibrational modes or "music" may represent a worthy field of investigation for "informative reprogramming" of cellular behavior. If such nanomechanical bioinformation can be identified, then nanomechanical/EMF patterns orchestrating stem cell commitment and differentiation might be retained and stored as an informative "nanomechanical signature" of the "sounds" or "music" emitted and functionally received by cells and organs. Such sounds might communicate the informational memory of the biofield and be used to enhance regulation of a variety of processes including differentiation, stem cell reprogramming, and the maintenance and manipulation of homeostasis.

BIOINFORMATION: TOWARDS A NEW LANGUAGE OF VIBRATION

In this article, we have presented a portion of the large and extremely rapidly growing body of evidence suggesting the existence of a vibrational bioinformation regulation system operating across the subcellular, cellular and organismic levels. To reiterate, it has been clearly demonstrated that the microtubular cytoskeleton has functional electronic properties beyond the stabilization of cellular shape, that endogenous EMFs generated by the intracellular network of microtubules, centrosomes and chromosomes play a fundamental role in regulating the dynamics of mitosis and meiosis,[139] and that endogenous EMFs in the nuclear DNA-containing chromatin also play a key role in chromosome packing during the mitotic cell-cycle phase.[205] EMFs thus play a fundamental role in the low audiofrequency asymmetric oscillations forming the basis for translational movements and configurational changes in nuclear chromatin domains (ChDs).[206] The mechanisms by which weak nonthermal EMFs' bioeffects can occur have been more clearly elucidated,[49,50,85,86] and the demonstration that NO modulates chromatin folding in human endothelial cells, suggests one pathway by which exogenous EMF-modulated NO activity could play a direct role in the regulation of gene expression.

The cytoskeleton acts as a dynamic bioinformation "track," promoting molecular and information transport in and out of the nucleus, and across the cell, enabling regulation of the expression of transcriptional regulators and transcription factors. Through the mechanism described above, ChDs may cluster together if they share appropriate oscillatory patterning, and thus the vibratory information contained in ChD dynamics could function as an organizer, determining the shape and dynamics of higher-order chromatin structures and thus regulating specific cellular activities. Specific epigenetic modifications of chromatin regions would thus relay specific chromosome rearrangements to upstream signals, resulting in alterations of both sub-nuclear chromatin and chromosome structures. The recent identification of the ubiquity of the TC network[141] provides further support for the existence of a system of EMF-vibratory intercellular regulation via a dense and highly convoluted dynamic cytoskeletal complex containing abundant microfilaments, microtubules, and the filament protein vimentin.[41] Such intercellular regulation is also reflected in the suggestion that electrical signaling activity within the neuronal cytoskeletal framework may be essential for understanding the rapid changes of functional neuronal connectivity necessary for cognition.[142] These dramatic findings strongly suggest that the cytoskeleton provides synchronization, coordination, and recognition patterns across multiple sources of vibration. A picture continues to emerge wherein molecular EMF vibrations and sounds, or "biomusic" oscillations, communicate a symphony of regulatory bio-information, governing activities from the atomic and molecular to cellular and multicellular levels. Thus, the concept of a field, borrowed from physics, may be the most appropriate means of describing the dynamic bioinformation network, or "biofield," intimately involved in regulating many vital biological processes.

One fundamental aspect of the concept of biofield regulation is the move from a mechanical, chemistry-based view of biology in which all significant activity results from reaction rates driven by chemical concentrations, to an information-based view, wherein biochemical activity occurs in resonant modulation with EMF-related cytoskeletal vibrations. This new, biofield-based view also reflects the more information-based findings of weak, nonthermal EMF resonance interactions, wherein effects occur in specific amplitude/frequency windows determined by the overall structure and function of the system, rather than through the linear deposition of energy.[49,85,86] Thus, the concept of biofield regulation suggests a view on biology wherein even very weak, or "subtle" signals and energies of interaction can have significant effects. This is supported also by the existence of the pT-nT EMF effects summarized above, the remarkable picomolar sensitivity observed for NO signaling and the clinical significance of the wide range of correlations with solar and geomagnetic activity. Sensitivity to such subtle sources of information may also shed light upon the growing number of reports of nonlocal neural correlations between spatially separated human subjects[207-209] and human neurons adhering to printed circuit boards.[210] Experiments performed with shielding suggest that these effects are not mediated by EMFs[207,210] and thus might involve some form of quantum entanglement.[211] However, a comprehensive biological theory of nonlocal connections would require the existence of a "subtle" biofield system

capable of responding in an informationally meaningful manner to extremely weak inputs to yield correlated higher-level EEG activity. A link between the cytoskeletal biofield system and brain activity is supported by the suggestion of biologically "orchestrated" coherent quantum processes in collections of microtubules as a possible source of the observed EEG correlates of consciousness.[212] This suggests the possibility that the cytoskeletal biofield information system described here may be merely a narrow glimpse of a much larger view of the role of mind and body in the connections between individuals, society, our planet, and the Cosmos.

