

Comparison Between Two Models for Interactions Between Electric and Magnetic Fields and Proteins in Cell Membranes

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Abstract

Investigations on exposure to electromagnetic have generated conflicting results both in epidemiological and laboratory studies, leaving their possible health consequences largely inconclusive. One of the well-reported reasons for the discrepancies is that there is no generally accepted theory to describe the interactions between the very weak electromagnetic fields and the living cells. This work presents a critical evaluation of three theories that describes the effects of weak electromagnetic fields on channel proteins in the cell membrane. The forced ion vibration model appears to explain the opening of ion channel proteins for exposures to low-frequency magnetic fields in the mili-Tesla range. No resonance frequencies or amplitude window effects are predicted in this method. We identify inconsistencies in the forced vibration model and show that the environmental magnetic fields that would be required to elicit opening of channel proteins are much stronger than predicted by the proposers of this model. The Ion Parametric Resonance model predicts a biological response at well-defined resonance frequencies for magnetic fields exceeding about 10 micro-Tesla. The oscillating magnetic field is assumed to act on proteins together with the earth's static magnetic field. This model predicts amplitude windows. We explain how a purely magnetic interaction, where in a two-stage ion magnetic resonance model, the conformation of a protein is changed under the influence of ions attached to its surface, which in turn, changes the function of the protein, can overcome the inherent signal-to-noise problem caused by electric thermal noise. The hydrogen nuclear polarization model predicts a biological response for oscillating magnetic field strengths above 0.1 micro-Tesla. The presence of a static magnetic field is required, and biological effects can be expected for frequencies below a few hundred hertz. All models except the forced vibration model can be applied for amplitude modulated microwaves.

Key words: electromagnetic field (EMF) exposure; Mobile Phones; Base Stations; High Voltage Power Lines; Interaction Models; Biological Effects

Introduction

STATIC MAGNETIC AND ELECTRIC FIELDS occur naturally; time-varying fields, however, do not. These man-made fields have health consequences remains a matter of debate. The question whether extremely weak and low frequency (50 or 60 Hz) magnetic and electric fields can interact with the living cell is highly controversial. Over 11,000 scientific articles have been devoted to this subject (Liboff, 2003; Belova *et al.*, 2007). Many have reported an influence on organisms, but conversly, many others were unable to find such an association. Most biological studies were not intended to clarify how these weak fields can interact with biological molecules; rather, environmental frequencies and unrealistically high

amplitudes were used for exposure (Falone *et al.*, 2007; Rodriguez *et al.*, 2008). A crucial problem that any interaction model must deal with is how a large enough signal-to-noise ratio ($S/N > 1$) can be obtained to enable the living cell to detect the signal. For strong signals (> 1 mT), how the biological effects are obtained is well understood. For example, strong microwave radiation will heat body tissue, mainly by setting water dipoles into rotation, and strong low-frequency electric or magnetic fields will induce electric currents in the body that lead to nerve excitation. On the other hand, for extremely weak electromagnetic fields ($\ll 100 \mu\text{T}$) there is no generally accepted theory that can explain all the biological effects reported in the literature. Early experimental data (Bauréus *et al.*, 2003) indicate that the transport of calcium ions over the cell membrane can be influenced by amplitude-modulated RF electromagnetic fields and low-frequency electric and magnetic fields. Calcium is an important signaling substance in the living cell, and a disturbance of the calcium balance in the cell might interfere with many functions of the cell. It is

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therefore believed that the cell membrane is an important site of interaction for electromagnetic fields. As the use of wireless communications is expanding, with one-fourth of the earth's population owning a mobile phone and the use of wireless networks increasing explosively, it should be considered whether proposed theoretical models that aim to explain the interaction between low frequency magnetic fields and biological matter, might also be applicable to amplitude modulated radiofrequency electromagnetic radiation. Some theoretical models, are discussed below, with special emphasis on the ability to modify the function of proteins in cell membrane.

Forced Vibration of Free Ions Near the Cell Membrane

The cell is the smallest unit of living organisms, also called the building block of life. Human organisms are multicellular with approximately 10^{14} cells, each with a typical size of $10\ \mu\text{m}$. A plasma membrane, also called cell membrane, covers each of these cells. There are free ions (ions that can move across the membrane), such as K^+ , Na^+ , Cl^- and Ca^{++} , on both sides of every cell membrane, but in different concentrations. These ions control the cell volume, help the signaling process, and create a strong electric field between both sides of the cell membrane (Panagopoulos *et al.*, 2000). The cell membrane contains ion channel proteins, the opening of which can be regulated by the transmembrane voltage, mechanical stress (mechanically gated channels gated by ion pressure) of chemical signals. The basic mechanism proposed by Panagopoulos *et al.* (2002, 2003) is the forced vibration of all the free ions on the outer surface of a cell membrane, caused by an oscillating electric field. It is shown by them (Panagopoulos *et al.*, 2002) that this vibration of electric charge is able to irregularly gate voltage-gated channels in the plasma membrane, and thus disrupt the cell's electrochemical balance and function. An oscillating external electric field will exert an oscillating force on the free ions on the outside of the cell and in the channel of the protein. The inside of the cell is considered to be at least partially shielded from the external field by the free ion layer illustrated in Fig. 1. Once the amplitude of the ions' forced vibration exceeds some critical value, the oscillating ions will give a false signal to the channel protein's

