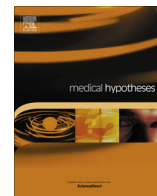




Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

Aging and magnetism: Presenting a possible new holistic paradigm for ameliorating the aging process and the effects thereof, through externally applied physiologic PicoTesla magnetic fields

Jerry Jacobson^{a,*}, Benjamin Sherlag^b^a Institute of Theoretical Physics and Advanced Studies for Biophysical Research, Jupiter, FL 33477, USA^b Department of Medicine, Cardiovascular Section, University of Oklahoma Health Sciences Center, Oklahoma City, OK 73104, USA

ARTICLE INFO

Article history:

Received 7 March 2015

Accepted 27 May 2015

ABSTRACT

A new holistic paradigm is proposed for slowing our genomic-based biological clocks (e.g. regulation of telomere length), and decreasing heat energy exigencies for maintenance of physiologic homeostasis. Aging is considered the result of a progressive slow burn in small volumes of tissues with increase in the quantum entropic states; producing desiccation, microscopic scarring, and disruption of cooperative coherent states. Based upon piezoelectricity, i.e. photon–phonon transductions, physiologic PicoTesla range magnetic fields may decrease the production of excessive heat energy through target specific, bio molecular resonant interactions, renormalization of intrinsic electromagnetic tissue profiles, and autonomic modulation.

Prospectively, we hypothesize that deleterious effects of physical trauma, immunogenic microbiological agents, stress, and anxiety may be ameliorated. A particle–wave equation is cited to ascertain magnetic field parameters for application to the whole organism thereby achieving desired homeostasis; secondary to restoration of structure and function on quantum levels. We hypothesize that it is at the atomic level that physical events shape the flow of signals and the transmission of energy in bio molecular systems. References are made to experimental data indicating the aspecific efficacy of non-ionizing physiologic magnetic field profiles for treatment of various pathologic states.

© 2015 Elsevier Ltd. All rights reserved.

Introduction

Theories about the process of aging address two sets of factors – those intrinsic and those extrinsic to the organism. Intrinsic factors operate on the body from within, such as the impact of genetic programming. Extrinsic factors are influences on the body essentially from the environment, such as the impact of cumulative stresses. From an intrinsic perspective, human telomeres are approximately 15–20 kb in length at birth, and shorten gradually throughout life in dividing cells; suggesting that telomere length may serve as a biological (as opposed to a calendar) timing mechanism. Cell senescence is activated once a critical shortened telomere length is attained. There are many published correlative studies demonstrating a connection between telomere length and aging, and there is evidence supporting an inherited component to telomere length [1,6,10,28,31–34].

* Corresponding author at: Institute of Theoretical Physics and Advanced Studies for Biophysical Research, 2006 Mainsail Circle, Jupiter, FL 33477-1418, USA. Tel.: +1 (561) 746 8719; fax: +1 (561) 748 8870.

E-mail address: drjijacobson@yahoo.com (J. Jacobson).

The first component of our hypothesis resides in the possibility that extrinsically sourced physiologic PicoTesla electromagnetic fields (PTEMF's) may be utilized to prevent telomere shortening. Theoretically, magnetic resonant energies may be target-specific, and through the mechanism of photon–phonon transduction, i.e. piezoelectricity, PTEMF's may stabilize the structural integrity of telomeres to prevent shortening upon cell division. Studies supporting this possibility will be discussed.

Secondly, extrinsic challenges of life produce various stressors, stimulation of the hypothalamic–pituitary–adrenal axis (HPA axis), and production of the stress hormone *cortisol*, a glucocorticoid naturally secreted during a stress response. Cortisol's primary function is the redistribution of energy through gluconeogenesis to regions that need it most, i.e. the brain and major muscles during a fight-or-flight situation.

Cortisol also acts to suppress the body's immune system, while aiding in fat and protein metabolism. Thus, we hypothesize that the natural exigencies of life produce increased heat energy, enhancing desiccation of tissue microstructures, increasing microscopic scarring, quantum *entropy* or disorder, and aging. Therefore, the second component of our hypothesis concerns electromagnetic

field modulation of vagal innervation and sympathetic innervation [1–5].

It is proposed that the challenges of life (physical, chemical, and emotional) all contribute to the actual longevity of an organism; seldom actualizing the maximum life span determined by the predisposing inherited characteristics of the genome. While the neuroendocrine system has been scrutinized as a major contributor to aging, we note that many lower organisms known to age over time have no well-developed neuroendocrine system. Neuronal loss in humans occurs in selective areas in the brain and age-related neuronal losses may be considered secondary to the production of biological senescence. Despite the fact that elderly individuals tend to develop hypertension possibly related to increased sympathetic system reactivity, impaired glucose tolerance, diminished thyroid function, and decline in gonadal function, these and other factors may be considered contributory to the aging process. It should be noted that most brain functions involved with *intelligence* are quite remarkably preserved throughout life [1–8].

The nature of aging

Metabolism is the sum of all the physical and chemical processes by which living organized matter is produced and maintained; and the transformation by which energy is made available for use by an organism. Energy metabolism is concerned with overall heat production in an organism, including intermediate metabolism (e.g. cellular oxidative stresses), dealing with chemical reactions within cells and tissues. Through metabolic adjustments, energy is provided for vital processes, whereby raw material may be assimilated. Yet, stress, tension, strain and anxiety challenge our cells to provide extra energy for the maintenance of homeostasis [4,5,8,9].

Basal metabolic rate (BMR) is defined as the amount of heat energy produced by the body to maintain life processes when the body is in a state of physical, emotional and digestive rest. Thus, while the maximum life span is encoded by our genes (involving telomeres, or end stops for chromosomes), levels of stress and strain (emotional and physical) place extra demands upon cellular functions, increasing metabolic rates with the production of heat energy. The presence of free radicals adds to the production of heat and slow burn of aging. With respect to intermediate metabolism, free radicals have been linked to a number of human diseases, including atherosclerosis, cancer, Alzheimer's disease, cataracts, osteoarthritis, and immune deficiencies [10]. Free radicals are molecules or atoms, which possess one or more unpaired electrons. In general, free radicals are formed by the rupture of a bond in a stable molecule with the production of two fragments, each with an unpaired electron. The resulting free radicals may participate in further heat yielding reactions. Radicals can be generated by thermal decomposition, electric discharge, photochemical reactions, rapid mixing of two reactants, as well as gamma or X-ray irradiation [5,6,8–11].

We note that free radicals can be chemically very reactive (for example, the methyl radical) or they can be very stable entities (for example, nitric oxide). Free radicals can be grouped into three major classes: atoms (for example H, F and Cl), inorganic radicals (for example, OH, CN, NO₂ and ClO₃) and organic radicals (for example, CH₃, CH₃CH₂, and C₆H₆). Such molecules are of great importance since they often appear as intermediates in thermal and photochemical reactions. Radicals are known to initiate and propagate polymerization and combustion reactions [11]. Additionally, oxidative phosphorylation is critical to metabolism, because the free energy of hydrolysis of ATP generated is used in the synthesis of, inter alia, nucleic acids, proteins and complex lipids; in addition

to processes of muscle contraction and nerve impulse signal transduction. Such processes are fundamentally affected by life challenges of stress, strain, anxiety and tension-imbued by enhancement of sympathetic stimulation [3,5,12].

It is noted that the energy state tonicity, and bioelectric potential of nerves may be modulated by PicoTesla electromagnetic fields [13,14]. Recalling our hypothesis that biomolecular resonance using non-ionizing EMF's may be target-specific Saxena et al. [13], studied the effect of low-level extremely low frequency (ELF) EMF's on the restoration of forelimb grip strength and radial nerve ultrastructure in mice with induced toxic motor neuropathy. Field intensities, gradients and frequencies were calculated with the Jacobson Resonance Equations [13] considering sub-cellular components vital for nerve function. Target molecules included nerve growth factor (NGF), microtubule associated protein (MAP), neurofilaments (NF), tubulin, acetylcholine, calmodulin, kinesin, and dynein. The results demonstrated a significant biological effect on restoration of subcellular structures required for nerve impulse conduction and metabolism in nerves, and consequently a grip strength recovery from motor neuropathy under controlled experimental conditions. Indeed, the renormalized, physiologic state of mitochondria, as observed, indicated normal membrane permeability and a recovery of ATP synthesis essential for nerve growth and repair. A link between EMF and renormalized Schwann cell function indicated that a non-neuronal control in the regeneration and growth of peripheral nerve fibers is possible. Yet, we need to understand what aging is from a fundamental physical point of view, in addition to the biochemical perspective e.g. a molecular and cellular level [13–22].

Entropy

Proteins, the building blocks of many tissues, as well as functional agents for life, are important to the aging process. Proteins encompass three-fourths of the dry weight of most cells, and are involved in structure, hormones, enzymes, immune function and essential life functions. Genes impart instructions for cellular function through transcriptional and translational processes providing these purported semi-crystalline piezoelectric structures that serve numerous functions [4,35,41].

