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BIOLOGICAL EFFECTS OF ELECTROMAGNETIC FIELDS

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1. Introduction

Molecular biology today appears to be the mainstream interpretative basis for all cellular and pathophysiological phenomena, even going so far as to embrace neuronal and psychic events. The explanation o disease processes, whether genetic or acquired, is sought and, where possible, located in mechanisms consisting in quantitative and/or qualitative modifications of particular molecules making up part of the various anatomical or physiological systems. In relation with the molecular paradigm of disease, also the medical treatment is today founded mostly on the conventional pharmacological approach. However, the need of further research in different fields is suggested by the fact that biological phenomena are characterized by high levels of organization, that many experimental data suggest to be due forms of inter-molecular and inter-cellular communications of biophysical nature. As suggested by Kroy [Kroy, 1989], in the living creatures there is an ancestral cybernetic order that is not based on the nervous system or on the humoral system (blood, hormones). This ancestral system is thought to be of an electromagnetic nature, because electromagnetic radiation is the most basic form of information present in nature. Electromagnetic signals have constituted (and still constitute) both the language of communication between atoms and molecules and the means whereby primordial organisms received a series of items of information on the environment (sunlight, other cosmic waves). There can thus be no doubt that living organisms have learnt to use electromagnetism as an information signalling system and thus as a means of communication between cells and tissues. According to the studies by Popp and coworkers [Popp, 1985; Popp *et al.*, 1989; Ho and Popp, 1994], many biological systems are capable of producing, receiving and even of "storing" electromagnetic waves such as light.

Moreover, considering most of major health problems such as neoplastic, degenerative, autoimmune, endocrine-metabolic, and neuropsychiatric diseases, it should be noted that they are not due to single modifications of specific genes/molecules, but often to subtle and minor changes of genetic predisposition to disease, which in turn react with a multiplicity of environmental factors to determine the final risk to develop disease and symptoms. Therefore, the understanding of the *organization* of the systems regulating these *interactions* is needed in order to properly deal with these diesases. The pursuit of a unitary approach, capable of assuring a multidisciplinary synthesis and of defining the nature of disease processes at higher levels of organization, is proving increasingly difficult using the molecular paradigm. In practice, though not in principle, the ongoing accumulation of notions and data proves inadequate as a means of furthering our understanding complex vital phenomena and thus of the phenomena relating to health and disease.

In this context, the emerging *bioelectromagnetic* paradigm will play an important role because it re-evaluates an important form of long-range communication not only at inter-molecular but also at supra-molecular levels of organization of biological systems. Moreover, a biophysical paradigm is necessary in order to develop working models and hypotheses explaining the possible effect of highly diluted remedies, often used by homeopathic doctors at dilutions far beyond the Avogadro number. There is still no exhaustive explanation of how a transfer of information from such remedies to the body can take place, but, if the problem is couched in physical and not merely in chemical terms, it is very likely that any such explanation must necessarily take account of sensitivity of living systems to small energies like those carried by electromagnetic fields.

The study of the effects of electromagnetic fields in the body has come to take on increasing importance and scientific dignity in recent years, while at the same time that aura of mystery which has favored the exploitation of such phenomena by charlatans has steadily declined. The renewed interest in interactions between electromagnetic fields and living systems consist in various factors, including the folofing: a) evidence has been building up regarding the efficacy of extremely-low-frequency (ELF) pulsed magnetic fields in therapy, and most notably in orthopedics; b) from the standpoint of public health, there is a heightened awareness of the risks associated with technological development and thus also with exposure to electromagnetic fields generated, for instance, by high-tension electrical power lines, video terminals, diagnostic equipment, household electrical appliances, and other sources; c) the topic is being tackled increasingly in experimental terms with studies on cell and molecular models, with the result that a number of possible explanations of the biological effects of low-energy magnetic fields are beginning to emerge.

These matters will be briefly illustrated here below, as a contribution to a better understanding of the emerging biophysical paradigm in medicine and thus of the possible relationship between electromagnetic phenomena and homeopathy. We feel we should stress that our discussion of these issues lays no claim to being in any way systematic, but rather constitutes an attempt to compare in outline and put into perspective many different problems and phenomena which are sill largely unclear from the scientific point of view.

