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Cellular ELF Signals as a Possible Tool in Informative Medicine

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According to Quantum Electro-Dynamical Theory by G. Preparata, liquid water can be viewed as an equilibrium between of two components: coherent and incoherent ones. The coherent component is contained within spherical so called "coherence domains" (CDs) where all molecules synchronously oscillate with the same phase. CDs are surrounded by the incoherent component where molecules oscillate with casual phases regarding each other. The existence of coherent domain in water has been demonstrated in a set of experiments on pure water exposed to high voltage, under this condition the electric field concentrates inside the water, arranging the water molecules to form high ordered structure.

Recently has been studied the influence of combined static and alternating parallel magnetic fields on the current through the aqueous solution of glutamic acid; outlining the relevance of low frequency electro-magnetic field in interacting with biological target. Additional results demonstrate that at combined static and alternating parallel, magnetic fields matching the ion cyclotron energy resonance of a particular charged molecule into biological tissue an intrinsic weak magnetic field is generated by ion currents in the cell.

These results should increase the reliability and the clinical feasibility of the use of electromagnetic field, tuned at ion cyclotron resonance of charged molecules, as a biophysical approach to interfere with biological mechanisms. We demonstrate that Exposure of human epithelial cell to ion cyclotron energy resonance generated by a commercial electromedical device (Vega select 719) tuned to calcium ion at 7 Hz act as a differentiation factor, thus opening up the possibility to use particular extremely low frequency electro magnetic field protocols, in informative medicine.

Keywords Resonance; ICR; Differentiation.

Introduction

Living organisms are complex electrochemical systems which evolved in a relatively narrow range of well-defined environmental parameters. For life to be maintained, these parameters must be kept within their normal range, since deviations can induce

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biochemical effects. Environmental natural electro-magnetic fields are a ubiquitous factor of nature. If nature gave certain organisms the ability to receive information about the environment via invisible electromagnetic signals, then there must also have been the benefit of an ability to discriminate between significant and meaningless signals. The most evident example of adaptation of living creature to the environment electromagnetic component is the visual system: the eye is a biological tool committed to the perception of the entire visible electromagnetic energy to regulate cellular or sensorial function such as in protein folding, circadian rhythm, and in central nervous system function. Bearing in mind that electromagnetic field can be perceived by living organism, we should not be surprised if they are consequently able to induce biological effects. The discovery that electromagnetic signal can be associated to specific biological function is known since the time of Galvani and Matteucci. In the past century, several studies indicated a correlation between some physiological and pathological processes and electromagnetic field.

Despite the fact that electromagnetic therapy is already used in clinical trial such as in orthopaedics, debate still continues about the mechanisms of the interaction between specific irradiation protocols and biological targets.

The Ion Cyclotron Resonance (ICR) Proposed Mechanisms

The mid-1980s was marked with the discovery by Blackman (Blackman et al., 1985) and Liboff (1985) of a surprising phenomenon: a low-frequency alternating (AC) magnetic field (MF) is capable of changing free calcium concentrations in nervous tissue only in the presence of a simultaneously acting static (DC) MF. The most prominent effect was observed at the AC field frequency close to the cyclotron frequency of a calcium ion. The cyclotron frequency is defined (Liboff, 1985) as

$$f_C = \frac{q}{2\pi m} B_0,$$

where q and m are the charge and mass of the ion, and B_0 is the DC field. This works opened a new line of research in the area of bioelectromagnetics.

There were three unexpected aspects to this phenomenon: (1) the necessity for simultaneous application of DC and AC MFs; (2) tuning the AC and DC MFs to the cyclotron frequency resonance condition; and (3) very small values of acting MFs, measured in tens of μ T, and extremely low frequencies of AC MFs, measured in tens of Hz or less. Therefore, these results evoked much suspicion in the scientific community. Afterwards, however, many confirmations for these data were obtained in works performed on different model systems and in different experimental situations (Liboff et al., 1987; Lerchi et al., 1991; Blackman et al., 1994; Zhadin et al., 1999; and others) which convinced the scientific community of the real existence of the above effects.

Earlier, there were attempts to understand the physical mechanisms of resonance action of combined MFs. Liboff (1985) considered the motion of free ions under action of these MFs, suggesting a mechanism similar to the one working for charged particles in free space under the influence of the Lorentz force. But at body temperature this idea can be realized only in very large systems capable of including the large radius of ion rotation, measured by meters. The idea (Lednev, 1991) that

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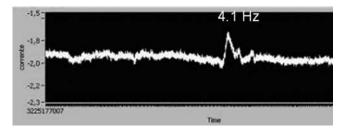


Figure 1. The effect of glutamic acid ion cyclotron energy resonance: the recorded current of glutamic acid at pH 2.9 when exposed to its ICR at 4.1 Hz.

parametric resonance might be responsible for such effects was also not very fruitful for lack of a necessary low frequency harmonic oscillator in living systems. Larmor precession also does not help in this situation, because of a lack of restoring force with proper parameters. The problem is likely solved using the quantum electrodynamics of condensed matter. According to the quantum electro-dynamical theory of Preparata (1995), liquid water consists of two components: coherent and incoherent. The coherent component is contained within spherical, so-called "coherence domains" (CDs) where all molecules synchronously oscillate with the same phase. CDs are surrounded by the incoherent component where molecules oscillate with random phases relative to one another. Diameters of CDs are measured in terms of tenths of a micron, and at room temperature the total volume of domains is about 40% of the whole water media. At resonance action of the ion cyclotron frequency, the ion is accelerated by the MFs, increasing its kinetic energy until escape from CD, jumping into the incoherent component of the water molecule where the ion became biologically available. This has been scientifically supported by experiments performed in different laboratories studying the behavior of glutamic acid at glutamic acid ion cyclotron resonance of 4.1 Hz. Glutamic solution in an electrolytic cell were irradiated under controlled condition at extremely low frequency and the current flowing in the electrolite cell continuosly was recorded. When the resonant conditionwere reached at 4.1 Hz, a peack of dc current were recorded (Figure 1).