But, genes can be changed, as time-dependent processes increase levels of “entropy,” or disorder on fundamental levels. Thus, we note that vital structural and functional integrity of critical molecules are challenged with age, and the atomistic signal transductive coupling mechanisms for molecules and molecular assemblies are therein denigrated.

In chemical and biological systems, it is impractical to determine the entropy of a system by counting the number of ways it can assume the most probable state.

Rudolph Clausius [23] proposed:

$$\Delta S \geq \int_{\text{initial}}^{\text{final}} \frac{dq}{T} \quad (1)$$

where T is the absolute temperature at which the change in heat (dq) occurs and ΔS is the change in entropy. Any system becomes progressively disordered (with increased entropy) as its temperature rises. Eq. (1) holds for processes in which the system remains in equilibrium throughout the change. These are known as reversible processes. For biological processes, Eq. (1) reduces to:

$$\Delta S \geq \frac{q}{T} \quad (2)$$

Therefore, the entropy change of a reversible process at constant temperature can be determined from measurements of heat transferred and the temperature at which this occurs.

However, since a process at equilibrium can only change at an infinitesimal rate (as equilibrium processes are by definition unchanging), real processes can approach, but never attain, reversibility. Therefore, the universe's entropy change in any real process is always greater than its ideal (reversible) value. When a system departs from and then returns to its initial state via a real process, e.g. transient states of sympathetic system stimulation, the entropy of the universe must increase even though the entropy of the system (a state function) does not change. In this regard, we consider a bio system as an intrinsic universe of electromagnetic interactions in constant flux, oscillating about a steady state system [23–26].

Now, genes can exhibit deletions, substitutions, or cross-linking. The cross-linking of genes refers to increasing numbers of bonds formed between critical molecules, to impart errors in communications. Improper genetic information transfer (e.g. cancer) results in abnormally structured proteins, like enzymes that make chemical reactions go. [27] We hypothesize that such biochemical dysfunction is based in EMF anomalies stemming from incoherent atomistic communications. It is known that various oncogenic transformations are the result of a unique combination of germline and somatic mutations, e.g. nucleotide substitutions, insertions and deletions, chromosomal rearrangements and copy number changes in protein-coding or regulatory components of genes; changes in DNA methylation and chromatin structure, that have impact on gene expression [28].

Age changes have also been found in chromatin structure, necessary for repair of DNA. With age, special trophic factors (like nerve growth factor) are either not available in sufficient quantities or are abnormally structured. Even immune function becomes less efficient with age, examples of which are interferons and interleukins, vital agents for intercellular communication [13,27–30].

Considering our genomic biological clocks

We have mentioned that telomeres are essentially biological clocks; and decrease in length with age. Certain tissues, like blood, the G.I. tract system, and skin, produce some telomerase, an enzyme that increases telomere length.

Perhaps the production of this reverse transcriptase enzyme is a natural cellular defense mechanism. However, ironically, cancer cells produce heightened levels of telomerase to increase telomere length—increasing longevity of the actively dividing cancer cells. Telomerase inhibition is currently being researched for a possible new treatment for cancer. And, telomere length measurements in human cells provide an estimate of the approximate number of cell divisions that may be remaining. Once a critically shortened telomere length is attained, cellular senescence is activated, and when a sufficient number of cells undergo senescence in a tissue or organ, a decline or loss of function of that tissue is predicted to occur that could contribute in substantial ways to aging. Changes due to chromatin instability, DNA damage, and other stress signals (such as overexpression of oncogenes) may result in a more immediate cessation of normal cell growth [6,7,31–34].

We note that cancer stem cells in primary tumors are quiescent, thus telomerase inhibition must be used adjunctively with chemotherapy, because cancer stem cells do not produce telomerase as the actively dividing cells do [6].

Now, telomeres are bound by a series of single and double-strand DNA-binding protein. Telomeres shorten with each cell division due to incomplete lagging strand synthesis. Importantly, when conformational states of proteins are altered, this information can be transmitted to other structures, e.g. DNA; through non-linear vibrations of protein piezoelectric structures. These structures convert mechanical energy into electrical energy,

or vice-versa. The atomic quasi-crystalline lattice structure of many proteins in the human body are known to be piezoelectric [5,6,13,16,35–41].

Thus, it is hypothesized that interatomic communications through electromagnetic forces are at the root of all communications, i.e. signal transductive coupling mechanisms in living systems. Therefore, even though telomeres are considered noncoding repeating DNA sequences, when the binding protein undergoes atomic conformational changes as a result of incomplete lagging strand DNA synthesis, (mechanical error), electromagnetic communications may be sent to the rest of the DNA, inhibiting normal genetic information transfer mechanisms. It is also hypothesized that telomeres may serve as targets for magnetic resonance energies. It may also be possible to target telomerase (or components thereof) with the inhibition of same in cancer. Such considerations point to the necessity for research in this area.

Preliminary studies at Mississippi State University executed by Coyne, [42] screened a number of PicoTesla range magnetic field schedules. Calculations using the Jacobson Resonance equation were based upon molecules thought to be associated with human mammary carcinoma cell populations (HTB-126 and MCF-7) in multi well tissue culture plates. Two schedules were found to compromise the viability and/or proliferation rate of HTB-126/MCF-7 cell types relative to untreated negative reference controls. Over the course of replicate studies ($n = 7$) these PicoTesla schedules were observed to consistently inhibit the viability and/or proliferation rate between 31% and 35% compared to untreated negative reference controls. Additionally, Coyne identified membrane-associated complexes that were expressed at elevated or decreased levels in MCF-7 populations. Several mRNA sequences were detected ($n = 3$) that were expressed at higher levels ($n = 1$) or uniquely expressed ($n = 2$) in MCF-7 populations. Interestingly, these cells were exposed to magnetic resonance energies for thirty minutes each time in five treatment sessions, compared to exposure times of fifty-six minutes, twice weekly, for 8.5 weeks as was executed in nerve regeneration studies at Fairleigh Dickinson University for the in-vivo study. It is the experience of the authors that outcome measures are generally directly related to exposure time- in addition to the conditions of resonance determined by accuracy of flux densities and frequencies.

Nevertheless, collective interpretation of experimental findings revealed an ability of a multi-frequency, multi-amplitude PicoTesla range magnetic schedule to induce alterations in viability/proliferation rate and expression profiles of: (1) cytosol-soluble and membrane associated protein fractions; and (2) genetic transcription of mRNA sequences compared to negative (non-exposed) reference controls. In this context, these alterations appear to be of a different pattern when experimental samples were immediately processed following MCF-7 exposure to the fifth and final schedule. In contrast, different and slightly more subtle differences were appreciated when an intentional delay of several hours was implemented between the final exposure and sample preparation. Appreciation of this observation implies that maximum alterations in protein expression and mRNA transcription may occur during or shortly after periods of exposure. In addition, there was also a relative difference in the biological affect excited by individual single frequency techniques contained within the “Master” multi-frequency PicoTesla schedule. Ultimately, these laboratory findings may serve as an experimental foundation for future research investigations devoted to delineating (1) time frames that PicoTesla magnetic fields exert a biological affect, (2) duration of PicoTesla magnetic field induced molecular/genetic alterations, (3) identity of PicoTesla magnetic fields that selectively exert specific biological affects in living systems, and (4) identify molecular/genetic “targets” that PicoTesla magnetic fields interact with in a manner that creates a biological affect.

When the ultimate propitiators of order and balanced function, i.e. atoms, are disrupted by external factors to a system, then entropic states must result [13]. Disorder produces extra demands for energy on all levels: atomic, molecular, cellular...etc. and the heat energy enhances entropy and the slow burn of aging, and microscopic scarring [5].

Chromosomal damage, cross linking, improper genetic information transfer, and improperly structured proteins will lead to an increase in scar tissue production; much like a slow burn, resulting in desiccation of tissues-globally.

And, another critical factor reported in the literature is increasing concentrations of metal ions in cells [5,27]. Sources of ions (electrically charged species) like calcium, magnesium, copper, zinc, sodium and potassium, are in food and the air we breathe. Excess metal ions, or metal ions improperly distributed in the cells will produce errors in the cell's genetic information transfer, and other intracellular pathways, e.g. perhaps by denigrating the balance of tissue EMF profiles [5,13,27,43–45].

Biophysical Theory

Our bodies are a collection of trillions of atoms that must communicate incessantly, cooperate and “work together”, to produce functionality of the whole organism. Atoms constitute all matter, and atoms are permanent spinning magnets. Einstein [46–48] said that all matter is condensed electromagnetic field; comprised of fundamental elementary electrically charged particles. For example, protons (positively charged nucleons) are themselves composed of three ‘quarks,’ manifesting electrically charged states. From a classical perspective the electrons are miniaturized atomistic planets orbiting atomic nuclei within specified energy shells, and are negatively charged. And, the electrical charge distribution in space and time can balance atoms for neutrality. Our atomic magnets communicate through long-range electromagnetic forces, carried by photons (quanta) or packets of energy [13,16]. Heat energy is an electromagnetic wave, having lower frequency than visible light. Now, when the atomic structures of cells are challenged and denigrated, the quantum order and balance of life is impugned; with the gradual increase in entropy [5,13].

