SECTION 17

Electromagnetic Medicine

Non-Inductive Non-Thermal Modalities

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I. INTRODUCTION

The area of electromagnetic medicine (EM) encompasses the applications of electricity and magnetism to medical practice. Although this includes both diagnostic and therapeutic applications, the medical community is far more familiar with the former, notably with techniques such as magnetic resonance imaging (MRI), electromyography (EMG), electroencephalography (EEG), electrocardiography (EKG), and magnetocardiography (MKG). There are historical reasons for the medical unfamiliarity (even antipathy) with electromagnetically-based therapies. One has only to look at the beginnings of modern medicine in the United States, specifically the 1910 Flexner report [1,2] that provided the basis for medical education today. Prior to this report there was widespread use of electromagnetic techniques in medicine, often little more than late 19th century versions of snake-oil cures. In great measure the present aversion to electromagnetic therapies built into modern medicine is a direct result of Victorian age quackery.

Another reason for this antipathy, apart from the constraint on the teaching curriculum, has been the extraordinary success of, first, the germ theories of Pasteur and Koch, and, second, the development of molecular biology following the work of Watson and Crick. These have engendered a sense of completeness, a feeling that there is no place for alternate, radically new approaches to the way that illness is treated. Even when electromagnetically-based therapies have proven beneficial, they have been usually ignored. There is little impetus to replace the existing approach, since it is firmly believed that nothing is more fundamental than the existing paradigm, that questions of wellness and illness are ultimately biochemical in nature.

The divisions in electromagnetic medicine are outlined in Fig. 1. Beyond the separation into diagnostic and therapeutic applications another distinction is made for applications of weak-field ELF magnetic in the treatment of illness. The description ***non-inductive non-thermal*** helps emphasize that the effects obtained by applying low intensity low-frequency electromagnetic fields to biological systems are not the result of either inductive emf generation or the delivery of thermal energies through Joule heating. By contrast, a number of clinical devices that make use of Faraday induction or Joule heating are recognized by the medical community not only because they are effective, but also because the applied voltages, currents or heat are fully consistent with what is expected biochemically. In sharp contrast, the non-inductive non-thermal category includes clinical applications where this is not true, that is, where the electromagnetic variables that are part of the therapy fall outside those permitted by the current medical paradigm.