Calcium Ion Cyclotron Resonance to Transfer Information at Biological Level

We recently published that exposing keratinocytes cell to Calcium ICR causes rearranging of actin filaments leading to an increase in actin expression and in formation of stress fibers that cross parallel to the cells. Since modification of cellular growth rate and gap junction number with the consequent cytoskeleton rearrangement are implicated in cells transformation, we analyzed the expression of involucrin as a differentiation marker of keratinocytes. In human epidermis, involucrin is first observed in the cytoplasm of spinous and granular layer cells. In transition cells, it is equally distributed between the cytoplasm and the nascent corneified envelope, while in the corneocytes it is largely corneified envelope associated. In our experiments, involucrin expression in the exposed cells is increased compared to control (Figure 2). Since involucrin is a keratinization-associated molecule, our observation may suggest that the exposed cells are at an upper differentiation level than controls. Exposed cells showed a higher number of lamellipodia, specialized structures for cell-cell contact. The augment of cell-cell contact junctions, is also supported by the different distribution in



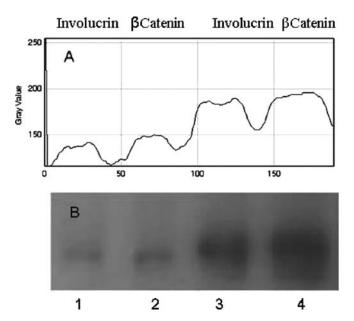


Figure 2. 7 Hz Calcium ICR β Catenin and Involucrin modulation by Western Blot. In lane 1 and 2 proteins extracted in control cells non exposed cells; in lane 3 and 4, proteins extracted in 7 Hz Calcium ICR exposed cells. The profile plot is shown in the upper panel. The amount of proteins inoculated is the same for control and exposed samples, quantitated by Lowry test.

 β -Catenin as reported in Figure 2. β Catenin is a protein implicated in cell-celladhesion, binding cytoplasmic domain of cadherin, and in signal transduction cell adhesion molecules and their association with actin cytoskeleton play an important role not only in the maintenance of tissue integrity, but also in proliferation and differentiation. The modification of cytoskeletal assept, and expression of adhesion and differentiation markers confirm our previous data that exposed cells are at an upper differentiation level. This is a very important point suggesting a possible application of electrotherapy in the therapy of proliferative diseases. It would be very interesting, for example, to analyze the possibility of using Calcium ICR electrotherapy as non invasive chemoterapic agent. Our results strongly suggests the possibility to use physical agents such as magnetic or electromagnetic field, in support to chemotherapy to fight epithelial proliferation diseases, as well as all the diseases in which cells are characterized to a lower differentiation state.

Bioresonance in Regenerative Medicine

For bone remodeling field, it has been suggested that bone marrow-derived Mesenchymal stem cells (MSC) could be considered as a potential therapeutic tool. Using the Ca++-dependent specific differentiation potential of the ELF-MF 7 Hz ICR, we showed that exposure of human MSC to these same conditions of MF, enhanced expression of osteoblast differentiation markers such as alkaline phosphatase, osteocalcin, and osteopontin, as analyzed by real-time quantitative PCR, without affecting cell proliferation. As expected, while the differentiation marker factors were up regulated, the ICR electromagnetic field down-regulated osteoprotegerin gene expression, a critical regulator of postnatal skeletal development and homeostasis in

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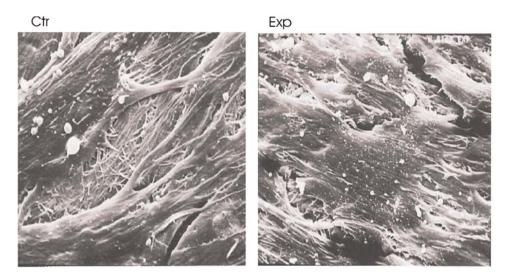


Figure 3. ICR exposure and bone marrow-derived Mesenchymal stem cells morphology Scansion electron microscopy of control and exposed 7 Hz ICR exposed human Mesenchymal cells.

humans as well as mice. Exposure to the ICR-tuned low-frequency electromagnetic field for five days resulted in changes in plasma membrane morphology (Figure 3).

Conclusions

Since the time of Galvani, evidence has accumulated indicating that living systems make useful use of electromagnetic field. The major particles that constitute the functional organization of living systems are associated with electromagnetic fields. Organisms might be considered aggregates of electromagnetic fields that are embedded within or correlated with atomic and molecular structures. Albeit electromagnetic medicine is still in its beginning, the evidence reported here, that ICR exposure can tune eucariotic cell towards cell differentiation and maturation influencing physiological processes, let us foresee a possible future application of electromagnetic protocols for the treatment of human deseases.

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