Heat is the energy associated with the random motions of the molecules, atoms or smaller structural units of which matter is composed. From the perspective of thermodynamics, it is convenient to define all energy while in transit, but unassociated with matter, as either heat or work.

In this regard, matter and electromagnetic wave energy are distinguished. Thus, heat is that form of energy in transit due to a temperature difference between the source from which the energy is coming and the sink toward which the energy is going. Even more specifically, radiant heat energy (infrared radiation) is one form in which heat can be transferred. It occupies the electromagnetic spectrum between light and radio waves, i.e. in the wavelength range 740 nm to 0.3 mm. Heat is measured by the same physical units as work (joules) [11].

A burn is a lesion caused by heat or any cauterizing agent. While heat energy is a normal product of metabolism basically under genetic control, environmental factors can negatively influence the natural processes of life. When emotional insults, disease or injury strike, the intrinsic defense mechanisms of life proceed to provide increased energy meeting demanded exigencies. Increased levels of energy will be utilized to reorder systems, but entropy will nevertheless increase within small volumes of tissues, to increase microscopic scarring. Gradually, in spite of meeting physiologic exigencies, aging is the inevitable result when metabolic states are forced to increase over extended time frames [5,13].

As life challenges progress, magnetic profiles of tissues are changed in accommodation to the requirements for maintenance of physiologic homeostasis. That is, atomic and subatomic structures will be reoriented in space and time as a natural sequelae to transient disequilibria, i.e. changing magnetic moments and spin angular momenta of electrons and protons. With changing stress levels, magnetic profiles of tissues may become too strong, too weak, or unbalanced. These electromagnetic profiles (representing the fundamental structures of which biological tissues are composed) must be renormalized to reestablish a state of global health [13,49,50].

Now, appreciating the fact that cell membranes are barriers to electric fields above 1000 Hz, it is feasible to conclude that the magnetic force is the most important vehicle for intercellular and intracellular communications. Magnetic forces pass unimpeded through all biological structures, and the regulatory capacity of the force acts on all levels of structure and function, as a consequence of biologically coherent resonant amplifications [18,39].

Magnetic resonance therapy (MRT)

How can we assist the body to more rapidly and with greater efficiency heal itself? We realize that improved efficiency in the renormalization of homeostasis (with a decrease in energy requirements) is useful for the slowing of aging.

The answer to the foregoing conundrum may be forthcoming. Normal physiologic magnetic profiles of human tissues have been measured directly with superconducting quantum interference detectors, or atomic magnetometers. These magnetic fields have been found to be in the PicoTesla range. One PicoTesla is fifty million times weaker than the geomagnetic field (the Earth's steady magnetic field).

The existence of the brain's magnetic field and the difference between the magnetic field profile of the normal brain versus the pathologic brain, has been known from the classical work of David Cohen [51] and several recent works of others using the superconducting quantum interference detectors (SQUID); on patients with epilepsy and other neurologic disorders [52–57]. These investigators measured the intensity profile of the human brain magnetic field and found that it is on the order of 0.5 PT (PicoTesla) or 5×10^{-9} gauss for alpha brain waves. Cohen found that a DC magnetic field on the order of 5×10^{-8} gauss (5 PT) was associated with delta brain waves, and a maximum measurement of the human heart magnetic field profile was on the order of 5×10^{-7} gauss (50 PT). Anninos [56,57] found that a maximum magnetic field profile for the human brain was about one micro gauss (100 PT). Therefore, from a practical point of view, the PicoTesla range of current interest is from about 0.5 PT to about 100 PT.

Can MRT Maintain Structural Integrity of Telomeres?

Since telomeres are repeating DNA sequences (TTAGGG) and the prime molecular weight is about 1.681 kD, the following intensities and correspondent frequencies are suggested for research protocol:

2.37 PT @ 0.66 Hz, 4.74 PT @ 1.32 Hz, 7.11 PT @ 1.98 Hz, 9.48 PT @ 2.64 Hz, 12 PT @ 3.3 Hz, 14.4 PT @ 3.96 Hz, 16.6 PT @ 4.62 Hz, 19.2 PT @ 5.28 Hz, 21.3 PT @ 5.94 Hz, 23.7 PT @ 6.6 Hz, 26 PT @ 7.26 Hz, 28.8 PT @ 7.92 Hz, 31.2 PT @ 8.58 Hz and 33.6 PT @ 9.24 Hz.

Since atomic structures are so small, it is understandable why from a microscopic point of view, the natural magnetic profiles

of tissues are subtle energies. Living systems evolved into a complex array of many trillions of atoms, and our functional nature involved intrinsic regulation of atoms through the long-range communications carried by electromagnetic waves.

Supporting literature

Pico-Tesla electromagnetic fields. (PTEMFs) have been demonstrated to affect brain waves [56–60] and enhance regeneration of nerve ultrastructure [13], affect autonomic nervous system tonicity, e.g. enhance parasympathetic stimulation to cardiac inputs and regulate atrio-ventricular conduction mechanisms of the heart [61] (affecting rate and rhythmicity), modulate endogenous opioid activity (e.g. enkephalin, endorphin) [14,62] and affect benefits in neurological disorders such as Parkinson's disease [63], multiple sclerosis [14,64], and epilepsy [53,54], speed wound healing [65], and regulate thoracic spinal neuronal potentials after administration of noxious chemicals to the heart (which stimulated nociceptive afferent fibers [14], just to cite a few of the many studies conducted at major universities, indeed, research over the past 30 years has revealed more and more that extrinsically sourced, low-level, extremely low frequency electromagnetic fields (many orders of magnitude weaker than the membrane potential gradient in the pericellular fluid) do modulate actions of hormones, antibodies and neurotransmitter molecules at cell surface receptor sites. The observed sensitivities are as low as 10^{-7} volts per centimeter in the extremely low frequency spectrum [37,39,40].

Other examples of subtle field effects also include: altered rate of cell growth [66], suppression of T-lymphocyte cytotoxicity [67], increases in the growth related enzyme ornithine decarboxylase [68], altered quantities of RNA transcripts and proteins [69–71], altered cell surface properties [40], and effects on development [72].

The plethora and diversity of reports in the literature concerning biological effects from non ionizing radiation (NIR's) may be based upon a fundamental initial underpinning physical mechanism: a new particle–wave equation, $mc^2 = BvLq$, known as Jacobson Resonance. And, many of the cited studies utilized calculated PicoTesla range magnetic field signal parameters derived from this new theory [5,8,13–22,29,30,35,43,50,61–63].

Bone repair [73–75] neurotransmission intensification [13,76,77] and DNA synthesis [78] have all been linked to the same causal modality, namely pulsed low-intensity magnetic fields. All the foregoing phenomena are intimately connected to metabolism and physiologic homeostasis. Indeed, the ultimate regulators of growth and repair are the genes and normal genes are homologs of oncogenes, the essential propitiators of atypical growth. It is then relevant to note that operator genes respond only to the particular regulator elements of their own system. The controlling elements do not correspond to stable loci on the chromosome but move. Barbara McClintock [16,79] called this capacity to change position “transposition.” Transposition is itself a property regulated by activator genes. The normal DNA of cells can rearrange itself in response to signals from other parts of the DNA. These signals are subject to influence by the internal environment of the cell. For the very sequence of genes to depend on factors beyond the genome, information has to flow bi-directionally, that is, from cytoplasmic protein to DNA. Additionally, viral DNA can insert itself into the DNA of its host cell and subsequently detach itself. For years, scientists cataloged chromosomal alterations that seemed to go with certain cancers. Now, logical connections have been made between oncogenes (discreet transforming DNA segments), and translocations, deletions and other much studied chromosomal changes. One example is the *myc* oncogene, moving from its normal position in chromosome 8 to a region of chromosome

14, where it lands close to one of the genes for immunoglobulins [16]. We have noted that proteins (good conductors of electricity), DNA and transforming DNA segments may function as piezoelectric atomic lattice structures. Also, genes continually structurally change during the lifecycle, as demonstrated by Susumu Tonegawa while outlining the genetic principle for generation of antibody diversity [16,21]. The force carriers (photons) of electromagnetic fields are long-range interatomic messengers, unlike stochastic interactions, which are short range and key-lock in nature. Therefore, we must ask the question, “Could it be that genetic recrystallizations and translocations are related to the very weak apparently physiologic magnetic fields measured by the superconducting quantum interference detector; manifesting a sort of quantum gravity in biological systems?” [80].