2. Electromagnetic fields

For the purposes of making it easier to understand the basic concepts used in bioelectromagnetism and the experimental evidence reported here below, we will briefly explain the terminology and the measurement units used. A diagram illustrating the various types of electromagnetic waves, together with their wavelengths and frequencies is given in Figure 1.

Fig. 1. Electromagnetic radiations of various wavelengths and frequencies.

The frequency of an electromagnetic field is the number of cycles per second of the electromagnetic wave, or the number of pulsations of the field itself per second and is measured in Hertz (Hz). The wavelength (●) is the distance between two wave peaks and is measured in meters (or in multiples of submultiples of a meter). Obviously, the higher the frequency, the lower will be the wavelength.

Electromagnetic waves are used, as is known in the case of telecommunications, as *information vectors*. For this purpose a *carrier* wave is used with a frequency selected in a very broad range according to the transmission and reception systems. This carrier wave is specifically *modulated* in relation to the information to be conveyed, i.e. its length and height are subtly altered and can be slightly increased or reduced to a variable extent over time (frequency and amplitude modulation, respectively). In this way, a piece of equipment *tuned* to the carrier wave can perceive the modulation and, after decoding it, the information contained in it.

The *intensity* of the electrical field is provided by the electric potential over a given distance and is expressed in volts/meter (V/m) or millivolts/centimeter (mV/cm). When a biological system is exposed to an electrical field, the mobile charges shift in the direction induced by the field itself, thus forming a *current*, which is measured in amps (A) or in submultiples of an amp. With reference to a certain area of tissue or organ traversed by electrical charges, there will be a certain density (J) of the current itself, which is measured in amps/square meter (A/m^2) or in mA/cm^2.

The electric field and the magnetic field are closely related according to Faraday's law of induction. When a pulsed magnetic field is applied to an electrically conducting material (such as living matter), an electric field is introduced perpendicular to the direction (vector) of the magnetic field. This electric field obviously depends on the surface of the area concerned and is proportional in intensity to the frequency of the magnetic field and its intensity.

The intensity of the magnetic field is measured in Gauss (G) or, to use the more modern SI unit, in tesla (T) or submultiples of a tesla ($1\ T = 10^4\ G$). To have two terms of comparison, the intensity of the earth's magnetic field is of the order of 0.02 to 0.07 mT (0.2 to 0.7 G), whereas that used in diagnostics by magnetic resonance is of the order of 0.1 to 10 mT (1 to 100 G) [Walleczek, 1992].

3. Effects on the organism

We intend here to examine low-energy, low-frequency radiation, which acts with very different mechanisms compared to ionizing radiation. The latter causes biological effects through ionization (detachment of electrons from the atomic orbits) of the molecules and thus gross alterations such as damage to chromosomes, peroxidation of lipid membranes, and so on. In contrast, the energy of radiation with frequencies from 0 to a few hundred GHz is too low to cause physicochemical changes of this type and at most is able to yield thermal effects (heating, used, amongst other things, in the functioning of microwave ovens).

The effects of non-ionizing electromagnetic fields on the human body may be both of a pathological type and useful for therapeutic purposes. As regards the damaging effects most commonly studied, we have to refer essentially to studies which appear to demonstrate an increase in tumors in exposed subjects [Pool, 1990]. The topic is much debated and the epidemiological data have been confirmed only with regard to a number of childhood tumors (leukemias). As regards the uses for therapeutic purposes, the techniques most extensively employed are electromagnetic stimulation of osteogenesis, in cases of pseudoarthrosis and retardation of fracture consolidation [Chiabrera *et al.*, 1984]. This is not the place for a detailed review of the pathological or therapeutic effects of electromagnetic fields, this today being an area of major development, and so we will confine ourselves to outlining the basic molecular and cellular aspects.

There are many natural sources of weak electromagnetic fields: sources outside the body include, for instance, the earth's magnetic field (which is exploited by a number of birds, fish and dolphins for direction-finding), signals from the earth's ionosphere (Schumann waves at 7.8 Hz that are related to the accuracy of biological rhythms [...]), radiation from the stars which emit radiofrequencies, the sun itself (particularly in certain phases of its activity) [Konig, 1989], the waves irradiated by telecommunications and radar systems, and electrical power lines. The sources inside the body are multiple and range from the electrical activity of the brain (e.g. hyppocampus at 7.8 Hz), the nerves and muscles to the electric fields generated by a number of fish and other marine organisms (used for the purposes of recognition in the dark and for defense), to the generation of light by cells such as leukocytes (chemiluminescence).