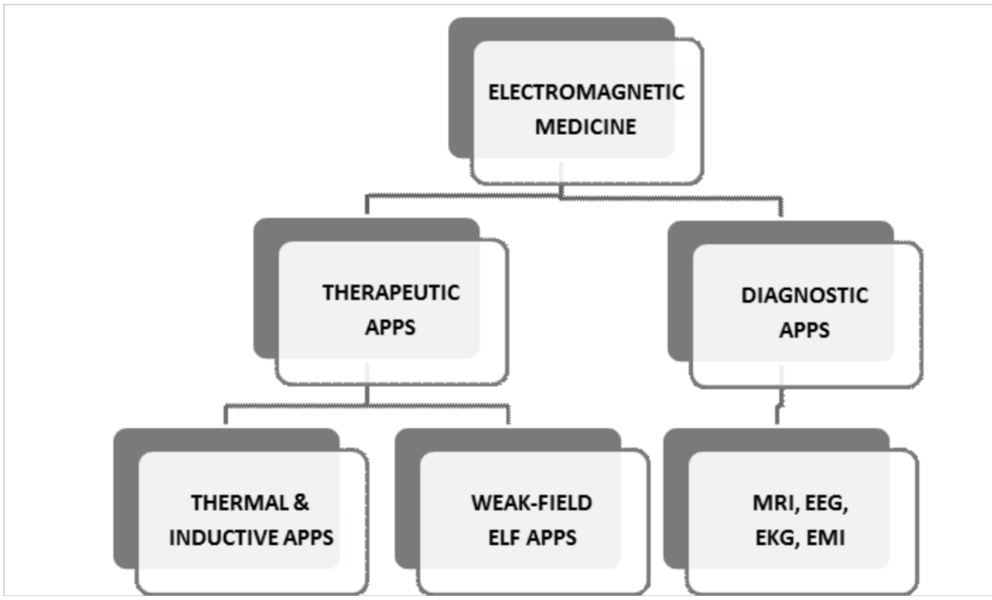

Fig. 1. Divisions comprising Electromagnetic Medicine

II. WEAK-FIELD ELF APPLICATIONS: SCIENTIFIC BASIS

There is a wealth of evidence showing that weakly intense ELF fields affect the metabolic responses in cells. It was found in the 1980s that ELF magnetic fields too weak to be considered as inductive sources of potential differences are nevertheless capable of affecting DNA synthesis in mammalian cell culture[3,4]. Since that time, there have been numerous reports (Table 1) that magnetic fields on the order of several microTesla and in the 3-300 Hz ELF frequency range can affect a wide range of biological systems. A short list of such reports, given in Table 1, emphasizes both the variety of systems in which these effects have been found, and the difficulty in providing an explanation, as evidenced by the fact that these studies have a history extending back more than 25 years. The lack of a reasonable explanation is not a trivial distinction, since there is great reluctance to accept observational evidence, regardless of replications and the number of supportive reports, without a reasonable biomolecular basis

Biological Model	YEAR	Reference
Rat behavior	**1986**	**Thomas et al**[5]
Diatom motility	**1987**	**Smith et al**[6]
Protein synthesis in salivary gland cells	**1988**	**Goodman and Henderson**[7]
Mitogenesis in lymphocytes	**1989**	**Cossarizza et al**[8]
Production of glycosaminoglycans in cartilage	**1991**	**Smith et al**[9]
Neuroblastoma cell metabolism	**1992**	**Smith et al**[10]
Expression of Insulin Growth Factor II	**1995**	**Fitzsimmons et al**[11]
Regeneration of planarians	**1995**	**Jenrow et al**[12]
Analgesia in snails	**1996**	**Prato et al**[13]
Rat EEG	**1998**	**Vorobyov et al**[14]
Growth Rate in plants	**2005**	**Galland and Pazur**[15]
Stem cell differentiation	**2009**	**Gaetini et al**[16]

Table 1. List of reports indicating that non-inductive ELF magnetic fields are biologically interactive. Note that these reports are by no means isolated. A number of these have been independently replicated, for example the studies on rat behavior, lymphocytes, planarians, and plants.

In 1998 a group led by Zhadin[17] discovered that these effects are also found at much lower intensities. AC magnetic fields as low as 40 nT can shift the electrical conductivity of polar amino acids in aqueous solutions. This work, independently replicated[18,19,20], is typified by a sharp change in conductivity at one specific frequency, as shown in Fig. 2. The explanation for this remarkable effect makes use of quantum electrodynamics to provide a means of reducing the viscosity of water sufficiently to allow Lorentz forces to be observed on solvated biological ions, thereby establishing a straightforward reason for the many difficult-to-explain magnetic stimulation reports claiming a connection to ion cyclotron resonance[21].

Ion cyclotron resonance (ICR) as it applies to biological systems was first discovered[22,23] to be a critical underlying factor in connection with previously observed[24] electromagnetically-induced changes in free calcium in brain tissue (Ca-efflux experiments). In the presence of a static magnetic field the most prominent effects are always observed for parallel AC magnetic fields with frequencies very close to the cyclotron frequency of the calcium ion. The majority of subsequent ICR cellular studies have focused on the Ca^{2+} ion. As a second messenger it is involved in regulation at all stages of growth and development, including proliferation, and in the organization of cytoskeletal elements. Indeed some of the results shown in Table 1 are examples of Ca^{2+} ICR stimulation.