It does seem feasible that physiologic Pico-Tesla range magnetic fields may be utilized to regulate the atomic structure and functional behavior of genes. In this regard, we must wonder about the ability of exogenously sourced magnetic profiles to regulate telomere lengths and telomerase activity [13].

$mc^2 = BvLq$ (Jacobson Resonance) is used to establish the magnetic flux density (B) of an externally applied magnetic field to the whole organism, having longest dimension (L). (mc^2) represents the intrinsic energy of a target mass (m) which can be any atomic or molecular species, e.g. peptide hormone trophic factor, enzyme, neurotransmitter, DNA structure such as a telomere (TTAGGG), or any immunogenic particle. ($BvLq$) represents the electromagnetic interaction energy (wave energy), wherein the body of length (L) containing the mass (m) interacts with the magnetic field (B) to provide a system of dual resonance, i.e. $mc^2 = BvLq$. It is hypothesized that a coherent excitation is produced in the target mass (m) via a photon–phonon transduction or conversion, i.e. the piezoelectric effect. (v) may be any inertial velocity such as Earth orbital velocity, because Newton's second law of motion does not distinguish between terrestrial and celestial velocity; and, (q) represents a unit electrical charge, or a single ab-coulomb in the CGS system of physical units; established by defining electromotive force as energy per unit charge. A detailed description of this physico-mathematical model is available in the literature; including the derivation, rationale for the variables m , B , v , L and constants c and q ; and the correlation to other known resonance phenomena: ion cyclotron resonance and Zeeman resonance. Whereas, (c) is the velocity of light, and also the velocity of the force carrier (photon) for a magnetic field moving independently of the inertial frame of reference/source [13,16,46–48].

Within the context of this presentation a sample calculation follows to show how the theory may be applied to biological systems. After the magnetic flux density (B) is derived from $mc^2 = BvLq$, the derived (B) field is inserted into the ion cyclotron resonance equation, $f = qB/2\pi m$, to derive the associated frequency [13,15,16,80].

Sample calculation

Nerve growth factor (NGF) exhibits trophic influences on a variety of neuronal populations; promoting survivability, regulation of synaptic transmissions, and plasticity at adult synapses in many regions of the central nervous system; and homeostatic regulation of intrinsic neuronal excitability. NGF contains an anti-apoptosis inducing segment to prevent cell death. Choosing NGF as a target, we consider the following:

- (1) NGF is 26,500 Dalton, or 4.425×10^{-20} g
- (2) $C^2 = 9 \times 10^{20}$ cm² s⁻²
- (3) (L) is the height of a human, or 177 cm
- (4) (V) is Earth orbital velocity, or 3×10^6 cm s⁻¹
- (5) (q) is one ab-coulomb (unit charge by definition)

The CGS system of physical units is chosen, because, in the MKS (SI) system force is determined between moving charges, whereas in the CGS system force is determined between stationary charges. Therefore, we desire:

$$mc^2 = BvLq$$

$$(4.425 \times 10^{-20} \text{ g})(9 \times 10^{20} \text{ cm}^2 \text{ s}^{-2}) = (7.5 \times 10^{-8} \text{ Gauss})(3 \times 10^6 \text{ cm s}^{-1})(177 \text{ cm})(\text{ab-coulomb}) \quad (3)$$

Then, we note that (q) is normalized in CGS. Consequently, when converting from CGS to MKS, $mc^2 = BvLq$ becomes $mc^2 = BvL(10q)$, because 1 ab-coulomb is equal to 10 coulomb. Therefore, when using the MKS expression, $f = qB/2\pi m$, we must use $f = 10qB/2\pi m$, and we note:

$$f = \frac{10(1.6 \times 10^{-20} \text{ ab-coul})(7.5 \times 10^{-8} \text{ Gauss})}{(6.2832)(9.11 \times 10^{-28} \text{ g})} = 2.1 \text{ Hz} \quad (4)$$

where, (q) is the charge of an electron and (m) is its mass.

Normalization permits the process of introducing a numerical factor into an equation and is of importance in quantum mechanics. Furthermore, the signal, 7.5 Pico-Tesla @ 2.1 Hz, has been successfully utilized in the treatment of Parkinson's disease, improving the quality of life for these patients [13,55,63].

Table 1 presents the results of a Phase II double blind; placebo controlled and randomized clinical study in Parkinson's patients exhibiting motor fluctuations. Twelve subjects experienced 24 sessions of total body immersion in PicoTesla range magnetic fields administered over 8 weeks. Standardized motor and non-motor assessments were performed prior to treatment, at endpoint, and monthly for 3 months. It was demonstrated that PicoTesla range magnetic fields may improve motor and non-motor features of PD beyond that achieved with standard medical therapy, and these effects are long lasting. Larger placebo controlled studies to confirm and further investigate the benefit of this unique non-invasive, non-significant risk and potentially promising therapy are indicated.

The signs and symptoms of PD result from widespread neuronal degeneration, resulting in downstream cortical and subcortical

dysfunction. We postulate that the beneficial effect of EMF results from its piezoelectric effects. As a result, synaptic activity in neurons at various levels of dysfunctional cortical-basal ganglionic loops in PD might be favorably affected. Further research will obviously be needed to clarify this mechanism of action [63,99].

Additional supporting studies

Clinical studies using Pico-Tesla range magnetic fields at low frequency (<300 Hz) demonstrated improvement of brain stem evoked potentials and cognitive responses in multiple sclerosis patients; possibly by modulating axonal and synaptic transmission as well as molecules crucial for immune responses [58].

Ca⁺⁺ cyclotron resonance at 7 Hz was applied to human cardiac stem cells continuously for 5 days, and the level of transcription and translation of the cardio sphere were significantly increased [81].

A double blinded, randomized and placebo- controlled study determined the efficacy of calculated MF signal parameters on subjects suffering with knee pain secondary to osteoarthritis. One hundred seventy-six patients pooled from four sites completed the study. Subjects were randomly assigned to one of two groups, the placebo group (magnet-off) or the active group (magnet-on). Each group received eight treatments over a two-week period. Each subject rated the pain level from one minimal to ten maximal before and after each treatment session on three separate instances; before treatment trials, during the treatment trials, and two weeks after treatment had terminated. Subjects recorded their pain intensity while out of the treatment environment. The magnetic fields used in this study were generated by the Jacobson Resonance device, which consisted of two 18 inch diameter coils of 30 gauge copper wire connected in series (Helmholtz configuration), placed 9 inches apart. The coils were connected to a power supply e.g. HP3325A function generator and an attenuator to obtain the desired field in the space between the coils. The calculated flux densities were in the Pico-Tesla range and associated ELF frequencies (<10 Hz) were utilized. On average, subjects in the 'on' group perceived a 46% reduction in pain after a treatment

Table 1
Key findings of pilot II results: baseline to endpoint.

	Baseline	Endpoint week 8	% chg	Washout week 16	% chg
<i>PDQ-39 (SI)-summary index QoL</i>					
Treatment	20.01 ± 12.26	11.61 ± 7.44	(-42%)	10.86 ± 9.47	(-46%)
Control	24.52 ± 6.93	22.70 ± 6.84	(-7%)	17.96 ± 8.94	(-27%)
<i>PDQ-39 (Mobility)-motor</i>					
Treatment	25.00 ± 24.75	13.33 ± 13.48	(-47%)	12.92 ± 15.69	(-48%)
Control	35.42 ± 12.19	33.33 ± 16.56	(-6%)	24.58 ± 16.00	(-31%)
<i>PDQ-39 (ADL)-activities of daily living</i>					
Treatment	25.00 ± 18.07	9.03 ± 6.67	(64%)	17.36 ± 14.05	(-31%)
Control	22.92 ± 5.74	20.83 ± 6/97	(-9%)	18.06 ± 3.40	(-21%)
<i>PDQ-39 (BD)-body discomfort/pain</i>					
Treatment	27.78 ± 15.52	19.45 ± 6.80	(-30%)	16.67 ± 13.95	(-40%)
Control	22.22 ± 14.59	25.00 ± 20.41	(+13%)	25.00 ± 22.98	(+13%)
<i>Back depression inventory II-depression</i>					
Treatment	12.33 ± 4.76	6.50 ± 5.32	(-47%)	5.83 ± 4.02	(-53%)
Control	12.17 ± 7.25	12.00 ± 4.94	(-1%)	11.50 ± 5.89	(-6%)
<i>UPDRS II (On)-activities of daily living</i>					
Treatment	9.83 ± 6.34	4.33 ± 4.08	(-56%)	5.17 ± 3.17	(-47%)
Control	11.67 ± 4.27	8.33 ± 2.25	(-28%)	8.83 ± 2.48	(-24%)
<i>UPDRS III (On)-motor</i>					
Treatment	23.50 ± 12.99	14.00 ± 7.56	(-40%)	15.67 ± 6.83	(-33%)
Control	29.67 ± 7.94	23.83 ± 11.44	(-20%)	27.67 ± 11.55	(-7%)
<i>FSS-fatigue</i>					
Treatment	34.44 ± 10.23	26.67 ± 9.29	(-22%)	28.00 ± 8.99	(-18%)
Control	35.17 ± 8.93	33.33 ± 9.65	(-5%)	35.33 ± 19.29	(+5%)

session. On average, subjects in the 'off' group perceived an 8% reduction in pain after a treatment session (see Fig. 1).

