Evidences of regulatory and signalling role of electromagnetic fields in biological objects (review of literature and own studies)

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Abstract: There are growing evidence supporting the role of electromagnetic fields and interactions in biological processes. In this paper we're trying to theoretically substantiate the feasibility and necessity of the "Theory of Electromagnetic Biological Regulation and Signaling" **(TEBRS)** development. To support the idea we attempted to describe and systematize some existing data and own research experience from a perspective of the TEBRS.

Key-Words: - electromagnetic field, cell, viruses, antibodies, biological regulation, signalling.

1 Introduction

According to a known definition of Friedrich Engels, life is the mode of existence of protein bodies. It is necessary to note that "existence of protein bodies" implies a continuous process of most diverse interactions among protein (and not only protein) entities of all kinds. Any processes of development, differentiation, physiological reactions and pathological conditions imply presence of interaction, transmittance and recognition of signals at molecular, intracellular, intercellular, systemic and other levels. Successful and purposeful exploration of the mechanisms of such interactions requires knowledge of their nature, for example - correct understanding of the physical forces which mediate (or cause) the flow of nervous impulses through neuron branches and their transmission in the synapses, promote interaction of active sites of enzymes and their substrates, participate in the regulation of cellular membrane permeability, immune interactions and in many other vital activities.

Modern science is aware of only 4 types of interactions between objects, therefore, however complex and unusual activities and events are explored by investigator — one must always seek for action of one or several forces from this known set [1]:

1) Gravitational interaction;
2) Electromagnetic interaction;
3) Strong interaction (strong nuclear force);
4) Weak interaction (weak nuclear force).

Gravitational interactions between living organisms, their organs and biomolecules are negligibly small due to a known cause: the mass of the living organisms is too small for the Gravitational forces to have any significant effect. Since the range of nuclear interactions (Strong and Weak nuclear forces) does not exceed diameter of a medium sized atomic nucleus, such forces cannot play a role even in interactions between the smallest biomolecules. Therefore the only type of Fundamental Forces (interactions) able to participate in all of the vital activities is the Electromagnetic interactions. One can already find an abundance of supporting evidence for this fact in the modern science, for example – in the "Electromagnetic Biology and Medicine" journal. Nevertheless, scientific knowledge in this field is still incomplete and disembodied, therefore needs additional exploration. In the paper we attempted to summarize some current medical, biological data and own experience to support the Regulation and Signalling role of Electromagnetic fields in living systems. We believe that it will be helpful for development of a comprehensive "Theory of Electromagnetic Biological Regulation and Signalling" (**TEBRS**) in nearest future.

2 Evidences of electromagnetic forces participation in biological regulation.

Participation of electromagnetic interactions in various chemical and biological processes looks very natural and essential. Numerous interactions between biological molecules presuppose strictly specific spatial orientation of their reactive sites (e. g. antigenic site and corresponding antigen binding site of a specific immunoglobulin molecule) and sometimes – preliminary directed transport and approximation of the interacting molecules. It seems unlikely that such events occur exclusively thanks to chaotic Brownian motion. Dr. McCaig et al. fairly mentioned in their review that "electric fields are present in all developing and regenerating animal tissues, yet their existence and potential impact on tissue repair and development are

largely ignored. This is primarily due to ignorance of the phenomenon by most researchers, some technically poor early studies of the effects of applied fields on cells, and widespread misunderstanding of the fundamental concepts that underlie bioelectricity" [2].

2.1 Electromagnetic forces in Immunity

It is known that one of the most important and ancient system of the body is immune system, its role is to preserve the constancy of antigenic composition of the body by protecting it from mutated proteins and from invasion of foreign genetic information products. It was found that electrical charge of antigens and antigenically-active sites (antigenic determinants) of biomolecules significantly influence their immunogenicity: the most immunogenic are regions of a protein that have negative electrostatic potential [3]. Purposeful change of surface electric charge of antigens, for example, cationization - cause alteration of their immunogenic properties [4]. Moreover, a straightforward correlation has been found between the net electrical charge on a variety of natural and synthetic antigens and the type of antibody they elicited [5]. These facts clearly demonstrate the regulatory function of electric charges in immune recognition and immune response.