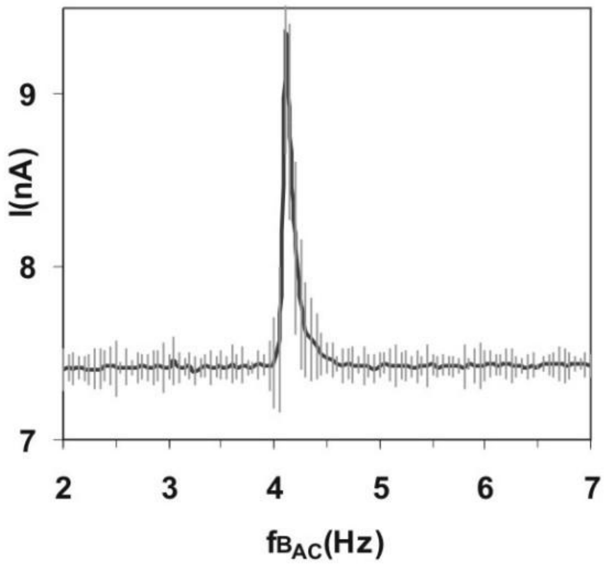

Fig. 2. Data taken by Pazur[18] illustrating the Zhadin effect[17]. A very weak AC magnetic field (40 nT) is applied to an aqueous solution of glutamic acid and the conductivity of the glu^+ ions is continuously monitored in terms of nA. The magnetic frequency in Hz is slowly ramped upwards. A sharp change in conductivity is observed at a frequency (4.25 Hz) close to the ion cyclotron resonance value for glu^+, (4.8 Hz).

The expression for the ICR resonant angular frequency is given as $w = (q/m)B_o$, where q and m are the charge and mass of the ion, and B_o the DC magnetic field. Confirmation that the charge-to-mass ratio was explicitly involved in this effect was obtained when isotopic $_{45}Ca$ was substituted for $_{40}Ca$ in a study on lymphocyte proliferation[25], showing that the frequency where the maximum ICR effect on proliferation occurred was shifted down by a factor of 12%, exactly what is to be expected for a change of mass of 5 parts out of 40.

Because these ICR effects appeared to violate simplistic analysis involving magnetic induction at first they evoked much suspicion in the scientific community. Many subsequent confirmations, however, performed on different model systems in diverse experimental situations , in part listed in Table 1, proved that these weak low-frequency effects are indeed real. It is clear that magnetic field combinations when tuned to ion cyclotron resonance, can act to regulate the flow of biological information, a conclusion that has important ramifications for electromagnetic medicine. Consider the following, from a recent review[26] of this subject:

The inescapable conclusion…is that the ICR mechanism, whatever its molecular basis, is of enormous biological significance. We are able to make reproducible and consistent physiological changes of various sorts in the widest imaginable range of genera simply by applying weak magnetic fields tuned to the charge-to-mass ratio of various biological ions. It is very clear that [this] must be part of a heretofore unknown system that carries physiological information/instructions, and that better understanding will open the way to providing a radically new means of controlling wellness.

In addition to medical applications already initiated using ICR techniques there are also a number of potential advances that are likely to be further developed in the future. Consider for example the observations found in a number of ICR studies that indicate merely changing the resonance condition from one ion to another will result in the opposite result. This phenomenon was first observed by S D Smith in his studies on diatom motility[6] and later reported by others[9,27-31] (Table 2). One explanation is that this effect likely reflects the endogenous nature of bioresonance, wherein multiple ion resonances are occurring simultaneously giving rise to a balanced physiologic outcome. If this is true then it should be possible in principle to selectively reduce the undesirable in favor of the desirable. There is evidence[32] indicating that ICR applications can increase the rates of proliferation in neuroblastoma cell culture. Is It possible that there exist yet-to-be-tried ICR conditions that would have the opposite effect, namely to reduce the rates of proliferation in cancer cell lines, thereby opening the way to new cancer fighting techniques?