The results showed a significant difference between the two groups. A two-way ANOVA (GLM) of the treatment sessions showed that the reduction in pain was significantly greater in the magnet 'on' group ($p < 0.001$) than the magnet 'off' group. Additionally, of the 101 magnet 'on' patients evaluated in the treatment sessions, 96% received statistically significant ($p < 0.000$) reduction in pain levels. The $N = 97$ (96%) patients who experienced a reduction in pain had on average a 53.25% reduction in pain [62].

This study indicated that the prediction of the Jacobson Resonance Theory regarding the possibility that Pico-Tesla range MFs are physiologic should be considered. The results of this study point to a subtlety of life that has yet to be fully appreciated, as the benefits were shown to be durable [13,62].

Albert Szent-Gyorgi [82] first proposed an electronic theory of cancer. He believed in the need of a solid-state, physics approach in studying living systems (bioelectronics), since living systems are a complex and ordered quasi-crystalline organization of atomic-molecular and bioplasmic systems. Bio plasma is characterized by a high degree of order, consisting of charged particles, electrons and protons, with an especially high density in mitochondria (10^{16} – 10^{17} electrons per cubic centimeter). Production of electromagnetic oscillations with a frequency greater than 10^{12} Hz (IR) is noted. According to Wolkowsky [41,83,84] bioplasma electromagnetic emissions are in a range of infrared (about 10^{13} Hz, wavelength about 0.02 mm) to short waves (about 10^8 Hz, wavelength about 3.2 m).

It has been hypothesized that physiological, homeostatic mechanisms of living systems operate on atomic, molecular and cellular levels; thus promulgating the idea of electromagnetic immune response mechanisms, i.e. adjustment mechanisms to maintain the balance of total systems in accordance with quantum theory [13,29,30]. Quantum mechanics affords statements relating to apparently discontinuous transitions from one total condition to another without yielding a representation of the specific process. This is connected to the notion that this theory does not operate with the single system, but with a totality of systems. With this interpretation of quantum mechanics, it is readily ostensible why this theory does account for the fact that

weak disturbing forces are able to provide alterations of any magnitude in the physical condition of a system; such that only small alterations of the statistical density in the ensemble of systems occurs. Hence, only infinitely weak alterations of single systems, e.g. PicoTesla magnetic field signals, are required for profound amplifications within complex systems, e.g. biological systems. It appears that a disturbance of the physical parameters of the flow of electrons (mass/energy) whatever the cause, produces a change in the oscillation frequency of the electronic bioplasma, and indirectly disturbs the processes of homeostasis. It is thought that the adjustment mechanisms that maintain ordered states of matter are based upon photon-phonon transductions or conversions, i.e. the piezoelectric effect. We note that a phonon is a quantized vibration of an atomic crystal lattice structure. Wherein, mechanical vibrations are converted to electromagnetic oscillations, or conversely, electromagnetic oscillations are converted to mechanical vibrations. This possibility also points to the semi-conductive nature of biological matter [13,16].

The ordered nature of bio plasma may be consistent with electron and proton vectorialized flows, currently recognized as essential features of cell metabolism. Various biological structures, e.g. keratin, collagen, alpha and beta sheaths of proteins, genes, etc., form an uninterrupted reticulum that may act as piezoelectric communications networks. Recent biophysical knowledge has suggested that piezoelectricity may be considered the common denominator for the aspecific actions of the various non-ionizing order-inducing biological/clinical/physical therapies. Indeed, piezoelectric mechanisms may be present spontaneously in physiology. For example, piezoelectricity may be at work in cells specialized in the reception of external stimuli (heat, pressure and sound) [16].

The cells are able to subsequently convert the specific types of energy they are sensitive to, into the electric energy of the nervous impulse. Furthermore, several tissues and basic biomolecules may have piezoelectric properties by virtue of being made up of electrets: parallel molecular assemblies wherein the microscopic subunits and the macroscopic whole have stable and permanently ordered dipoles. Piezoelectricity may well account for the transmission of electromagnetic oscillations at different frequencies, which are then coherently recognized by resonant molecules [16,41].

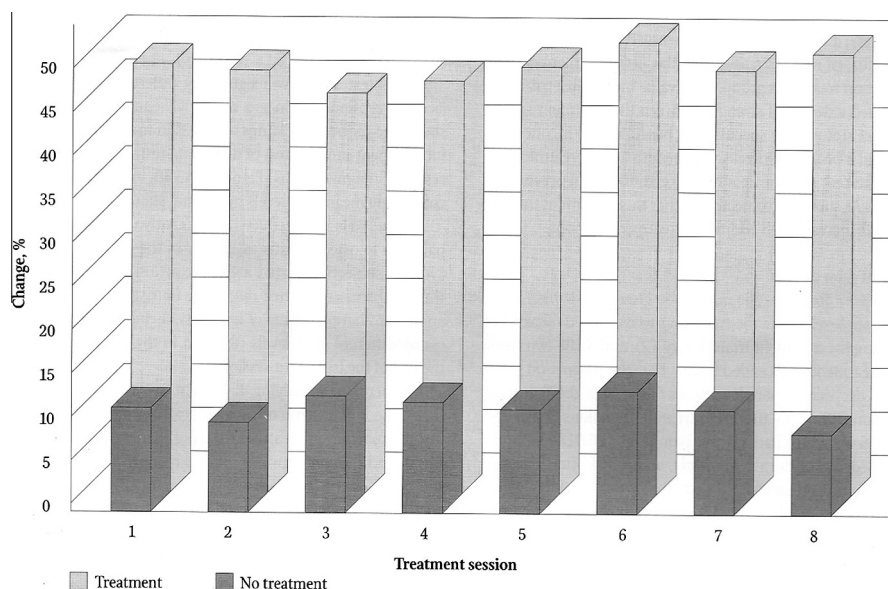


Fig. 1. Comparison of mean percentage reduction in pain level.

We note that when an electric field is changing, the molecules of the medium readjust their positions in response to this change, and this motion of the molecules (actually of the charges within the molecules) constitutes an electric current. Thus, a changing electric field causes an electric current, which in turn generates a magnetic field. There is a fundamental symmetry between electric and magnetic fields. According to Faraday's law, a changing magnetic field induces an electric field; according to Maxwell's principle, a changing electric field induces a magnetic field [85]. Due to the nature of the magnetic force, in that it passes unimpeded through biological structures (unlike electric fields that are attenuated significantly by membranous structures), it seems quite logical to pursue research in the utilization of physiologic, safe, and potentially efficacious non ionizing magnetic fields to establish resonant, coherent and cooperative systems to hopefully renormalize homeostatic function on a global basis in living systems. Indeed, this is the foundation of magnetic resonance therapy, and the magnetic field profiles in the PicoTesla range (naturally occurring) are carrier waves for extremely low frequency ranges, analogous to normal brain wave rhythms.

One of the great pioneers in the field of Bioelectromagnetics was W. Ross Adey. Adey said, "One of the great but often unrecognized accomplishments in the quest for order in biological systems is the revelation of an exquisite succession of structural and functional hierarchies that interact within and between each other. It is at the atomic level that physical, rather than chemical events now appear to shape the flow of signals and the transmission of energy in biomolecular systems. These recent observations have opened doors to new concepts of communication between cells as they whisper together across barriers of cell membranes. Fields, millions of times weaker than the membrane potential gradient modulate cell responses to surface stimulating molecules. The evidence supports nonlinear, non-equilibrium processes at critical steps in transmembrane signal coupling" [40].

In accord with the diversity of possibilities presented herein, concerning biological effects secondary to application of non-ionizing extremely low intensity and low frequency EMFs, we point to studies conducted at the University of Oklahoma Health Sciences Center, Arrhythmia Research Institute.

Truly, it appears that a distinctive, and quite unique potential is unfolding from the radiological sciences for ameliorating the aging process and the effects therefrom.