In our studies we showed possibility to increase immunogenicity of various antigens by regulated alteration of ionic composition of the antigen's surface. As a result of these studies "Method for enhancement the immunogenicity of antigens" was developed and patented [6]. The method allows to increase the immunogenicity of proteins, vaccines and other immunobiologicals.

2.1.1 Correlation between biological features of cells and their electrokinetic potential

There is a comprehensive review describing role of electromagnetic fields in vital activities of different types of cells [2]. Therefore in our paper we just shortly mention few aspects of this huge scientific field.

It is known that cell membrane potential plays an important role in cell activity and in signal transduction [7]. Especially sensitive to any "electrical signals" and changes in ion composition of environment must be cells having low membrane resting potential: for example, cancer cells. In these cells, even mild changes of transmembrane potential may cause substantial changes in membrane permeability and apoptosis [8]. Especially impressing are data demonstrating possibility of modification of cell genome expression pattern because of alterations in cell ion environment [9]. It is obvious that an inverse regulation also exists. The genetically determinated regulation of processes of ion membrane transport can explain experimental data which demonstrated that differences in electrophoretic mobility of immune cells are associated not only with the functional peculiarities of the cells, but also with their maturity stage. For example, the author has shown that mature T-cells from peripheral blood possess relatively high electrophoretic mobility, and the thymocytes at various stages of maturation are characterized by medium to low electrophoretic mobility, which is closer to the electrokinetic characteristics of B-cells. Most of the lymphocytes isolated from bone marrow also had low electrophoretic mobility [10]. H. Walter successfully separated "young" erythrocytes from "old" ones using differences in their surface charge and electrophoretic mobility [11].

The role of charged particles and electromagnetic forces in biological systems is not limited to various intracellular activities. It is obvious that electric forces are a very important mediator of intercellular and stromal-cellular relationships. Brief analysis of Glycocalix function would be enough to prove this thesis. The opinion exists that glycocalyx is an "executive apparatus, which mediates interaction of a cell with intercellular medium and neighbouring cells". In terms of Informatics, glycocalyx is needed for perception, recognition, transmission, and modulation of incoming and outgoing cell signals in the form of substance, energy, and information. Glycocalyx is formed from free fragments of plasmalemma's glycoproteins interconnected whith anionic-cationic movable bridges.

It was shown that surface charge of some immune cells changes during activation and immune response [12]. Besides, there are data implicating cell surface sialic acids and enzyme Neuraminidase as a potential modulators of immune cell interaction [13][14]. Pertinent mechanisms seems understandable. It is considered that many functions of glycocalyx are mediated via electric charge of its components and by changes of this charge. For example, glycocalyx inhibits non-specific, spontaneous adhesion of cells (particularly, blood cells). This happens because the glycoproteins of glycocalyx create negative charge on cell surface. And the like charges repel in accordance with law of physics. To a significant degree the electric charge of glycocalyx is caused by negatively charged residues of sialic acids. Desialisation of glycocalyx glycoproteins significantly weakens the mutual repelling force between the cells and facilitates their specific binding [15]. Interestingly, immune system actively uses the mechanism of changing the charge of glycocalyx as a regulator for specific intercellular contacts. For example, activation of

monocytes under influence of cytokines, such as interferon gamma or tumor necrosis factor (TNF-alpha), leads to desialisation of their glycocalyx molecules, particularly CD43 (leukosialin, or sialophorin) [16]. Removal of sialic acids, and, consequently, reduction of negative surface potential lead to decrease of electrostatic repulsion between cells and facilitated heterotypic adhesion of monocytes on various cells of a body. The authors supported the role of sialic acids in the regulation of adhesive properties of monocytes with the evidence that exposure of cells to neuraminidase or monoclonal antibodies against sialic acid-containing epitopes also increased the adhesive activity of monocytes.

In addition to the function described above, decrease of cell surface potential facilitates penetration of activated T-cells through vascular wall into the infection sites. Thus, alteration of cells surface potential has important functions in immune mechanisms.