Practically all organisms emit light at a rate from few photons per cell per day to several hundred photons per organism per second. This emission of "biophotons", as they are called, is distinct from chemiluminescence of leukocytes and of bioluminescence of fireflies, that is associated with specific organelles. Biophoton emission occurs at very low intensity but is universal to living organisms, where is thought to represent a long-range form of communication, capable of generating synchronous and coherent phenomena [for a review, see Ho and Popp, 1994]. The most intriguing findings on bioluminescence (see "*Biophoton theory*") are discussed in the contribution by Bischof in this volume.

The electrocardiogram and electroencephalogram are no more than two methods of measuring the endogenous electrical activity of the heart and the nerve centres. Electrical activity is also generated in bone when it is deformed; such activity can be defined as piezoelectric and appears to be important for directing the growth of bone trabeculae along lines of force. In actual fact, one of the first clinical uses of weak magnetic fields was precisely the induction of bone repair [Bassett *et al*., 1974].

Animal organisms have developed very marked sensitivity to electromagnetic waves. Without going beyond the most obvious field, we need only mention the sensitivity of the eye to light, which makes it capable of perceiving only a few photons.

The experiments by Smith and Monro [Smith *et al*., 1985; Monro, 1987; Smith, 1988; Smith, 1989; Smith, 1994; see also the contribution of Smith in this volume] illustrate the concept of "sensitivity" to minimal perturbations of electromagnetic fields. These investigators (Smith works in the Department of Electronic and Electrical Engineering of the University of Salford) have reported a series of experiments performed in collaboration with allergologists from Hospitals in London and Dallas, in which they succeeded in inducing allergic manifestations in patients with immediate hypersensitivity to many substances, simply by bringing them into close contact with sources of electromagnetic radiation. The allergic manifestations could set in rapidly at particular frequency bands ranging, according to the individual patients, from only a few mHz to a large number of MHz. It was not, then, so much the intensity of output of the oscillator (a few V/m) that was important as the *frequency* and *coherence*.

It is not only curious that these investigators demonstrated the ability to trigger allergic attacks with electromagnetic waves, but also that the patients sensitive to this type of stimulation themselves produced electromagnetic signals during the allergy attacks, though the latter were provoked chemically. For details, see the contribution "X" by Smith in this volume and [...], referenced to in the contribution "X" by....

It has been demonstrated that a number of species of fish are capable of perceiving and responding to electric fields with intensities as low as 0.000001 V/m [Bullock, 1977], which corresponds to the most marked sensitivities found in allergic subjects. Again according to Smith, such sensitivities may enable the fish to locate food at great distances: it has been seen, in fact, that living cells, such as, for instance, yeasts, emit electromagnetic waves in radiofrequencies at levels of approximately 0.1 V/m [Smith, 1988; Pollock and Pohl, 1988].

In the course of the allergometric tests in the sample of hyperreactive patients, the researchers realized that allergic reactions triggered by contact with chemical agents could be neutralized by treating the patients with particular frequencies. If the same frequencies were used to treat pure water, the latter acquired the neutralizing therapeutic properties. If, on the other hand, the water was exposed to frequencies capable of triggering the attack, it acquired the properties of an allergen. For respective experiments with amphibia, see X...

The treatment of the water was done by inserting glass test tubes containing the water in solenoids or thoroids powered by an oscillator. The changes induced in the water, capable of triggering allergic attacks in hypersensitive patients, persisted for 1-2 months. Incidentally, at this point it is interesting to note that the stability of the homeopathic remedy in aqueous solution is traditionally short-lived, of the order of months, whereas since Hahnemann in homeopathy water-alcohol solutions are used precisely because they were much more stable and long-lasting (years).