In our initial experimental study we used 2 different sized Helmholtz coils to apply micro Gauss (μG) levels of electromagnetic fields (EMFs) either to the vagosympathetic trunks or across the chest of anesthetized dogs [86]. From previous reports on frequency analysis of heart rate, the parasympathetic activity averaged 0.043 Hz. Using the Jacobson ($mc^2 = qvBL$) and Cyclotron Resonance ($f = \frac{qB}{2\pi m}$) equations, we calculated the correspondent EMF amplitude value of 2.87×10^{-6} Gauss for parasympathetic activity. Applying these EMFs at the vagal trunks invasively or across the chest non-invasively, we found enhanced parasympathetic effects on the heart rate and atrioventricular conduction (AVC), both properties influenced by parasympathetic innervation. The maximal heart rate changes in the experimental versus control groups was 29% versus 12% ($P = 0.03$). The same EMF stimulation decreased the voltage applied to the vagal trunks by 60% in the experimental group versus a 5% increase in the control group ($P = 0.005$). We note the right and left femoral veins were cannulated for delivery of fluids and anesthetics, and for the insertion of an electrode catheter which was advanced and positioned against the lateral atrial wall in the low right atrium for atrial pacing. Using another level of EMF, (amplitude, 0.34 μG and 2 kHz) determined empirically, applied as above, there was a significant increase in atrial arrhythmias, including atrial fibrillation (AF)

atrial premature depolarization, and atrial tachycardia, which could be suppressed by applied EMF, (2.87 μG at 0.043 Hz). It should be pointed out that 2 kHz is a non-physiologic frequency and 0.34 μG is sympathomimetic.

A shortcoming of these studies was the lack of a mechanism underlying these responses to low level EMFs. Subsequently, a series of experimental studies have been published [87–91] in which we used low-level vagosympathetic trunk electrical stimulation at levels 10% and 50% which did not slow the heart rate or slow atrioventricular conduction (AVC). In an experimental model of induced AF, we found that the nerve clusters called ganglionated plexi (GP) found in specific vulnerable sites in the atria became hyperactive under the influence of excessive release of cholinergic (parasympathetic) and adrenergic (sympathetic) neurotransmitters [92]. In this regard, Smith et al. [92] tested the function of the GP, weeks after separation of the vagal and sympathetic nerves from the aforementioned structures. Not only did the intrinsic GP neurons remain viable but their responsiveness was enhanced. To emphasize this point, we severed the neural connection from the brain to the GP in experimental animals and found after 10 weeks there was a progressive increase in the occurrence of paroxysmal atrial fibrillation. Low-level vagal nerve stimulation markedly attenuated the hyperactive state of the GP, thereby suppressing AF. In a recent experimental study, we recorded the neural activity of the GP and found that several hours of induced AF caused a significant increase in the amplitude and frequency, whereas low level vagal nerve stimulation not only suppressed AF propensity but also the increased amplitude and frequency of the hyperactive GP [92]. A recent clinical report from our group has confirmed that low-level vagal nerve stimulation can mitigate AF in patients with the paroxysmal form of this arrhythmia [88].

Since electrical stimulation of nerves induces its actions via release of chemicals called neurotransmitters, we found that a specific peptide, vasostatin-1 was released at low-levels of vagal nerve stimulation (50% below the voltage that causes slowing of the heart rate) and even at very low levels of vagal nerve stimulation (80% below the slowing threshold). Indeed, further studies in our experimental model of induced AF, showed that vasostatin-1 suppressed AF by inhibiting GP hyperactivity by an anti-autonomic action mediated by nitric oxide [93].

Returning to the earlier studies using low level EMFs to affect heart rate and rhythm, we inserted the molecular weight value for vasostatin-1 into the Jacobson and Cyclotron Resonance equations to derive the amplitude (0.034 μG) and frequency (0.952 Hz), respectively. Applying these EMFs at the vagal trunks and across the chest we found that these low level fields significantly suppressed AF and also decreased the amplitude and frequency of the neural activity of the hyperactive GP [94].

A fundamental question is: Why do these neural tissues (GP) on the heart become hyperactive in some of the population, in particular, disproportionately in persons from 60–80 years old? An early report by Kaijser and Sachs [95] studied healthy women and men comprising groups, age 20–40, 40–60, and those between ages 60–80. Using simple procedures, such as handgrip and the response to the dive reflex test on heart rate and blood pressure, they found, "There seems to be only a moderate attenuation of autonomic cardiovascular responses to about 60 years, after which there is a more rapid decline." Since these cardiovascular responses are mediated by the autonomic innervation from the brain to the heart, these studies suggest that with age the control of the GP on the heart by the higher centers is markedly attenuated allowing these lower centers to become independently hyperactive. This would help to explain the increased incidence of AF in the elderly population compared to younger cohorts [96,97].

Now, although parasympathetic stimulation has been proposed as a generic approach to anti-aging, it must be pointed out that for

various indications, e.g. obesity, fibromyalgia, hypertension in cases usually refractory to pharmacological intervention, esophageal reflux, autism, and diabetes... etc., sympathomimetic electromagnetic field intervention may be useful. Understanding physiologic mechanisms underlying various clinical symptomatology is important, and requires extensive ongoing research.

Einstein once defined the grand aim of science as, “To cover the greatest number of empirical facts by logical deduction from the smallest possible number of hypotheses or axioms.” He believed in a basic universal field in which the multifarious manifestations are merely particular ephemeral forms or conditions of state [97]. Indeed, Lincoln Barnett said, “The urge to consolidate premises, to unify concepts, to penetrate the variety and particularity of the manifest world to the undifferentiated unity that lies beyond is not only the leaven of science, it is the loftiest passion of the human intellect [98].

Conclusion

The decreased need for metabolic activity greater than the BMR diminishes the rate of biological aging; by reducing heat energy production to meet exigencies of life. Through the enhancement of feelings of relaxation, e.g. parasympathetic stimulation, the level of stress, strain, tension and anxiety may be modulated and ameliorated. Externally applied, naturally occurring physiological magnetic profiles may also renormalize quantum-atomic states restoring interatomic cooperative communications networks, with concomitant resonant amplifications. Thus, magnetic resonant energies may restore homeostatic function on all levels of structure and function. Microscopic scarring from excessive production of heat energies may be prevented, further restoring hydration of systems, coherence of biochemical signal transduction pathways and diminution of errors in genetic information transfer-to maximize the lifespan of the individual.

Further to this end, PicoTesla range magnetic fields may restore atomic structures such that regeneration of disrupted tissues can result.

Even more particularly, PicoTesla range magnetic field signals may prove useful through the targeting of telomeres and/or telomerase subunits. In-vitro and in-vivo mammalian research is encouraged, to determine potentials for maintenance- stimulation-or inhibition of said targets, which may ultimately prove useful in medical therapeutics e.g. telomerase inhibition might be possible with externally applied Pico-Tesla magnetic fields in cancer therapy. Finally, it may be possible to target telomeres and/or binding protein to prevent telomere shortening in adult cells that produce little or no telomerase. While Pico-Tesla Magnetic Resonance Therapy is in its infancy, it looms as a possible new paradigm for the amelioration of the aging process and the effects thereof, and continuing research in this exciting new frontier is indicated.

Further theoretical details which need to be addressed include:

1. Further identification of target-specific EMF's, as well as other mass analogs that might be concomitantly affected by the same signal parameters; to confound outcomes/understanding of signal transduction coupling mechanisms.
2. Understanding the underlying physiologic bases for clinical symptomatology, e.g. ANS tonicity, required to standardize protocols for various indications.
3. Magnetic anisotropies typical in crystalline and liquid crystalline materials.
4. Magnetic interactions such as Fermi contact (or electron-nuclear hyperfine interactions) in free radicals.
5. Electron dipole-dipole interactions in the photo-excited triplet states and stable paired radicals.

6. Electron-spin orbit (Russell-Saunders) coupling in organo-transition metal complexes.

All of these magnetic interaction further split the Zeeman energy levels into several discreet energy levels. Spin-orbit and electron dipole-dipole interactions exist at zero applied field and hence the pathogenic particles that may contain these interactions may require corrections arising from these additional magnetic interaction terms (Hamiltonians).

Conflicts of interest statement

There is no conflict of interest.

Acknowledgments

We thank the following researchers for their tireless pursuit of truth in the emerging science of Bioelectromagnetics:

Prof Brij Saxena, Prof William Yamanashi, Prof Bjorn Nordentrom, Prof Franco Bistolfi, Prof Ross Adey, Prof Carlton Hazelwood and Prof Photios Anninos

Finally, we thank Faith Jacobson for her invaluable assistance in the typing and structuring of this manuscript.