voltage sensor for opening or closing the channel. Three forces are considered that influence each ion's movement: (1) an alternating force due to an external, alternating electric field, which will displace the ion; (2) a damping force, because the ion moves in a viscous medium. This force is proportional to the velocity of the ion; (3) a restoration force due to a slight distortion of the ion's equilibrium. This force is proportional to the displacement of the ion.

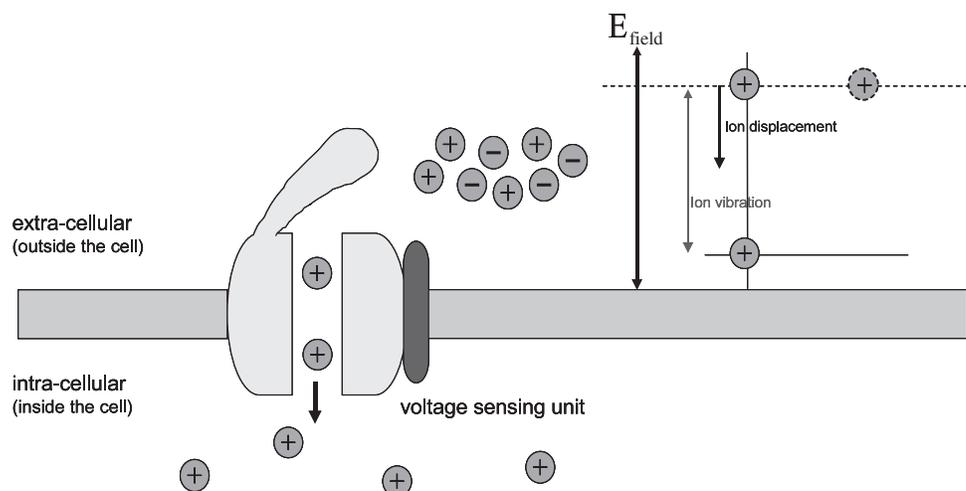
The ion, because of the above forces, will be accelerated and displaced. The movement equation of a free ion in the vicinity of a cell's plasma membrane under the influence of an external, alternating electric field constitutes a second order linear equation. Panagopoulos *et al.* (2002) show that the ion is displaced initially during the onset of the continuous signal and vibrates about the displaced location with an amplitude that is inversely proportional to the frequency of the applied field, and at the same phase as the applied field as in Figs. 1 and 2.

It is known that changes in the transmembrane voltage of about 30 mV are able to gate electrosensitive channels. It is shown Panagopoulos *et al.*, (2002) that a displacement of about $10^{-12}\ \text{m}$ can generate a force on the voltage sensor equal to that generated by a change of 30 mV in the transmembrane potential. From this we can derive the demand on the strength of the applied electric field as a function of the frequency of the field (Fig. 2). From the figure it can be estimated that an internal electric field at 50 Hz of at least 10 mV/m in the body is needed to influence channel proteins. Internal electric fields in the body can result from exposure to strong electric fields or be induced by exposure to time varying magnetic fields.

According to (Panagopoulos *et al.*, 2002), external electric fields acting on the human body in the order of 1,000 kV/m, or more realistically, magnetic fields well above one milli-Tesla, to induce this internal electric field. At higher frequencies, lower exposures would suffice to generate the internal field mentioned above, but on the other hand, higher internal E-fields are required, as is apparent from Fig. 2.

The authors (Panagopoulos *et al.*, 2002) developed a mathematical model by considering only one free ion in the vicinity of the voltage sensor of the channel protein. The displacement needed for gating the channel, $10^{-12}\ \text{m}$, is much smaller than the thermal movement of the ions. Although thermal movements have random directions and the forced vibration is in a

FIG. 1. Voltage-gated channel protein influenced by forced vibration of extracellular ions in an oscillating electric field and displacement.