MODEL SYSTEM	FREQ, Hz	B_o, mT	ION	RESPONSE
Diatom motility[6]	**16**	**20.9**	Ca^{2+}	**Motility✷**
	16	**41.0**	K^{+}	**Motility❋**
Embryonic bone[9]	**16**	**20.9**	Ca^{2+}	**Growth✷**
	16	**40.7**	K^{+}	**Growth❋**
Embryonic bone[27]	**16**	**20.9**	Ca^{2+}	**Growth✷**
	16	**40.7**	K^{+}	**Growth❋**
Plant growth[28,29]	**60**	**78.3**	Ca^{2+}	**Growth✷**
	60	**153.3**	K^{+}	**Growth❋**
Rat behavior [30]	**63**	**50**	Mg^{2+}	**More Active**
	38	**50**	Ca^{2+}	**More Passive**
Gravitropic response[31]	**35.8**	**46.5**	Ca^{2+}	**Up**
	54.7	**46.5**	K^{+}	**Down**

Table 2. Ionic tuning can drastically alter physiological outcome. Note that specific outcomes are observed for different magnetostatic fields at the same resonant frequency, or equivalently, for different frequencies at the same static magnetic intensity.

II. PRESENT CLINICAL ELECTROMAGNETIC PRACTICE

A number of diagnostic techniques based on electromagnetic principles, such as **Magnetic Resonance Imaging** (MRI), are universally accepted by physicians, to the point where objections are heard concerning the costs to the health care system because of overuse[33]. Neurologists universally use **Electromyography** (EMG) in their practice no less than **Electrocardiography** (EKG) is used by cardiologists and internists. It also should be understood that there are efficacious electromagnetic diagnostic tools that are used outside of the United States but not permitted in the US. The US Food and Drug Administration (FDA) oversee the introduction and use of medical devices with as much zeal as it supervises pharmaceuticals. The prospect of very expensive and time-consuming procedures for new devices tends to discourage the introduction of foreign devices, regardless of their efficacy and safety. This applies to both diagnostic and therapeutic devices.

One example of a foreign diagnostic device that is presently in clinical trials in the US is the Tissue Resonance Interferometer (**TrimProbe)**[34], invented by Clarbruno Vedruccio. Following its original use as an electromagnetic device for the remote detection of land mines and for airport screening, he discovered that microwave signals in the range 400 to 1350 MHz reflect differently from cancers as compared with healthy tissue. A hand-held non-invasive probe measures the degree of interference between the incoming and reflected signals, providing instant determinative results. It has been highly successful in prostate diagnosis, proving effective in distinguishing malignancies from prostate hyperplasia and prostatitis. This technique has also been used to detect bladder cancer. Because of its non-invasiveness, its speedy application and rapid diagnosis, all within a matter of minutes, this device has great potential as a tool for screening populations at risk.

It is clearly the case that the highly specific electrical nature of the nervous system should predispose it to exogenous electrical influence. This is shown in the great variety of electric medical procedures[35] presently in use as neurotherapies. Devices such as heart pacemakers and defibrillators are so widely known that they need no description. **Vagal nerve stimulation** (VNS) is widely used as an anti-convulsant therapy. **Deep brain stimulation** (DBS) uses electrodes in the brain to treat Parkinson's disease and other movement disorders. Chronic pain is treated using the non-invasive **Transcutaneous electrical nerve stimulator** (TENS) directly on the back or the **Cranial electrothermal stimulator** (CES) on the head. Insomnia is treated with **Low-energy emission therapy** (LEET) using an electrode positioned in the mouth. In general these devices are employed as surrogates for already existing physiological endogenous mechanisms that require a boost or improvement, with the cardiac pacemaker serving to regulate the timing of heart contractions as an illustrative example. Presently there is an extension of this concept, with widespread ongoing research aimed at mimicking the electric signals needed to restore eyesight and muscle function that may have been lost because of disease or accident.

Less well known are a number of medical accepted EM therapies that are sufficiently energetic to be acknowledged as based either on Faraday induction or Joule heating. **Transcranial Magnetic Stimulation** (rTMS)[36,37] is used to treat depression. In this procedure, approved by the FDA as efficacious and safe, a large pulsed current is sent through a coil placed strategically over the head, thereby inducing a current through the brain. In part, this serves as a modern alternative to the much older (1938) use of applied currents to treat depression, namely **ElectroConvulsive Therapy** (ECT), wherein pulses or sinusoidal voltages are applied to the scalp through electrodes, producing power levels of several hundreds of watts directly into the brain.