References

- [1] Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. *Molecular biology of the cell*. In: Garland science. New York: Taylor and Francis Group; 2002. 263–266, 421, 422, 649, 840, 1241, 2671.
- [2] Gilman AG, Goodman LS, Rall TW, Murad F, editors. *The pharmacological basis of therapeutics*. New York: Macmillan Publishing Company; 1985. 66–99, 209, 238, 1227, 1382–83, 1475.
- [3] Van De Graaff KM, Rhees RW. *Human anatomy and physiology*. New York: McGraw-Hill, Inc.; 1987. 124–167, 180–195.
- [4] *Stedman's Medical Dictionary for the Health Professions*. 6th ed. New York: Lippincott Williams and Wilkins; 2008. 749, 762, 976, 1081, 1280, 1351.
- [5] Jacobson JI. Is the fusion process the basis for growth, repair and aging? *Panminerva Med (J Ital Med Assoc/Europa Medica)* 1990;32(3):132–40.
- [6] Gelmann EP, Sawyers CL, Rauscher III FJ, editors. *Molecular oncology: causes of cancer and targets for treatment*. UK: Cambridge University Press; 2014. p. 442–51.
- [7] Campisi J, D'Adda di Fagnana F. Cellular senescence when bad things happen to good cells. *Nat Rev Mol Cell Biol* 2007;8:729–40.
- [8] Jacobson JI. A theoretical look at genes as magneto-targets. *Indian J Theor Phys* 1992;40(3):161–86.
- [9] Chen PS. *Inorganic, organic and biological chemistry*. 2nd ed. New York: Harper and Row Publishers; 1979. p. 156–78.
- [10] Murray M, Pizzorno J. *Encyclopedia of natural medicine*. New York: Three Rivers Press; 1997. p. 167–8.
- [11] Parker SP, editor. *McGraw-Hill concise encyclopedia of science and technology*. New York: McGraw-Hill Inc.; 1994. p. 810.
- [12] Kuchel PW, Ralston GB. *Oxidative phosphorylation*. Biochemistry. New York: McGraw-Hill, Inc.; 1988. 394.
- [13] Saxena A, Jacobson JI, Yamanashi WS, Scherlag BJ, Saxena BB. A hypothetical construct explaining the mechanism of biological amplification in an experimental model utilizing PicoTesla (pT) electromagnetic fields. *Med Hypotheses* 2003;60(6):821–39.
- [14] Qin C, Evans JM, Yamanashi WS, Scherlag BJ, Foreman RD. Effects on rats of low intensity and frequency electromagnetic field stimulation on thoracic spinal neurons receiving noxious cardiac and esophageal inputs. *Neuromodulation* 2005;8(2):79–87.
- [15] Jacobson JI. $Mc^2=BvLq$ coulomb: gravitational and EM potential in dual resonance. *Indian J Theor Phys* 1986;34:231–9.
- [16] Jacobson JI. A look at the possible mechanism and potential of magnetotherapy. *Journal Theor Biol (Academic Press)* 1991;149:97–110.
- [17] Jacobson JI, Yamanashi WS, Saxena A, Parekh P, Brown B, Shin D, et al. Effect of magnetic fields on mice sciatic nerves, in-vitro. *Front Perspect* 2000;9(1):6–11.
- [18] Jacobson JI. The intrinsic electro-gravitational mechanism of life, the basis of neoplasia, and the clinical method of repair. *Panminerva Med (J Ital Med Assoc)* 1990;32(4):159–71.
- [19] Jacobson JI. Speculation on the influence of electromagnetism on genomic and associated structures. *International Med Res Cambridge Med Pub* 1996;24(1):1–12.
- [20] Jacobson JI, Yamanashi WS. A possible physical mechanism in the treatment of neurological disorders with externally applied pico-Tesla magnetic fields. *Physiol Chem Phys Med NMR* 1994;26(4):287–97.