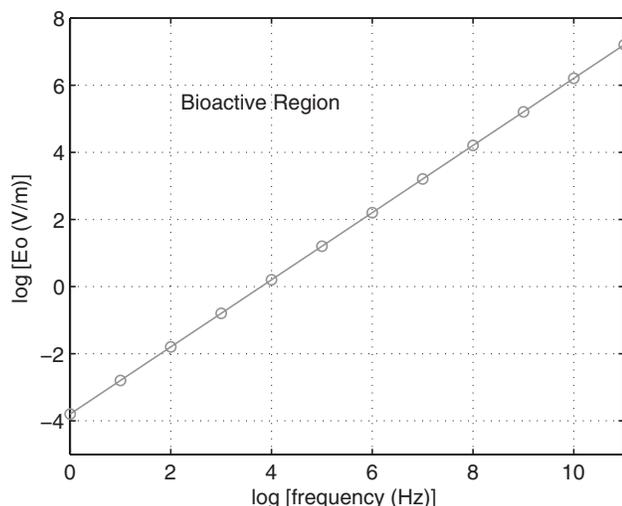


FIG. 2. Electric field bioactivity diagram: The electric field above the line induces the opening of the channel protein.

specific direction, it is not clear in a one-ion model (although the authors state differently) that the gating effect of the field driven ion movement would be larger than the effect of the random motion. If, however, the model presented were extended to the simultaneous action of several ions in the vicinity of the voltage sensor, the forces on the sensor of these ions, caused by thermal random displacements, would average a much smaller value. Another aspect to consider is that the response time of the sensor might be rather long, in which case it would work as a low-pass filter and high-frequency thermal electric fluctuations (in the GHz region) would simply not be detected. Such considerations make it unlikely, however, that microwave exposure might have the ability to open ion channels by the mechanism described. Also, the cell membrane's finite capacitance at high frequencies will make it transparent to the ionic currents and the transmembrane potential will be modified to a lesser degree.

The authors also consider purely magnetic (so-called) Lorentz forces on ions. However, the Lorentz force only acts on electric currents, and the only current in the channel model is the current through the channel when it is open. The motion of free ions in the vicinity of the voltage sensor is random, and the Lorentz force will not cause any systematic displacement of these ions. The third source the authors discuss for ion displacement is electric fields induced by external magnetic fields, as mentioned above. In their treatment, however, the facts are omitted that: (1) the induced electric fields are proportional to the flux change of the magnetic field through a surface, and thus increase with the frequency of the magnetic field, and (2) the induced electric field follows a circular path about the direction of the time varying magnetic field with increasing strength toward the periphery of the surface considered. The authors assume a constant contribution of 1 V/m in a fixed direction parallel to the Lorentz force.

The ion cyclotron resonance (ICR) model

In early studies, resonance phenomena in chicken brain preparations and with diatoms were found (Blackman *et al.*, 1982). In 1985, both Blackman *et al.* and Liboff (Blackman *et al.*, 1985a, 1985b) observed a dependence between the frequency

and the magnitude of the static geomagnetic field and amplitude windows (Blackman *et al.*, 1985a). These observations led to the formulation of the ICR theory (McLeod and Liboff, 1986). One of the first models that could explain the occurrence of resonance frequencies that were tied to the strength of the geomagnetic field was the ICR model, as proposed by McLeod and Liboff (1986). Cyclotron resonance occurs when an AC electric field is tuned to the cyclotron frequency of a specific ion moving in a static magnetic field B_{DC} , as in Fig. 3. The solution, in the absence of the electric field, can be written as

$$\omega = \left(\frac{q}{m}\right) B_{DC},$$

where ω is the circle frequency of the circular motion around the direction of the static field. The circle frequency is determined by the static magnetic field. Under cyclotron resonance condition, the ion is accelerated in the circular path by the time-varying electric field E , which is supposed to facilitate different biological processes such as ion transport through channel proteins. The cyclotron frequency is proportional to the charge over mass ratio of the ion and to the strength of the earth (static) magnetic field. A problem with this model is that ions in a viscous medium will undergo so many collisions per second with surrounding molecules, that cyclotron movement with a frequency well below 2,000 Hz cannot occur.

Both classical and quantum mechanical models have been proposed (Lednev, 1991; Edmonds, 1992). Both resonance frequencies and amplitude windows can be explained by the model. Adair (1992) criticized the quantum mechanical model presented by Lednev. Engström (1996) extended the above models and also predicts the occurrence of superharmonic resonances. He could show that Adair criticisms were not valid and that Lednev's model is physically feasible. Experimental data by Blackman (Blanchard and Blackman, 1994) and Eberhardt (Bauréus *et al.*, 2003) support the model. Biological effects were observed for magnetic field strength $>10 \mu\text{T}$. In a newer model, Lednev (2003) considers the polarization of proton spins of water by weak time-varying magnetic fields and how this can influence biological systems. In this model, biological effects can be expected for all frequencies of the time varying magnetic field, but the magnitude of the biological response depends on the ratio of the amplitude of the magnetic field and its frequency. For a

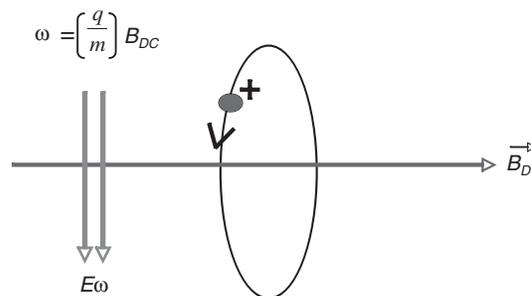


FIG. 3. Cyclotron motion of an ion about the direction of a static (earth) magnetic field, \vec{B}_{DC} . Ion, with mass m and charge q , is accelerated by an electric field E_ω tuned to the cyclotron frequency.