FROM A FUNCTIONAL GENOMIC PERSPECTIVE TO HUMAN WELL-BEING

Biological regulation requires multilevel, multidirectional information processing. For example, the nervous system uses both afferent and efferent activity in sensory and activatory feedback and feed-forward mechanisms, and actions as diverse as enzymatic activity, gene expression, phosphorylation, and cytokine activity employ simultaneous excitatory and inhibitory actions to create robust systems capable of generating temporal activity and detecting relative, rather than absolute, changes in activity.[213] In gene expression, such positive and negative feedback and feed-forward loops have been shown to produce regulatory systems of astonishing complexity, rendering understanding of the function of regulation pathways difficult or impossible, and complicating the interpretation of experimental data.[214] A "systems biology" approach has been suggested as a means of obviating some of these difficulties,[215] suggesting a more holistic perspective integrating mathematical modeling with experimental and clinical results to better understand complex problems in biology.[216] In a similar vein, the evidence we have presented for bioregulation via rhythms and oscillatory patterns extending from the single-cell to the organismic levels suggests also that a reverse flow of information may occur, from the macro to micro levels. This is supported by observations that emotions are intimately correlated with physiology, and in particular, that cultivation of positive emotions can produce beneficial changes in a wide variety of physiological, neurological and psychological parameters.[6] Thus, human feelings, thoughts, psychological attributes, and perhaps even life choices may resonate with the molecular cellular level and affect even these most subtle processes of life.[217] Although the idea that higher-level activities such as thoughts and feelings could affect gene expression may seem radical, substantial evidence exists supporting just such a confluence of psychology, neuroscience, and molecular genetics. For example, numerous investigations of neuroplasticity have shown that the adult brain can continue to form new neural connections and grow new neurons in response to learning or training even into old age, and the term *psychosocial genomics* has been introduced to describe the developing field of inquiry into the modulating effects of human experience on gene expression.[218,219] A review of successful psychotherapeutic methods identified five areas of biological change that are directly dependent upon precise shifts in gene expression[220] and it has been shown that human emotions such as loneliness are correlated with down-regulation of genes bearing anti-inflammatory glucocorticoid response elements and up-regulation of genes bearing response elements for pro-inflammatory NF-kappaB/Rel transcription factors.[221]

Ample evidence already exists that psychological and psychosocial factors do in fact influence gene expression. Growing interest in the clinical benefits of yoga, meditation, tai chi, and relaxation practices has brought forth a flood of new studies, and is beginning to show that mind-body disciplines can also modulate gene expression.[220] Of particular interest to the topics we have presented above, one study considered two psychological states in opposition to each other: threat awareness and mindfulness meditation.[222] This study examined the effects of these two psychological states on effects on cellular aging, with one measure of aging being telomere length (a measure of longevity at the chromosomal level), finding that mindfulness meditation can reduce telomeric shortening, decrease stress arousal, and upregulate hormonal factors that may promote telomere maintenance.[223] Genetic profiling in whole blood from subjects practicing deep relaxation has shown significant alterations in cellular metabolism, oxidative phosphorylation, generation of reactive oxygen species, and response to oxidative stress that may counteract cellular damage related to chronic psychological stress.[224] Other studies of yoga and meditation practices have provided a large body of evidence for psychological and physiological effects,[225] and a recent review has summarized changes in gene expression from yoga and meditative practices[222] and in peripheral blood lymphocytes,[226] lending further support to the notion that yogic/meditative practices can modulate gene expression at the molecular level. Other genetically relevant observations associated with yoga and meditative practices are a reduction in inflammatory cytokine IL-6 in regular practitioners of yoga[227] and a reduced sense of loneliness and decrease in the loneliness-correlated pro-inflammatory NF-κB-related gene expression in older adults.[228] A study on the effects of laughter and meditation found that laughter decreased markers for progression of diabetic complications, with concomitant changes in the expression of relevant genes, and meditation altered the expression of genes associated with cellular metabolism and oxidative stress, suggesting the inhibition of cell injury due to chronic stress.[229] In addition, genomic profiling of neutrophil transcripts in Falun Gong Qigong practitioners showed enhanced immunity, downregulation of cellular metabolism, and alteration of apoptotic genes in favor of a rapid resolution of inflammation.[230]

Also, a remarkable study recently found that the human body is able to distinguish at the molecular level between two different internal states: eudaimonic well-being, derived from "striving toward meaning and a noble purpose beyond simple self-gratification," as compared to hedonic well-being, that which is derived from "positive affective experience."[231] Although hedonic and eudaimonic well-being produced similar subjective feelings of happiness, they were found to engage distinct gene regulatory programs. In particular, the CTRA gene expression profile is characterized by increased expression of genes involved in inflammation, decreased expression of genes involved in type I IFN antiviral responses, and decreased IgG1 antibody synthesis, and is associated with inflammation-mediated cardiovascular, neurodegenerative, and neoplastic diseases and resistance to viral infections. In this study, the CRTA profile was down-regulated in subjects evincing a eudaimonic pattern and upregulated in subjects with a hedonic well-being profile,[231] suggesting a distinct change in gene expression with deep emotional content. Hence, not only chemicals and physical energies like EMFs and sound vibrations, but even our emotions, thoughts, beliefs, and the way we develop our intentions and life rhythms can deeply transform our gene expression patterning at the cellular level. This finding may disclose unexpected chances to develop self-healing processes based on further utilization of this remarkable human potential.