Another purely inductive device, **Pulsed Magnetic Field** therapy (PMF), has found great success in treating bony nonunions, a rather common problem in which fractures do not knit properly. This device was introduced by Bassett and Pilla[38] following a long history showing that living bone enjoys remarkable electric properties[39] that can be used to advantage in growth and repair processes[40]. In a very real sense, the PMF work on bone in the 1970s was the springboard for the development 25 years later of rTMS.

Electromagnetically-induced hyperthermia (**Oncotherm**)[41] and **Electrochemical Treatment** (EChT)[42] have both been found useful in treating late-stage cancers, the former mostly in Europe and Asia, and the latter in China. The Oncotherm device applies carefully directed radiofrequency devices to tumor sites, slightly elevating the local temperature, which has the interesting effect of killing off cancer cells without affecting healthy tissues. Neither procedure has as yet been approved by the FDA.

A much older device, dating back to the 1930s, **Diapulse**, applies radiant Joule heat deep into tissues. Because this device was introduced prior to the establishment of the FDA, its acceptance was ”grandfathered”, that is, allowed to be advertised and marketed on the basis of earlier widespread use. Electromagnetic energy is directed to specific areas of the body in the form of 600 pulses/s with each pulse lasting 65 ms. Although it was originally used to provide pain relief the extent of the therapeutic claims now includes “neurologically associated problems”. Along with a number of other devices making therapeutic claims related to radiofrequency use, the prominent frequency employed was 27.15 MHz, which has no special biological qualities, but is merely a frequency of choice permitted by the Federal Communications Commission (FCC).

This 27.15 MHz frequency has also appeared as the carrier wave in a similar arrangement to that used in the LEET insomnia device mentioned above, where one electrode is again placed in the mouth, in this case to treat cancer[43]. A much lower frequency, in the tens of Hz, modulates the 27.25 MHZ carrier. Presumably this ELF component represents the active anti-oncogenic component in this device.

Even higher frequencies, at 50 GHz and larger have also been reported as therapeutic aides. These devices, generally described as **Microwave Relaxation Therapy** (MRT)[44] machines are widely used in Russia and the Ukraine for mood behavior, and (anecdotally) to strengthen the immune system.

The author has previously attempted[45] to characterize neuroelectromagnetic therapies as falling into three categories: **subtle, gross, and disruptive**. The procedures of rTMS and ECT can be regarded as **disruptive**, considering that seizures have been associated with both, either deliberately or by accident. Similarly **gross** neurotherapies properly describe the great number of neural stimulators in use today. The term **subtle** is meant to convey the great difficulty in understanding how vanishingly small electric and magnetic signals are able to affect biological systems. It is abundantly clear that such signals cannot be the result of either Faraday induction of voltage or thermal changes due to Joule heating.

III. NON-INDUCTIVE NON-THERMAL MEDICAL APPLICATIONS

The question of subtle electromagnetic effects in biology is not new. Observations indicating that minutely small electric currents, at levels far weaker than allowed by simple energetic estimates, are capable of profound biological effects. These were first reported in connection with living bone. Electret applications[46], likely supplying no more than a few hundred nanoAmperes, were found to significantly affect growth rates in bone. This fact was subsequently used in a number of orthopedic devices operating at 1-2 mA to repair bony non-unions[47]. The great advantage of the PMF techniques mentioned above was that currents at this level could be introduced at the repair site in a completely non-invasive way.

More recently, the FDA-approved application of ion cyclotron resonance magnetic fields to the problem of bone repair[48] has all but replaced the use of both weak electric currents and PMF pulses. Magnetic fields from a portable coil tuned jointly to Ca^{2+} and Mg^{2+} are applied for 30 minutes a day over a period of weeks. It should be emphasized that the efficacy of this application, achieving repair rates of 70% or more, remains unexplained, except insofar as one considers ion cyclotron resonance phenomena as empirically factual.