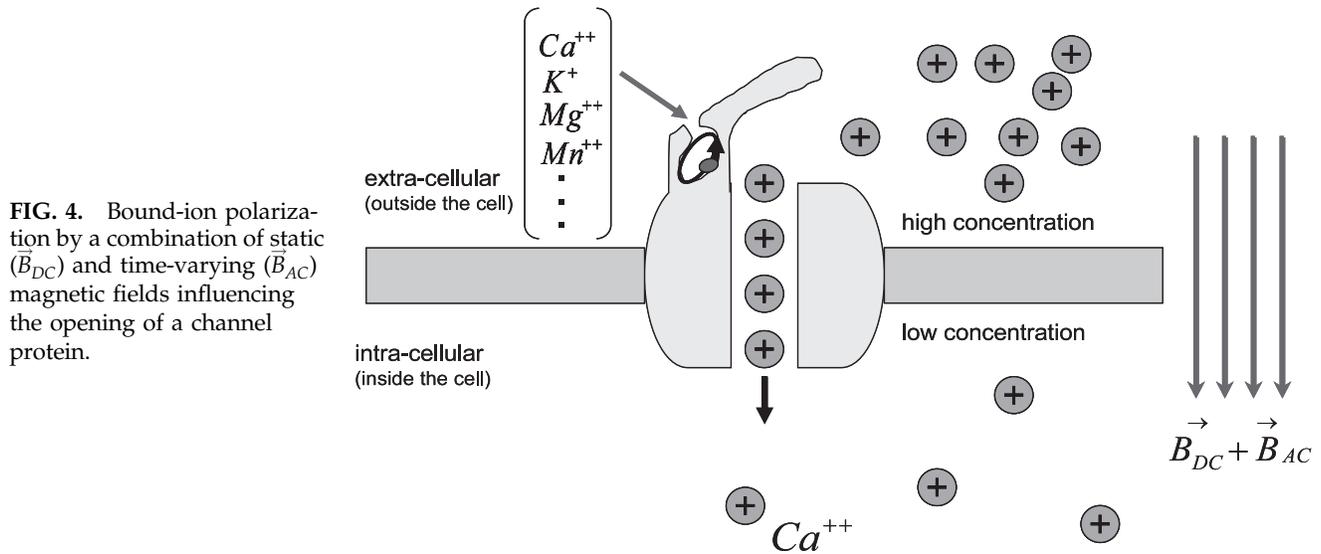


FIG. 4. Bound-ion polarization by a combination of static (\vec{B}_{DC}) and time-varying (\vec{B}_{AC}) magnetic fields influencing the opening of a channel protein.

example, 50 Hz magnetic fields with an amplitude of $\approx 1 \mu\text{T}$ would elicit a biological response.

The ion parametric resonance model

Because basic signal-to-noise issues could not be resolved in the ICR model, a new model was proposed by Lednev, the ion parametric resonance (IPR) model (Lednev, 1991). When combination of static and alternating magnetic fields is applied to a biosystem biological effects can be observed at the cyclotron frequency ω and is given by

$$\omega = \frac{1}{n} \left(\frac{q}{m} \right) B_{\text{stat}}, \quad (1)$$

where m is the mass, q charge and B_{stat} is a combination of static and alternating magnetic fields. Lednev considered an ion, bound in a trap or binding site on the surface of a protein, as a charged oscillator characterized by some vibrational energy levels, as in Fig. 4.

Lednev interpreted the cyclotron resonance in a new way. Whereas Liboff considered the effects of AC and DC magnetic fields acting on the free ions to be transported across the cell membrane, Lednev considers the effects of magnetic fields on ions bound to a biologically active molecule. Biological effects are hypothesized to be obtained as a secondary effect by electric interactions (energy transfer) between the (magnetically disturbed) bound ion and the protein. In a simple classical picture, the orbital magnetic moment of an ion in a potential well will exhibit a precession movement in a static magnetic field (Larmor precession). The Larmor precession appears because of the static magnetic field, and will be modified by an oscillating magnetic field parallel with the static field. The precession frequency will remain the same, but its speed will be accelerated or decelerated depending on the resulting total field strength, as in Fig. 5. According to Lednev, if the frequency of the AC magnetic field is tuned to twice the Larmor frequency, the angular momentum of the ion in its excited state will be polarized and the emission of photons due to deexcitations in a plane perpendicular to the

direction of the magnetic field will no longer be isotropic, but more intense in some directions than others. Incidentally, this frequency is the same as the cyclotron frequency.