2.1.2 Electric charge of antibodies and possible significance of this parameter

To further explore the role of electromagnetic forces in immune system function we performed a comparative study of electrokinetic potential of specific influenza antibodies and serum inhibitors of haemagglutination. It appeared that influenza anamnestic antibodies and antibodies that are produced in response to a current viral infection differ in their electrokinetic properties [17]. Functional role of this difference is still uncertain. However, the discovered peculiarity already opens new diagnostic opportunities. Particularly, we have shown that knowing the ratio between average population levels of negatively and positively charged specific serum antibodies to definite influenza antigens, it is possible to assess epidemic danger of a certain influenza virus strain for studied human population (e. g. for population of a city or a region) [18]. This approach has been successfully used for upcoming influenza epidemic strain prognostication for Odessa region of Ukraine in 1996-1998.

2.2 Correlation between Electrokinetic potential of virions and biological features of virus strains

Electromagnetic fields and surface potentials play a role not only in cells and "highly developed" organisms, but in viruses too. We have studied relationships between biological peculiarities of influenza viruses, their molecular biological structure and electrokinetic potential of virions [19]. It appeared that average electrokinetic characteristics of virions in virus population were closely correlated with the virus strain virulence, immunogenicity and capability to cause persistent infection [20]. It was shown that high relative contents of negatively charged virions in virus population often correlates with both: high immunogenicity of the virus and its ability to cause acute, quickly resolving infection in animals and humans. And vice versa: populations of persistent strains (causing prolonged, asymptomatic infection) contain high percentage of virions with positive surface potential. These results allowed developing of a method for rapid assessment of biological properties of new influenza strains and field isolates [21]. Possible reasons of the revealed correlation were suggested based on experimental data, peculiarities of flu virus structure and reproduction. In brief they are as follows:

A necessary prerequisite to successful and abundant influenza virus replication is high functional activity and sufficient amount of the major antigen Haemagglutinin (**HA**) on virus surface (the HA is responsible for attachment and internalization of virions to the host cells). In such conditions manifested, acute and quickly passing virus infection is highly probable. At the same time, the HA receptor-binding pocket binds not only cells, but also various small sialic acid-containing compounds which are negatively charged, hence, their binding adds negative charges to virion's surface. That is why negative charge of virions correlates with their high immunogenicity and definite type of infection (the acute infection) they can cause. And vice versa: positive surface potential of virions means low specific contents of HA in virions and/or low functional activity of the virus HA. This is accompanied by hindered attachment of virions to the host cells. As a result, virus reproduction and antigenic stimulation of the body are poorly manifested, and the infection itself becomes slow, up to formation of persistent infection [20][21]. This example shows possible functional regulatory role of electromagnetic forces in biological processes on population level.

3 Examples of practical usage of the TERBS Theory

Taking into account significant biological regulation potential of electromagnetic field our attempts to use it for treatment of different pathology looks absolutely appropriate. Indeed, electromagnetic fields have been used for therapeutic purposes for many decades. Numerous protocols utilizing physical fields of different characteristics for disease treatment are well known and constitute the Physiotherapy branch of Medicine. Therefore we'll just briefly mention below some of our elaborations in this field.

We have been studied mechanisms of biological effects of electromagnetic fields and possibilities for their therapeutic usage for 20 years. Positive effects of millimeter-range electromagnetic radiation with definite selected parameters (power and frequency) on cell immunity have been shown [22][23]. Treatment regimen for the millimeter range fields application in women before and after surgical operations for pretumor and tumor gynecological pathology has been elaborated [24] [25]. Efficacy of this approach was demonstrated in clinical study which enrolled 120 women with cervical dysplasia. Control group of the patients were subjected to standard cryotherapy of the cervical lesions, and two Study groups in addition to the cryotherapy obtained millimeter-range electromagnetic irradiation of different regions of the body. Shortening of the terms of total epithelisation of cervix uteri ($p<0,001$) and decrease of incidence of chronic adnexitis in postoperative period were statistically significant in both Study groups in comparison with Control Group [26].

Biological effects of magnetic (including geomagnetic) fields has been studied [27][28]. These studies resulted in elaboration of several protocols and devices for magnetotherapy of inflammatory and other diseases of woman's reproductive system [29][30].

4 Conclusion

Electromagnetic fields and interactions participate in regulation of numerous biological processes. Further exploration of direct and indirect mechanisms for participation of electromagnetic interactions in various biological activities is feasible and may yield many interesting results both: of theoretical and clinical significance.

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