Adey also recognized the fact that such signals caused effects that were not readily explained. In attempting to understand results obtained in his laboratory showing a distinctly nonlinear response in connection with the calcium-efflux experiments, he suggested that low-energy transmission occurs at cell membranes by means of solitonic waves[49].

The results listed in Table 1 for effects related to ELF magnetic fields have their counterparts in experiments conducted with AC electric fields. In some ways these are unexpected. Unlike the transparency of biological matter to low-frequency magnetic fields polarization effects in the extracellular medium and the large electric field at the cell membrane make it difficult to apply AC electric fields to cells. Some of the weak AC electric-field clinical approaches involve the use of invasive electrodes. Nonetheless these are noteworthy, considering the poor prognoses attached to illnesses such as glioblastoma.

Thus, one recent very promising therapy entails the use of electric fields at frequencies equal to or less than hundreds of kHz (**Tumor-Treating Fields**, or TTF) to treat aggressive glioblastoma and lung cancer[50,51]. Low-intensity electric fields, on the order of 1-2 V/cm, are found to slow the proliferation of all cells, cancer cells included. This is particularly advantageous in the treatment of brain cancer, because healthy brain cells tend not to proliferate in any case. Therefore the application of such fields is effective in slowing the increases in cancer cell production while leaving healthy cells unaffected. A somewhat similar effect has been discovered, but for applications at 50 Hz instead of hundreds of kHz. In this approach[52], a weak applied AC electric field is also used to fight cancer, not by reducing the proliferation of cancer cells, but by reducing their resistance to multidrug chemotherapy.

It is important to point out that these findings on the effectiveness of AC electric fields on cancer cell proliferation help illuminate why possible similar results that might be obtained using magnetic fields are so interesting. For one thing, there are problems related to AC electric field polarization effects that add constraints on how the cells are stimulated. By contrast because of tissue transparency to ELF magnetic fields, their clinical use will not only always be non-invasive, but also capable of being applied in more general ways.

Comparable effects of the sort observed using AC electric fields have already been observed using weak ELF magnetic fields. A number of reports have found changes in cell proliferation[8], particularly in lymphocytes, as a result of weak magnetic field stimulation. Further, in direct contrast to the electric-field reduction in chemotherapeutic resistance Liburdy discovered[53] that the resistance of breast cancer cells to tamoxifen was increased using 60 Hz magnetic fields.

Two interesting reports by Novikov highlight the clinical potential of weak magnetic fields. In the first case[54] he found that Ehrlich ascites cancer in rats can be dramatically reduced through the use of combined, ostensibly cyclotron-resonance tuned magnetic fields. In the second case[55] he demonstrated that these fields can also be used to hydrolyze, that is, break down, polypeptides by merely tuning to the charge-to-mass ratios of the constituent amino acids. One obvious clinical direction suggested by this work is to use this approach to break down the b-amyloid plaque protein associated with Alzheimer's disease. Experiments have indicated that this is indeed possible in animal models, but it is not yet clear if this plaque is a cause of this disease or simply one of its symptoms.

The last entry in Table 1 indicating that weak ELF magnetic fields can play an important role in stem cell applications[16] is particularly exciting. The most difficult aspect to treating heart failure is the inability of damaged heart muscle to regenerate, leading when possible to heart transplants. Stem cell regeneration of heart tissue is an obvious remedy to this problem but the results to date have in general been slow. This stalemate has been dramatically changed through the use of weak ICR magnetic fields. It was demonstrated that cardiac stem cells from humans when exposed for five days to ELF resonance fields tuned to Ca^{2+} enjoyed significantly greater proliferation and differentiation, perhaps paving the way for a minimally manipulative means of regenerating diseased hearts. Because of this result there is now heightened interest in the use of ELF magnetic fields to enhance the implementation of regenerative medicine and tissue engineering.