Magnetic resonance imaging (MRI) is a medical imaging technique that can be used to investigate the internal structure and the body function. The same resonance conditions, as described above, occur in MRI, but with static magnetic fields in the order of Teslas. The main difference between IPR and MRI is that in IPR, the static and dynamic magnetic fields are parallel to each other, whereas they are perpendicular to each other in MRI.

In a quantum mechanical treatment, the ion is thermally excited from its ground state to an excited state. This state is three-fold degenerate in the absence of external fields. A small static magnetic field will remove the degeneracy and the excited state is split into three sublevels, as in Fig. 6. If a time-varying magnetic field is now added parallel to the static magnetic field, with a periodicity equal to the difference between frequencies of the vibrational substates, interference between the substates can be observed by observing the emitted radiation when the ions decay to the ground state. The emitted energy is absorbed by the protein, and the change in the probability of radiation in the plane perpendicular to the direction of the external magnetic field will reflect itself in a biological reaction that can be observed. A nonisotropic distribution of emitted photons is expected not only for frequencies of the AC magnetic field as described above, but also for subharmonic frequencies at $1/2$, $1/3$, etc., of the basic resonance frequency, as shown in Fig. 7. As in the ICR model, the resonance frequency is determined by the charge over mass ratio of the ion considered and the strength of the static magnetic field.

According to the IPR model, the magnitude of the biological effects is expected to show amplitude windows as in Fig. 7b. Because the strength of the earth magnetic field is of the order of $30\text{--}70 \mu\text{T}$, it is obvious from Fig. 7b that the biological effect can be expected for time-varying magnetic fields exceeding about $10 \mu\text{T}$. For stronger static magnetic field strengths, of course, as in MRI, the resonance frequencies are

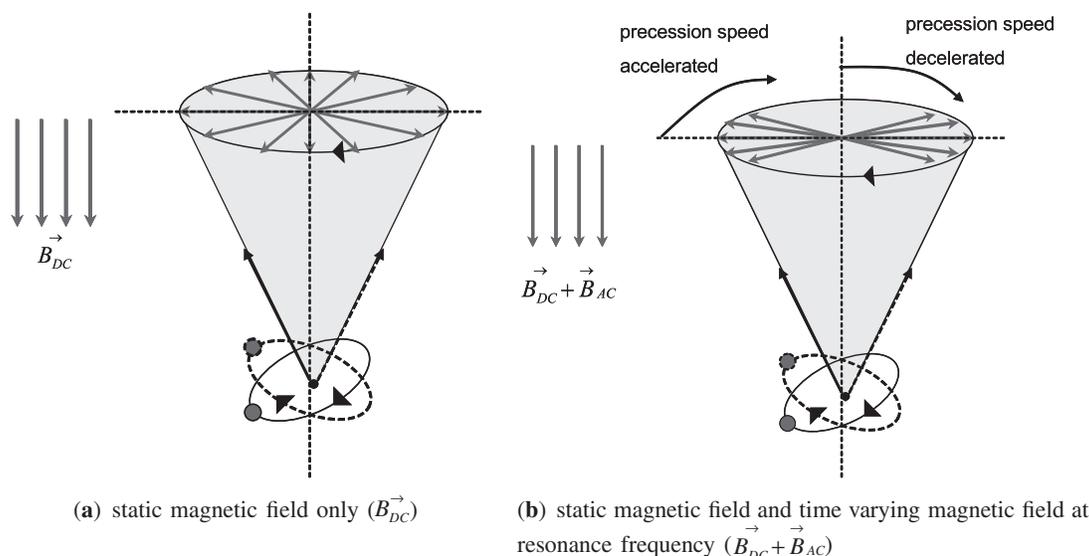


FIG. 5. Larmor precession of an ion orbital. The Larmor precession is the conical movement performed by the magnetic moment around its own axis.

much higher (see Fig. 7a). Because the biological effect depends on B_{AC}/B_{DC} (Fig. 7b and 7c), the required AC fields have to be higher for larger B_{DC} .

In this model, the signal-to-noise ratio between the magnetic signal and the electric noise in the living cell due to thermal movements of ions is highly improved, because a magnetic interaction can only be disturbed by magnetic disturbing fields. There should be no, or very little, intrinsic magnetic noise in the cell. The most important electric disturbance is the Stark effect caused by the surrounding ions, but fortunately it does not constitute a problem, because it displaces the Zeeman levels all in the same direction, and hence, there would be no broadening of the levels. The same is valid for the Doppler effect, the intrinsic level splitting by the magnetic field is conserved. The first version of the IPR model was proposed in 1991 (Lednev, 1991) and considers the oscillation (in a given direction) of an ion bound to a protein

(Calmodulin), in a time-varying magnetic field. The model is criticized by Adair (1992) and defended and extended by Engström (1996). One objection made by Adair was that the trap containing the ion must be extremely spherical and symmetrical to enable the interference between substates to occur. Another objection was that the lifetime of the excited ion state must be of the order of the periodicity of the Larmor precession; otherwise, the precession movement would be interrupted and the biological effect could not occur. Lednev addressed these objections by generalizing his theory to the case of continuous excitation (1996). He hypothesizes that biological effect is related to the degree of polarization of the ion orbit in the trap. Energy transfer between the ion and the protein is not required any more in this model. In Lednev's view, the polarization of the ions influences its escape probability from the trap, and thus the efficacy of the protein involved. In principle, in this model, no extremely spherical symmetrical potential is required, although, for simplicity, Lednev considered a spherical symmetrical potential in his derivations. Resonance frequencies occur as in the first theory, but the dependence of the degree of ion polarization as a function of the strength of the time varying magnetic field is now altered (see Fig. 7c).