- [21] Jacobson JI. Exploring the potential of magneto-recrystallization of genes and associated structures with respect to nerve regeneration and cancer. *Int J Neurosci* 1992;64:153–65.
- [22] Jacobson JI. The question of ameliorating the aging process, even macula regeneration with magnetic fields. *Panminerva Med* 1991;33(4):205–8.
- [23] Voet D, Voet J. *Biochemistry*. New York: John Wiley & Sons; 1990. p. 47.
- [24] Nordenstrom BEW. Biologically closed electric circuits: clinical, experimental and theoretical evidence for an additional circulatory system. *Nordic Med Pub* 1983. 69–74, 112–150, 152–172, 269–313.
- [25] Nordenstrom BEW. The paradigm of biologically closed electric circuits (BCEC systems). Presidential address. *Eur J Surg* 1994;574:7–23.
- [26] Jacobson JI. Influence of electromagnetism on genes and associated structures. *Isr J Med Sci* 1994;30:245–8.
- [27] Eichhorn GL. Aging, genetics and the environment: potential of errors introduced into genetic information transfers by metal ions. *Mech Aging Dev* 1979;9:291–301.
- [28] Hanahan D, Weinberg RA. Hallmarks of cancer; the next generation. *Cell* 2011;144:646–74.
- [29] Jacobson JI. Oncogenes and magnetic resonance energies unified algebraically. *Panminerva Med* 1987;29:97–104.
- [30] Jacobson JI. A testable theoretical model for magnetotherapy potentially applicable to such diverse concerns as oncogenic, CNS trophic factors, and viral disorders. *Indian J Biochem Biophys* 1990;27(1):58–62.
- [31] Slagboom PE, Droog S, Boomsma DL. Genetic determination of telomere size in humans; a twin study of three age groups. *Am J Hum Genet* 1994;55:876–82.
- [32] Von Zglinicki T. Oxidative stress shortens telomeres. *Trends Biochem Sci* 2002;27:339–44.
- [33] Wu X, Amos CI, Zhu Y. Telomere dysfunction: a potential cancer predisposition factor. *J Natl Cancer Inst* 2003;95:1211–8.
- [34] Aviv A. Telomeres and human aging: facts and fables. *Sci Aging Knowledge Environ* 2003;51:43–5.
- [35] Bistolfi F. A new approach to the interaction between ionizing radiation and bio structure: the dual compartment interaction model. *Radiat Med* 1991;81(1):99–108.
- [36] Cope FW. Discontinuous magnetic field effects (BarKhausen noise) in nucleic acids is evidence for room temperature organic super conduction. *Physiol Chem Phys* 1978;10:233–45.
- [37] Adey WR. Interaction mechanisms of low-level electromagnetic fields in living systems. UK: Oxford University Press; 1992. p. 44–77.
- [38] DelGuidice E, Doglia S, Milani M. Self-focusing and ponderomotive forces of coherent electric waves; a mechanism for cytoskeleton formation and dynamics. In: Frolich H, Kremen F, editors. *Coherent excitations in biological systems*. Springer: Berlin; 1983. p. 122–7.
- [39] Adey WR. Whispering between cells: electromagnetic fields and regulatory mechanisms in tissue. *Front Perspect* 1993;3(2):21–5.
- [40] Adey WR. Physiologic signaling across cell membranes and cooperative influences of extremely low frequency electromagnetic fields. In: Frolich Herbert, editor. *Biological Coherence and Response to External Stimuli*. Springer-Verlag; 1988. p. 148–70.
- [41] Bistolfi F. Biostructures and radiation order disorder. Edizioni Minerva Medica. Torino 1991: 27,53,67,73,91,103.
- [42] Coyne C, Jacobson JI. Inhibition of the viability and/or proliferation rate of human mammary carcinoma cell populations (HTB-126/McF-7) with pico-Tesla range magnetic fields. From: conference on the effects of pico-Tesla range magnetic fields on biological systems. Mississippi State University, College of Veterinary Medicine; 2001.
- [43] Jacobson JI. Normal and diseased states related to interdependence of electromagnetic fields, growth, repair and genetic regulation of metabolic function. *Indian J Biochem Biophys* 1988;25:442–6.
- [44] Jacobson JI. The influence of magnetism on genes. *Chin Med Sci J (Chin Acad Med Sci)* 1993;8(1):44–8.
- [45] Bistolfi F. A hydrogen-harps model for intracellular communication and its implications for the second genetic code. *Panminerva Med* 1990;32(1):4–8.
- [46] Einstein A. *Ether and the theory of relativity: an address delivered on May 5, 1920 in the University of Leyden. From: sidelights on Relativity*. New York: Dover Publications, Inc; 1983. p. 3–24.
- [47] Einstein A. *The meaning of relativity including the relativistic theory of the non-symmetric field*. Princeton: Princeton University Press; 1956. p. 165–166.
- [48] Einstein A. *Relativity: the special and general theory*. New York: Crown Publishers; 1961. p. 1–100.
- [49] Jacobson JI. On the electromagnetic nature of life. *Panminerva Med (J Ital Med Assoc)* 1989;31(4):151–64.
- [50] Jacobson JI. The mathematical framework essential for magneto-therapy in the treatment of genomic and associated disorder, including cancer, AIDS, and CNS regeneration. *Panminerva Med* 1989;31(1):1–8.
- [51] Cohen D. Detection of the brain's electrical activity with a superconducting magnetometer. *Science* 1972;175:664.
- [52] Williamson SJ, Kaufman I. Analysis of neuromagnetic signals. In: Gevens AS, Remond A, editors. *Methods of analysis of brain electrical and magnetic signals. EEG Handbook Revised*; 1987; 11. p. 411–417.
- [53] Anninos PA, Tsagas N. Localization and cure of epileptic foci with the use of MEG measurements. *Int J Neurosci* 1989;46:235–42.
- [54] Anninos PA, Tsagas N, Sandyk R. Magnetic stimulation in the treatment of partial seizures. *Int J Neurosci* 1991;60:141–71.
- [55] Sandyk R. Magnetic fields in the therapy of Parkinson's. *Int J Neurosci* 1992;66:209–35.
- [56] Jacobson JI. A brief review of picoTesla range magnetotherapies. *Estratto Da Gazzetta Medico Italiana-Archivo Per IE Sci Med* 1988; 157(2): 37–41.
- [57] Anninos PA, Jacobson JI, Tsagas N, Adamopoulos A. Spatiotemporal stationarity of epileptic focal activity evaluated by analyzing magnetoencephalographic (MEG) data and the theoretical implications. *Panminerva Med (Ital Med Assoc)* 1997;39(3):189–201.
- [58] Bistolfi F. Extremely low frequency pulsed magnetic fields and multiple sclerosis: effects on neurotransmission alone or also on immunomodulation. Building a working hypothesis. *Neuroradiol J* 2007;20:676–93.
- [59] Sanders RD. Rapporteur report: weak field interactions in the central nervous system. *Radiat Prot Dosim* 2003;106(4):357–61.
- [60] Mathie A, Kennard LE, Veale EL. Neurons in chemicals and their sensitivity to extremely low frequency weak electric field affects. *Radiat Prot Dosim* 2003;106(4):311–5.
- [61] Scherlag BJ, Yamanashi WS, Jacobson JI, Hov Y, Jackman WM, Lazzara R. Magnetism and cardiac arrhythmias. *Cardiol Rev (Lippincott Williams and Wilkins)* 2004;12(2):85–96.
- [62] Jacobson JI, Gorman R, Yamanashi WS, Dayton M, Haltiwanger S, Saxena BB. PicoTesla range magnetic fields tested in four-site double blind clinical study for treatment of osteoarthritis knees. *Alter Ther Health Med* 2001;7(5):54–69.
- [63] Klepitskaya O, Kumar R. Efficacy and safety of low level electromagnetic field treatment in Parkinson's disease. *Move Disorders* 2008;23(1):1628–37.
- [64] Sandyk R. Successful treatment of multiple sclerosis with magnetic fields. *Int J Neurosci* 1992;66:237–50.
- [65] Trostel TC, McLaughlin RM, Lamberth JG, Cooper RC, Elder SH, Pool AR. Effects of PicoTesla electromagnetic field treatment on wound healing in rats. *Am J Vet Res* 2003;64:845–54.
- [66] Liboff AR, Williams T, Strong DM, Wistar R. Time varying magnetic fields: effect on DNA synthesis. *Science* 1984;223:818–20.
- [67] Lyle DB, Wang X, Ayotta R, Choptart A, Adey WR. Calcium uptake by leukemic and normal T-lymphocytes exposed to low frequency magnetic fields. *Bioelectromagnetics* 1991;12:145–56.
- [68] Byrus CV, Kartum K, Preper S, Adey WR. Increased ornithine decarboxylase activity in cultured cells exposed to low energy modulated microwave fields and phorbol ester tumor promoters. *Cancer Res* 1988;48:4222–6.
- [69] Goodman R, Henderson AS. Exposure of salivary gland cells in low frequency electromagnetic field alters polypeptide synthesis. *Proc Natl Acad Sci* 1989;100:216–20.
- [70] Goodman R, Weil X, Xu J-C, Henderson AS. Exposure of human cells in low frequency electromagnetic fields results in quantitative changes in transcripts. *Biochem Biophys Acta* 1989;109:216–20.
- [71] Goodman R, Henderson AS. Transcription in cells exposed to extremely low frequency electromagnetic fields: a review. *Bioelectrochem Bioenergety* 1990;25:335–53.
- [72] Delgado MR, Leal J, Manteague JL, Garcia MG. Embryological changes induced by weak extremely low frequency electromagnetic fields. *J Anat* 1982;134:533–51.
- [73] Marino AA, Becker RO. Piezo electric affect and growth control in bone. *Nature* 1970:228–473.
- [74] Marina AA, Cullen JM, Reichmanis M, Becker RO, Hart P. Sensitivity to change in the environment: a new bioelectric effect. *Am J Physiol* 1980;39:424.
- [75] Bassett CAL, Mitchell N, Gaston SR. Pulsing electromagnetic field in ununited fractures and failed arthrodeses. *JAMA* 1982;247:623–7.
- [76] Borgon RB, Bonhart DM. The response of mammalian spinal axons to an applied DC voltage gradient. *Exp Neurol* 1997;45:376–89.
- [77] Wikswo J, Barach J, Freeman J. Magnetic field of a nerve impulse: first measurements. *Science* 1980;208:53–5.
- [78] Decker C. Elf-zapped genes speed DNA transcription. *Science News* 1990; 229.
- [79] Keller EF. *A feeling for the organism: the life and work of Barbara McClintock*. New York: WH Freeman; 1983. 8–11.
- [80] Jacobson JI, Yamanashi WS. An initial physical mechanism in the treatment of neurologic disorders with extrinsically sourced picoTesla magnetic fields. *Neurol Res* 1995;17:144–8.
- [81] Lisi A, Ledda M, de Carlo F, Pozzi D, Messine E, Gaetani R, et al. Ion cyclotron resonance as a tool in regenerative medicine. *Electromagn Biol Led* 2008;27(2):127–33.
- [82] Szent-Gyorgi A. Towards a new biochemistry? *Science* 1941;9:609.
- [83] Wolkowski ZW, editor. *Interactions of non-ionizing electromagnetic radiation with living systems. Proceed International Symposium on Wave Therapeutics. Versailles* 1979.
- [84] Wolkowski ZW, Sedlak W, Zon J. The utility of bioelectronics and the bioplasma concept in the study of biological terrain and its equilibrium. In: Wolkowski [83]: 114–122.
- [85] Brancasio PJ. *The nature of physics*. New York: Collier-Macmillan Pub; 1975. p. 368–371.
- [86] Scherlag BJ, Yamanashi WS, Hou Y, Jacobson J, Jackman WM, Lazzara R. Magnetism and cardiac arrhythmias. *Cardiol Rev* 2004; 12:85–96.
- [87] Li S, Scherlag BJ, Yu L, Sheng X, Zhang Y, Ali R, et al. Low-level vagosympathetic stimulation a paradox and potential new modality for the treatment of focal atrial fibrillation". *Circulation* 2009;2:645–51.
- [88] Yu L, Scherlag BJ, Li S, Sheng X, Lu Z, Nakagawa H, et al. Low-level vagosympathetic nerve stimulation inhibits atrial fibrillation inducibility: direct evidence by neural recordings from intrinsic cardiac ganglia. *J Cardiovasc Electrophysiol* 2011;22:455–63.

- [89] Sheng X, Scherlag BJ, Yu L, Li S, Ali R, Zhang Y, et al. Prevention and reversal of atrial fibrillation inducibility and autonomic remodeling by low-level vagosympathetic nerve stimulation. *J Am Coll Cardiol* 2011;57:563–71.
- [90] Sha Y, Scherlag BJ, Yu L, Sheng X, Jackman WM, Lazzara R, et al. Low-level right vagal stimulation: anticholinergic and antiadrenergic effects. *J Cardiovasc Electrophysiol* 2011;22:1147–53.
- [91] Yu L, Scherlag BJ, Sha Y, Li S, Sharma T, Nakagawa H, et al. Interactions between atrial electrical remodeling and autonomic remodeling: how to break the vicious cycle. *Heart Rhythm* 2012;9:804–9.
- [92] Smith FM, McGuirt AS, Leger J, Armour JA, Ardell JL. Effects of chronic cardiac decentralization on functional properties of canine intracardiac neurons in vitro. *Am J Physiol Regul Integr Comp Physiol* 2001;281:R1474–82.
- [93] Stavrakis S, Scherlag BJ, Fan Y, Liu Y, Liu Q, Mao J, et al. Antiarrhythmic effects of vasostatin-1 in a canine model of atrial fibrillation. *J Cardiovasc Electrophysiol* 2012;23:771–7.
- [94] Yu L, Dyer JW, Scherlag BJ, Stavrakis S, Sha Y, Sheng X, et al. The use of low-level electromagnetic fields to suppress atrial fibrillation. *Heart Rhythm* 2015;12:809–17.
- [95] Kaijser L, Sachs C. Autonomic cardiovascular responses in old age. *Clin Physiol* 1985;5:347–57.
- [96] Kane WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. *Am J Cardiol* 1998;82:2N–9N.
- [97] Einstein A. *The Quotable Einstein*. Collected and edited by Alice Calaprice. Princeton University Press; 1996. p. 165–85.
- [98] Barnett L. *The Universe and Dr. Einstein*. Bantam Books. New York: (7th printing) William Morrow & Co.; 1974. p. 111.
- [99] Jacobson JI. *Reason for life*. Abbott Press (a division of writers digest) Bloomington, Indiana 2012:117–8.