A very different approach to ICR medical therapy is found in the **Seqex** device[56] which applies an oscillating magnetic field to the patient's entire body while simultaneously taking advantage of the local parallel vertical component of the earth's magnetic field to achieve resonance. Its most celebrated use has been to treat the debilitating depression that often accompanies chemotherapy following cancer remediation[57], but there have also been numerous anecdotal reports claiming success in treating other diseases, for example multiple sclerosis. There is reason to believe that the efficacy of this device may be related to its dramatic effect on antioxidants. In addition to the fact that this device employs holistic application of the combined fields, it is unique in that the applied ICR frequency is not calculated from ionic charge-to-mass ratios, but is determined by first finding in a prior separate evaluation the specific frequency conditions that sharply alters the whole-body bioimpedance. Once determined this frequency information is stored on a "smart card" for future treatments on that patient. It is worth noting that the change in whole-body bioimpedance at resonance is consistent with the sharp changes in ionic conductivity that were observed by Zhadin and others. This device has not as yet been introduced into the United States for clinical evaluation.

IV. WELLNESS AND ILLNESS: THE ELECTROMAGNETIC PERSPECTIVE

The medical community continues to regard therapeutic regimens based on weak magnetic fields with great suspicion. This fact is best illustrated by contrasting the interest shown in the use of AC electric fields to treat cancer while similar results using magnetic fields have all but been ignored. We do not seek to diminish the potential importance of these electric field effects, but it is apparent that ELF magnetic field research is still thought of as too far outside the mainstream. One useful rationalization in trying to explain the AC electric field effects has been to implicate voltage-dependent ion channels as the key interaction site. This allows one to avoid the thorny question surrounding the intrinsic difficulty in the lack of penetration of AC electric fields into the cell. By contrast, even though there appears to be no such thing as magnetically responsive ion channels, ELF magnetic fields are not impeded by the large electric field of the cell membrane, reaching all compartments inside the cell equally.

One alternate view, when looking at electromagnetic effects, may be to regard a common parameter found in both the electric and magnetic cases, perhaps involving frequency or some function of frequency, as the key distinction. This has already been hinted at in connection with ICR biological interactions.

Recently the author and colleagues[26] advanced a radical new view of electromagnetic effects in biology, suggesting that these strange new electromagnetic interactions can be explained in terms of an endogenously available substrate resonantly coupled to biological ions that enables information transfer for purposes of regulation. In this approach the tweaking of biological systems with weakly energetic electromagnetic signals reveals an underlying order to organisms, one in which the electromagnetic is elevated above the biochemical.

However, even if this generalized concept of systemic electromagnetic wellness is correct, there still remains unexplained the molecular basis that might tell us why nanoAmpere currents can help initiate bone formation or why nanoTesla magnetic fields can hydrolyze proteins. These fully replicated observations are well outside the simplistic electrical engineering that is so often used to discuss such effects. For example, it is inappropriate to express this work in terms of

Specific Absorption Ratio (SAR), because a different yardstick is required. The low levels of power absorbed by the biological system are literally many orders of magnitude below the 1 Watt/kg prescribed as safe. We know that very low levels of electromagnetic can affect biological systems, but do not know how this happens. One clearly obvious truth yet to be generally accepted, yet of vital importance to everyone, is that these effects are profoundly quantum mechanical in nature[17-21], and have little connection to the traditional safety limitations imposed by electrical engineers.

V. CONCLUSIONS

There can be little doubt that weakly energetic electromagnetic fields are biologically interactive to the point where they can be usefully applied in medically relevant therapeutic procedures. Not only does this fact suggest a bright future for the role of electromagnetism in medicine, but it also underscores the need to be very cautious when examining the effects of low-level electromagnetic fields on people. This conclusion, slightly rephrased, was expressed by the author when he wrote[58]:

> ***In the long run, [weak-field exposures for medical purposes] may be the only way to prove the case for biological plausibility among those who presently choose to deny that weak field low frequency magnetic fields do indeed interact with biological systems.***

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