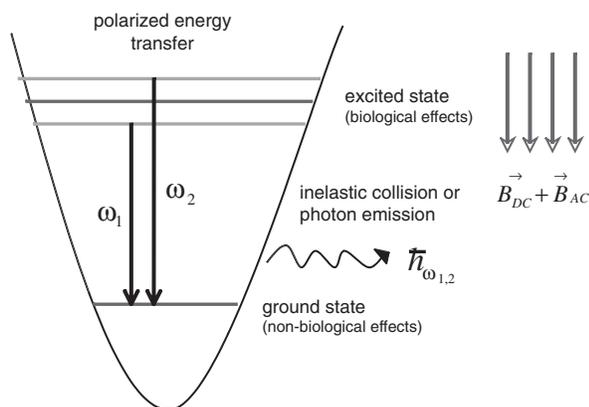


FIG. 6. Zeeman splitting of a bound ion's first excited state by an external magnetic field.

The hydrogen nuclear polarization model

While verifying the above models, Belova and Lednev found in 2001 that the gravitropic bending of flax seedling deviated anomalously from the expected values at very low amplitudes $0.075 < B < 5 \mu\text{T}$ of the time-varying magnetic field. Lednev explained the results by assuming that the hydrogen nuclei in water molecules are polarized by the combination of coparallel static and dynamic magnetic fields (Belova *et al.*, 2007). The expected dependence of the biological effect (BE) on the amplitude of the time-varying magnetic field for a given frequency is given by in Fig. 7d and