Quite apart from the fact that only a minority of allergic patients exhibited this extreme sensitivity and were suitable for the execution of such tests, the demonstration of the ability of water to incorporate electromagnetic information and transmit it to individuals reactive to it remains, if independently repeatable, of great interest and significance. The respective multicenter esperiments of Endler *et al.* are described in detail in this book (X). In this study, amphibian larvae were exposed to thyroxine dilutions prepared according to a homeopathic protocol, whereby the liquid (as well as water control) were sealed in glassa ampoules that were brought into the basin water containing the animals. Highly significant effects on the metamorphosis rate, similar to those of the liquid added directly dropwise to the water, were observed. The authors also report findings on molecular information transferred by an electronic device or stored on a data carrier. This seems to be a valid argument in favor of the effective existence of metamolecular information and its presence in aqueous fluids.

4. Cellular effects

It is well known that electromagnetic radiation can cause substantial changes at cellular level, but the bulk of attention, up until not very long ago, was devoted to the potentially toxic effects of medium-to-high energy radiation, such as X-, gamma- and ultraviolet ray. As mentioned above, investigations into the mechanisms of the biological effects of nonionizing radiation have recently begun (see Figure 1).

Electromagnetic waves, even if of low energy and broad wavelength, are known to generate heat, when absorbed by biological matter. The question whether millimetric waves cause effects independent of absorption of heat, i.e. so-called nonthermal effects, has been the subject of lengthy scientific debate. The controversy regarding the existence of cell responses to low-energy waves is due both to the fact that the reproducibility of many experiments has proven difficult, and to theoretical objections that the energy of such weak fields would be less than the energy of the background noise due to the temperature at which the cells are studied (*thermal noise*). If we are to expect an effect of an electromagnetic field applied from the outside, this field will have to cause significantly greater changes than would in any event occur casually in biological systems even in the resting state (e.g. the continual opening and closing of ion channels, oscillations in membrane potentials and in many metabolic activities, etc., all these being processes which are in any event active at a certain temperature). Today, however, the existence of nonthermal effects of weak electromagnetic fields has been demonstrated in many experimental systems and may now be regarded as generally accepted [Kremer *et al*., 1988; Aldrich and Easterly, 1987; Magnavita, 1989; Tsong, 1989].

A major contribution to this issue can be found in a critical study published in *Science* [Weaver and Astumian, 1990]. These authors propose physical models according to which the cells are considered as detectors of very weak periodic magnetic fields and where the relationships between the size of the cell and the changes in membrane potential due both to temperature-induced fluctuations and to the application of electromagnetic fields are established. In the simplest version of the model, the calculation estimates at around 10^{-3} volts/cm the intensity of the minimum field to which the membrane macromolecules could be sensitive. However, if the model parameters considered take into account the so-called frequency "windows", i.e. the possibility that certain responses occur only within a restricted frequency band, then the theoretical intensity necessarily proves to be several orders of magnitude lower (10^{-6} volts/cm), thus closely approaching the data from various experiments in cells and animals.

The growth of the nerve processes is guided by weak electric currents [Alberts *et al.*, 1989]. When a nerve process lengthens in culture or even in connective tissue, at its apex a structure called a growth cone is formed, which appears as the expansion center of many long filaments (filopods) which look like continually slow-moving finger-like processes, making ameboid movements: some retract, and others stretch out, as if exploring the terrain. Within the filopods many actin filaments are to be found. The net vectorial shift of the growth cone in one direction is followed by a lengthening of the nerve fiber (at an estimated rate of 1 mm per day). The direction of the movement depends on various local factors, such as, for instance, the orientation of the fibers of the connective tissue matrix, along which the growth preferentially occurs, and even the existence of specific membrane recognition systems between adjacent cells. The cells, however, are also powerfully influenced by electromagnetic fields: the growth cones of neurons in culture are oriented and direct themselves towards a negative electrode in the presence of low-intensity fields (70 mV/cm).

The cells have an ability to receive and integrate light signals, perceiving both their frequency and direction. This has been demonstrated by means of special phase-contrast microscopy equipment with infra-red light [Albrecht-Buehler, 1991]. 3T3 fibroblasts in culture extend the filopods preferentially towards light sources, the most effective being the intermittent ones in the 800-900 nm range with 30-60 impulses per minute. According to the author of these experiments, the cell receptor for the radiation is the centrosome.

There is also evidence that cell proliferative activity is influenced by electromagnetic fields, albeit of very low intensity (0.2-20 mT, 0.02-1.0 mV/cm) [Luben *et al.*, 1982; Conti *et al.*, 1983; Cadossi *et al.*, 1992; Walleczek, 1992].