CONCLUSIONS: TIME FOR A NEW PARADIGM IN SCIENCE

In this review, we have drawn upon several new discoveries in biophysics, biology, epigenetics, neuroscience, psychology, and psychosomatics. Although many pieces of the puzzle have yet to be elucidated, we suggest that taken together, these findings point to the existence of a subtle "biofield" information processing system that is intimately involved in the regulation of basic biological processes, from the molecular to organismic levels. We also note how these connections suggest an essential link between the heart and the mind, between emotions and cognition. We have noted how these connections extend even to the interpersonal and cosmic levels, with the development of psychosocial genomics and the growing body of evidence for correlations between individuals and the natural geomagnetic environment of the Earth and Sun. The paradigm emerging here moves from a purely biochemical viewpoint, based solely upon physical concepts of energy and momentum transfer and their implications for biochemistry, to a holistic, information-based paradigm. Much as a whisper might carry more gravitas than shouted words, science may now be uncovering the basic principles of a more subtle informational biology in which specific signaling behaviors can carry the power for healing.

We suggest that such a holistic view is required to explain the data presented here, and is essential also for a deeper understanding of Life. While science has made extraordinary technical progress in recent years, it has thus far provided only a fragmented picture of the living world, often with little or no connection between closely related fields. As scientific knowledge has become more detailed and specific, this has forced researchers to focus upon smaller and smaller domains. This growth in specialization has created numerous, highly specialized scientific journals, often reaching only very specific groups of researchers. Although this trend toward specialization is a necessary result of the tremendous growth in scientific knowledge we are now experiencing, it has also made it more difficult for scientists from different fields to communicate, and has created a fragmented picture of the living world that ironically has made some scientific analyses more removed from life itself.

The data point toward a new paradigm that reconciles this disconnected situation. Such a new paradigm would be capable of unifying a variety of disciplines and revealing the interconnections between the living world, the social world, and the physical universe. Such a paradigm, based on interconnectedness, implies a deep transformation of the human-nature relationship, holds the promise of imbuing science with a greater sense of meaning, and is likely to help bring about a significant shift in medical and therapeutic approaches. One example is the clear evidence from psychosocial genomics that gene expression can be modulated not only by nonthermal EMFs and sound vibrations, but also through the activities of mind, emotion, music, art, ritual, culture, and spiritual life.[232] That these factors can alter gene expression—an action occurring at the most basic level of living existence—also holds great promise for the development of medical therapies that account for each person's unique emotional, physical, and social needs. Indeed, this development is already well underway and is evidenced by a deepening understanding of the efficacy of "complementary and alternative medicine" (CAM) practices[232] and growing acceptance within the biomedical community that CAM practices can be effectively integrated into mainstream medicine."[233]

In order to encourage a medical tradition that incorporates understanding of the patient's mental, emotional, and interpersonal life, sensitivity and compassion are needed on the part of the healer. Such a medicine crosses the boundary of Science and Art, as the doctor's own sensitivity, clear understanding, and capacity for pathos would play an important role. And just as music can have the capacity to touch our deepest sentiments, and evoke feelings across the entire spectrum of human emotion, as scientists begin to understand the language of health, emotions, and heart rate variability,[6] and begin to decode the language of cellular vibrations and biofield information, it may be possible to develop new forms of healing. As healers have used music for therapeutic purposes for

centuries, might cell-music or EMF "biomusic" be further developed as a kind of medicine? Such a medicine could not only draw knowledge of the modulation of gene expression using EMFs and sounds but also integrate techniques of yoga and meditation and knowledge of the psychosomatics of heart rate variability and other physiological parameters[6] and incorporate training in the human sensitivity of the practitioner. These ideas echo comments by Hazrat Inayat Khan on the use of music for healing:

> *This way of healing can be studied and understood by studying the music of one's own life, by studying the rhythm of the pulse, the rhythm of the beating of the heart and of the head. Physicians who are sensitive to rhythm determine the condition of the patient by examining the rhythm of the pulse, the beating of the heart, the rhythm of the circulation of the blood. And to find the real complaint a physician, with all his material knowledge, must depend upon his intuition and upon the use of his musical qualities.*[234]

Implicit in this recognition of an inherent connection between practitioner and patient, there is a crossing of the edge of objectivity, toward an understanding that the healer's own viewpoint and psychospiritual condition might also play an important role in healing. In this passage toward an integration of objective *knowledge* with subjective *knowing* lies a route toward bridging the boundary between Science and Art, the natural integration of Science with the Humanities, as a Science of Humanness.

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