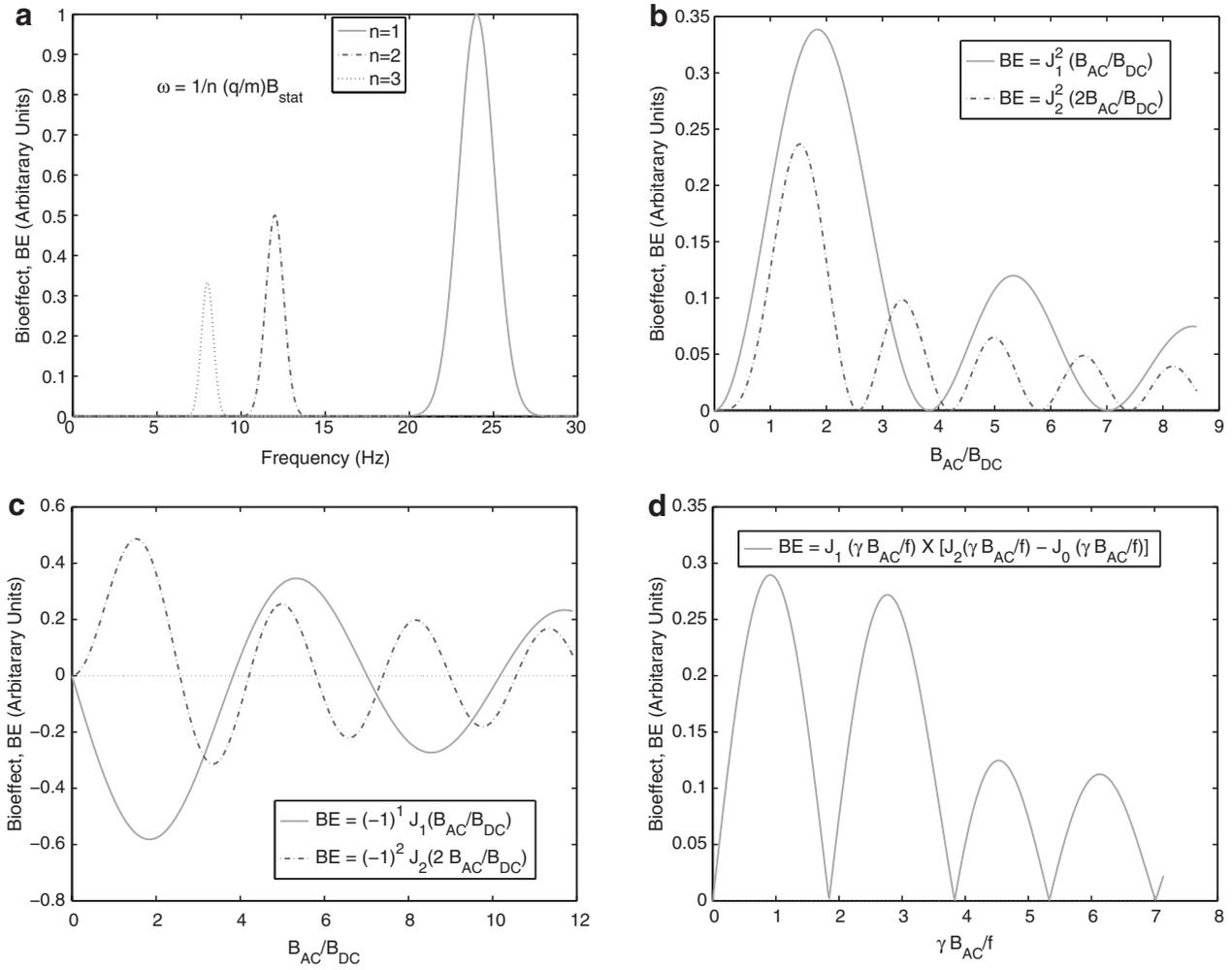


FIG. 7. Predictions of magnetic resonance models. (a) Resonance frequencies according to the IPR model for $^{45}\text{Ca}^{++}$ ions in a static magnetic field of $37\ \mu\text{T}$. (b) Expected biological effect as a function of the strength of the oscillating magnetic field according to the IPR model for the fundamental resonance frequency and the first subharmonic frequency. J_n are Bessel functions. (c) Expected biological effect as a function of the strength of the oscillating magnetic field according to the *modified* IPR model for the fundamental resonance frequency and the first subharmonic frequency. J_n are Bessel functions. (d) Biological effect as a function of the ratio of the time-varying magnetic field and its frequency for the hydrogen nuclear polarization model. γ is the gyromagnetic ratio of the proton $42.578\ \text{Hz}/\mu\text{T}$. J_n are Bessel functions.

$$BE = \left| J_1\left(\frac{\gamma B_{AC}}{f}\right) \times \left[J_2\left(\frac{\gamma B_{AC}}{f}\right) - J_0\left(\frac{\gamma B_{AC}}{f}\right) \right] \right|, \quad (2)$$

where J_0 , J_1 , and J_2 , are Bessel's functions of the first order. In this model, no resonance frequencies occur, so in principle, all frequencies that occur in the environment up to several hundred hertz, can give rise to biological effects. However, amplitude windows do occur (see Fig. 7d). The presence of the earth magnetic field in parallel to the time-varying magnetic field is still required, but the strength of this static magnetic field is not critical for the predicted biological effect.

Experimental evidence for the IPR model

Liboff and Parkinson (1991) studied transepithelial differences of potential in colonic tissue from the turtle (*Pseudemys scripta*) for various frequencies and AC and DC magnetic field conditions, and concluded that no cyclotron resonances

could be observed for each of the ions H^+ , Li^+ , Na^+ , K^+ , Ca^{++} , and Cl^- .

According to Lednev, this negative findings are to be expected, at least for the single charged ions, because the lifetimes of these ions in the traps would be too short for the Larmor precession to occur. Blackman and Blanchard (1994) tested the IPR model extensively by studying neurite outgrowth in NGF stimulated pheochromocytoma (PC-12) cells. The resonance found at 45 Hz was attributed to Mg^{++} bound to some biological molecule in the cell. The amplitude window predicted in the first version of Lednev's theory (1991) could be reproduced, but with a width of only half of the predicted value. Trillo *et al.* (1996) extended this work by tuning to the resonance frequency for H^+ ions. The resonance was found and the amplitude dependence of neurite outgrowth showed the same factor 2 difference as was found in the earlier work. (Bauréus *et al.*, 2003) studied the calcium flux through calcium channels in highly purified plasma membranes of spinach (*Spinacia oleracea* L.).

The calcium flux was modified at frequencies that corresponded to resonance frequencies for nonhydrated ions of $^{45}\text{Ca}^{++}$, Mn^{++} , and Mn^{+++} . The resonance frequencies were linearly related to the strength of the static magnetic field applied. However, as in the PC-12 experiments performed by Blackman and Blanchard (1994) a factor of 2 had to be included empirically in the argument of the Bessel function to explain the width of the amplitude window. Biological effects, BE , is given by

$$BE = (-1)^n J_n \left(\frac{B_{AC}}{B_{DC}} \right), \quad (3)$$

where $n \in 1, 2$, and J_n is the Bessel functions, B_{AC} and B_{DC} are AC and DC magnetic fields (Lednev, 1993).