It is important to note that on the basis of the literature data available to date it is impossible to draw any definite conclusions as to the positive or negative, stimulatory or inhibitory effects of weak electromagnetic fields on cellular or molecular systems and above all as to doses and application modalities [Walleczek, 1992]. In fact, the bioactive electromagnetic signals used vary very considerably in terms of intensity, frequency, duration, and waveform (sinusoidal, square, sawtooth, etc.). Moreover, the effect may also depend on the biological status of the cells exposed

[Cossarizza *et al*., 1989; Walleczek and Liburdy, 1990], indicating that mechanisms of very complex interaction between various different factors are involved.

Many enzymes and receptors appear to be sensitive to stimulations of a physical as well as a chemical type [Adey, 1988; Tsong, 1989; Popp *et al*., 1989]. The cell membrane, by virtue of its bioelectrical properties, is the site where influences of this type are most likely to be exerted [Kell, 1988], though other possible candidates are the large macromolecules organized in repetitive units, such as the nucleic acids [Popp, 1985], or the proteins of the cytoskeleton, particularly the microtubules [Hameroff, 1988].

The biological basis of the effect of magnetic fields on cells is highly complex and cannot be analyzed exhaustively here. The cell constitutes a typical electrochemical system, with a transmembrane potential difference (negative outside compared to inside) and a very large number of proteins endowed with electric charges of varying sign. According to the fluid mosaic model of the membrane (a model which is still valid, at least in general terms) in an ideal cell at rest, the proteins are distributed evenly over the membrane, but, in the presence of an electric field crossing the membrane, they undergo electrophoretic attraction or repulsion, tending to shift towards the poles which the cell presents in the direction of the electric field. A current of electrons or ions invading a cell flows around it, causing a movement of (electrically charged) proteins in the opposite direction.

The rearrangement of the position of the proteins on the surface of the membrane is not devoid of consequences, in that it favors contact between neighboring proteins and slows down contact between distant proteins [Chiabrera *et al*., 1984]. Since the functioning of receptors and membrane transduction systems depends on aggregations of proteins or at least on contacts between proteins, the consequences of the electric field for cell activation are easily imaginable. The aggregation phenomenon normally occurs in the case of a chemical signal, because the signal molecule may serve as a bridge between two or more receptors, which are mobile in the plane of the membrane. Of course, this model is a very substantial simplification of what happens in reality, where the concentrations of calcium, magnesium, sodium, potassium and hydrogen ions come into play, as well as the possible direct effect of the magnetic field on the macromolecules of enzymes, receptors or the cytoskeleton.

Across the double lipid layer of the biological membranes, measuring approximately 40 Å in thickness, an electrical gradient of a few tens or hundreds of mV is established, which means something like 10^5 volts/cm. Theoretically this gradient should constitute an effective electrical barrier against minimal perturbations such as those created by low-frequency electromagnetic fields present in the extracellular membrane. In other words, the natural electrical activity of the membrane would constitute a kind of "background noise" which would prevent the possibility of perceiving minimal variations in potential. Very recent research, however, has shown that electromagnetic fields various orders of magnitude weaker than the transmembrane potential gradient are capable of modulating the actions of hormones, antibodies and neurotransmitters at receptor and transduction system level. This suggests that *highly cooperative processes* are set up, i.e. that repeated minimal variations cooperate to cause major movements. It is an effect similar to that which occurs when a bridge starts to oscillate whenever a body of men cross over it at marching pace, or when a glass breaks as a result of resonance.

The sensitivities observed in these biological processes of electromagnetic modulation are of the order of 10^{-7} volts/cm in the E.L.F. (extreme low frequency) range. Note, for example, that electric phenomena responsible for the EEG create gradients of 10^{-1} to 10^{-2} volts/cm [Adey, 1988]. Moreover, many of these interactions depend on the frequency, i.e. they occur only in certain *windows of frequency*, which would suggest the existence of *nonlinear* regulation systems far from equilibrium [Adey, 1988; Weaver and Astumian, 1990; Yost and Liburdy, 1992]. Similar sensitivities have been detected in a broad spectrum of tissues and cells, indicating that we are faced with a general biological property characteristic of cells. Furthermore, also *windows of the intensity* of the field are postulated.