Blanchard and Blackman (1994) attempted to justify this factor of 2 on a theoretical basis, but Engström (1996) showed that it could not be derived from theory. In 1996, Lednev modified his model, to avoid some of the problems identified in the original theory (Lednev, 1991). In this modified version (see above) the amplitude window is described by the square of the Bessel functions J_n and BE is given by

$$BE = J_n^2 \left(\frac{nB_{AC}}{B_{DC}} \right). \quad (4)$$

A fit to Bauréus *et al.*, (2003) data demonstrates that the factor of two discrepancy is not resolved by Lednev's modified theory. Belova and Lednev (2000) tested the predictions of the modified IPR model by studying the gravitropic bending of flax stem segments (*Linum bienne*). Tuning for the resonance frequency for calcium ions, it was found that the amplitude dependence of the studied effect agreed well with the squared Besselfunction of the first order, as predicted by the modified theory (Lednev, 1996). In 2005, Sarimov *et al.* studied the hypothesis that proteins that incorporate zinc, which is important for the stability of conformation, can be influenced by combinations of DC and AC magnetic fields with frequency tuned to the resonance frequency of Zn^{++} . Some of these proteins controls apoptosis and cell proliferation. Several cancer cell lines were studied by the above authors. The amplitude of the AC magnetic field was chosen to be optimal according to Lednev's theory (1996), or Blanchard and Blackman's theory (1994). An inhibition of cell proliferation was observed only during the optimal condition according to Blanchard. In 1995, Prato *et al.* studied analgesia in the land snail *Cepaea*. The amplitude dependence of the opioid fuction studied agreed well with Lednev's (1991) predictions, but not with Blanchard and Blackman's (1994). In 1999, Zhadin *et al.* studied the effects of combined DC and AC magnetic fields on rat behavior. Resonance frequencies for different biologically active ions, especially Ca^{++} , Na^+ , K^+ , Cl^- , Mg^{++} , and Li^+ , were investigated. At the calcium resonance frequency, the locomotor and exploratory activities were lowered, whereas when tuning for magnesium, the same activities were enhanced. No changes in behaviour could be observed for the other ions.

Recently, in 2006, Pazur *et al.* studied the growth of etiolated barley plant seedlings under ICR conditions for Ca^{++} ions. Although the B_{AC}/B_{DC} ratio of 0.0055 ($B_{AC} = 0.5 \mu\text{T}$) is far from optimum according to the IPR model, the growth rate was reduced compared to sham exposed, and the total pigment content of protochlorophyllide and carotenoids were

significantly reduced. These results might, however, be explained by the proton polarization model proposed by Lednev (Belova *et al.*, 2007).

Discussion

The main purpose of any interaction model is to explain how extremely weak electromagnetic fields can be detected by the living cell. Several strategies are used for this purpose:

1. The regularity of the signal can be used to design a "pumping mechanism" by which many small energy steps add up to a detectable bioeffect.
2. Magnetic fields can be hypothesized as acting on small ferromagnetic substructures (grains of magnetite) that are found in certain cells. The interaction forces are in that case much stronger than the interaction between magnetic fields and paramagnetic structures.
3. By reducing the dispersion of energy in all directions from its original entry point, a directed transport toward a target molecule is facilitated. This increases the signal-to-noise ratio. Examples can be found in solitons in plasma membrane and along DNA-strings.
4. An interaction of the electromagnetic field with structures that are insensitive to electric thermal noise.

The models proposed by Lednev are good examples of the fourth category. Analogy to nuclear magnetic resonance (NMR)-spectroscopy and MR-imaging, the very small energy difference between different magnetic substates are insensitive to electric fields resulted from thermal collisions. Only disturbing magnetic fields can disturb these systems, and these are very small in biological tissue, leading to long relaxation times. It can be noted that the model of forced ion vibration relies on electric forces acting on free ions that are also subject to the electric forces of thermal collisions. In this model, therefore, external fields that are orders of magnitude higher, are required to induce a biological effect.

The recommendation of the International Committee of Nonionizing Radiation Protection (ICNIRP, 1998) for exposure limit value for low-frequency electromagnetic fields (EMF) and microwaves aim to protect against nerve stimulation and body heating, respectively. Signals far below the ICNIRP recommendations can be considered as weak, and the way they interact with biological matter is discussed in this article. Many epidemiological studies on residential and occupational exposure to extremely weak low-frequency (ELF) magnetic fields show varying, but in general positive, associations with different cancer forms such as Leukemia, brain tumors, and breast cancer. Finally, experiments should be devoted to test the predictions of interaction models, rather than just use 50 or 60 Hz signals in the mT range, which used in literature is rather unrealistic. Especially the predictions of the above #4) in the discussion are easily testable.

Conclusion

An important conclusion is that the models based on electric interactions have difficulties to obtain a high enough signal-to-noise ratio at low field strengths. The fields that are needed to explain the opening of a membrane channel protein are unrealistically high. On the other hand, models based on magnetic interactions can easily obtain a large enough

signal-to-noise ratio, because the level of magnetic thermal noise in tissue is low. The reason that these models work, is the same reason that makes the MRI technique possible.

Author Disclosure Statement

The authors declare that no conflicting financial interests exist.

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