5. Molecular effects

It is known that many molecular elements with receptor, structural and enzymatic functions are sensitive to changes in weak electromagnetic fields: photoreceptors [Alberts *et al.,* 1989], chlorophyll [Alberts *et al.*, 1989], receptors with 7 trans-membrane domains [Bistolfi, 1989], G-proteins [Adey, 1988], cAMP-dependent protein kinase [Byus *et al.*, 1984], protein kinase C [Adey, 1988], lysozyme [Shaya and Smith, 1977], receptors (aggregation) [Chiabrera, 1984], chromosomes [Kremer *et al.*, 1988], protein and lipid biopolymers [Hasted, 1988], Na^+/K^+ ATPase [Liu *et al.*, 1990]. Experimental data regarding these molecular systems will be detailed below.

Most protein molecules are capable of passing reversibly from one conformational state to another by virtue of various possible combinations of hydrogen bonds, disulfide bridges and hydrophobic forces. These passages occur by means of nonlinear changes, or hopping, to overcome the energy barriers between one state and another. The proteins are thus dynamic, vibrating structures whose components undergo continual oscillatory movements, which take place over a time scale ranging from femtoseconds (10^{-15} s) to several minutes. The most significant vibrations in biological systems are of the order of nanoseconds [Hameroff, 1988]. It is very important to stress the fact that, in biology, many proteins (and also other chemical species such as lipids) are assembled in multimeric or polymeric groups. In these structures, cooperative, or collective, interactions easily occur, with the result that the vibrations may propagate themselves in *coherent* ways and, as such, may take on a biological-informational significance [Frohlich, 1988; Del Giudice *et al.*, 1988b; Bistolfi, 1989; Ludwig, 1994; X].

The transfer of both chemical and electromagnetic signals from the external surface of the cell across the membrane consists in the transmission of conformational variations and oscillatory motions of proteins which have transmembrane domains (segments of the molecule). It has been claimed that a key role in this transmission is played by portions of proteins that have helical or folded-sheet-shaped fibrous structures [Bistolfi, 1989; Meissmer, cited from Ludwig, 1994, X...]. Such structures are characterized by a substantial degree of order and by arrangement in repetitive sequences, as well as by the existence of hydrogen bonds between the amine residues of adjacent amino acids arranged longitudinally along the fiber. These protein structures are characteristic in their ability to *resound* according to nonlinear modes of vibration as a result of interaction with electromagnetic fields.

The prototype of this type of receptor is rhodopsin, the light receptor in the retina, which consists of 7 ♋-helixes arranged in orderly fashion transverse to the plane of the membrane on which it is situated. In this type of receptor-transducer, the excitation resulting from absorption of the photon is linked to the pumping of a proton and to the stabilization of a transmembrane potential.

It should be noted, however, that this structure with 7 ♋-helixes crossing the membrane is also found in an extensive family of glycoproteins involved in cell transmission systems coupled to G-proteins: the ♌-adrenergic receptors, the muscarinic receptors for acetylcholine, various receptors for neuropeptides, the receptors for chemotactic peptides in the white blood cells and even the mutual recognition systems in yeast cells involved in replicative fusion [Alberts *et al.*, 1989]. It is therefore likely that these characteristic structural features render the transmission systems they are present in susceptible to electromagnetic modulation.

Studies conducted on electromagnetic modulation of collagen production by osteoblasts are consistent with this view. It has been demonstrated, in fact, that parathyroid hormone in osteoblasts binds to external receptors and activates the enzyme adenylate cyclase via the mediation of a G-protein. An electromagnetic field with a 72 Hz frequency and an electrical gradient of 1.3 mV/cm induced 90% inhibition of adenylate cyclase activation without interfering either with the receptor binding or with the enzyme itself. As a result, the inhibitory effect was attributed to blockade of the G-protein [Adey, 1988].

Cyclic AMP (cAMP) is an important element in controlling the function of many enzymes, particularly insofar as an intracellular increase in cAMP constitutes an activatory message for the protein kinases (enzymes which phosphorylate proteins). In precise experimental conditions of frequency and duration of exposure, the cAMP-dependent protein kinase of human lymphocytes has been inhibited by electromagnetic waves (field of 450 MHz modulated in amplitude to 16 Hz). Type C protein kinase, the involvement of which in important cell processes as well as in carcinogenesis is beyond doubt, can also be modulated by electromagnetic waves [data from Byus, cited in Adey, 1988].

The catalytic activity of the enzyme lysozyme is sensitive to electromagnetic waves (radiofrequencies from 0.1 to 150 MHz) [Shaya and Smith, 1977]. In these experiments, solutions of lysozyme were exposed, in the presence of submaximal doses of the competitive inhibitor n-acetyl glucosamine (NAG), to various electromagnetic frequencies supplied by an oscillator by means of a coil wrapped around a polycarbonate container of the enzyme solution. The main effect observed was a modification of the inhibition produced by NAG. Interestingly, specific frequencies (e.g. 40 MHz) increased the effect of the inhibitor, and other frequencies (e.g. 100 MHz) decreased the effect, enhancing the activity to the level of the uninhibited lysozyme, while yet other frequencies (e.g. 150 MHz) had no effect. Inspection of the whole range of frequencies between 0.1 and 150 MHz showed alternating peaks of stimulation and inhibition of the enzyme activity, without any apparent regularity. Subsequent measurements between 30 MHz and 50 MHz showed further fine details in the effects produced. Therefore, the relationship between frequency and activity appears to show a chaotic trend and fractal behavior.

According to Tsong and coworkers [Tsong, 1989; Liu *et al.*, 1990], the conventionally known forms of intercellular communication, such as ligand-receptor interaction, are slow processes operating over short distances, but cells also need rapid forms of communication over long distances, with the result that it has been postulated that the various biochemical reactions, which are in any event necessary, are regulated by forces of a physical nature. Given that oscillating weak electromagnetic fields are capable of stimulating or suppressing many cell functions and that, from the thermodynamic point of view, this is possible only if mechanisms of amplification of the signal exist, it is postulated that the cell membrane is an amplification site.

The experiments carried out be Tsong's team indicate that a weak electric field (20 V/cm) is capable of activating the function of Na^+/K^+-dependent ATPase only if specific frequencies are simultaneously used, corresponding to 1 kHz for the pumping of K^+ and 1 MHz for the pumping of

Na^+. These results have led to the formulation of the concept of “electroconformational coupling”. This model postulates that an enzymatic protein undergoes conformational changes as a result of a Coulomb interaction with an electric field (or with any other oscillating force field with which the protein can interact). When the frequency of the electric field corresponds to the characteristic kinetics of the conformational transformation reaction, a phenomenological oscillation is induced between different conformations of the enzyme. At the optimal field force, the conformations thus achieved are functional and the oscillations are utilized to perform the activity required, such as, for example, the pumping of Na^+ and K^+.

The organization of DNA in the chromosomes is affected by influences of an electromagnetic nature, as demonstrated in an extensive series of studies by Kremer and his coworkers [Kremer *et al.*, 1988]. These authors used the model provided by giant chromosomes of insects (larvae of *Acricotopus lucidus*), which are easily visible and can be studied under the microscope. It is well known that when information has to be transcribed from DNA to RNA, the chromosomes (compact rods containing thousands of genes packed and stabilized by istonic proteins) have to partially decondense, showing puffs of genetic material issuing from the rod in the relevant segment. This phenomenon is strongly and significantly inhibited - in the sense that the puffs are much smaller - by irradiation of the chromosome with frequencies of around 40 to 80 GHz and outputs of only 6 mW/cm^2. The nonthermal nature of the phenomenon has been demonstrated by many control experiments. It is worth pointing out that even DNA and RNA are characterized by a macromolecular organization that is extremely rich of hydrogen bonds, connecting complementary nucleotide pairs, a structure that makes them good candidate for resonating events.

In this quite recent field of investigation, many points remain still to be clarified and any conclusion, particularly in the field of therapeutical applications, should be regarded as hypothetical and preliminary. However, present knowledge allows us to suggest that this kind of ordered communication network of biophysical nature, coupled with the well known high sensitivity of complex and chaotic systems to small perturbations, could be a physiological substrate of the the interaction between the body and the information carried by low-doses or high-dilutions of pharmacologically active compounds and conceivably by low-energy electromagnetic fields.

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