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The Paradox of Magnetobiology: Analysis and Prospects for Solution

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Abstract—The formulation, content, and corollaries of the so-called *kT* problem are considered. The problem points to a paradox in the biological effect of weak low-frequency magnetic fields. The conventional formulation of the problem contains implicit assumptions that prove not fully valid according to the results of analysis.

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INTRODUCTION

The nature of biological effects of weak electromagnetic fields remains unclear in spite of a large body of experimental data. The difficulty in explaining such effects is usually attributed to the fact that a quantum of a low-frequency electromagnetic field is substantially smaller than the characteristic energy of chemical conversions, which is on the order of *kT*. It is generally accepted that this fact points to a paradox or even proves that magnetobiological effects are impossible. This thesis was specially termed the "*kT* problem" in the literature.

It should be specified that we are speaking of magnetic fields (MF) with an intensity on the order of the geomagnetic field and a frequency from a few to hundreds of hertz. Such fields do not produce appreciable inductive heating.

The *kT* problem was apparently formulated for the first time in 1960s in a broad sense, in relation to the then discovered biological effects of microwave electromagnetic fields (EMFs) with a low energy flux density (below 100 $\mu W/cm^2$) [1]. Microwaves modulated by a low-frequency signal proved to be particularly effective. It was found later that the modulating signal itself, in the form of a weak magnetic field, can produce a noticeable effect on organisms. For such effects, the *kT* problem has become especially dramatic since the field quantum is far smaller (by 11–12 orders of magnitude) than *kT*.

The *kT* problem in the above formulation contains three implicit assumptions: (i) the primary act of magnetoreception develops at the atomic–molecular level; (ii) the interaction between a varying MF and a molecular target is a single-quantum process; and (iii) the interaction of the field with the target occurs in thermal equilibrium conditions.

However, these assumptions (or postulates) are not fully substantiated and require refinement. The *kT* problem was considered at different times [2–5], but a unified point of view on the correctness of its formulation has not yet been worked out. In this paper, the postulates of the problem are discussed and their incomplete validity is exposed: in addition to molecular targets, an organism may contain relatively large particles with a nearly macroscopic magnetic moment. As regards molecular targets, their interaction with a low-frequency MF is of a multiquantum nature and may take place in the absence of thermal equilibrium.

SUBMICROMETER LEVEL OF MAGNETORECEPTION

Let us consider nanosize particles consisting predominantly of crystalline magnetite found in many living objects. The magnetic moment μ of such particles exceeds the elementary magnetic moment by 7–9 orders of magnitude. The energy of their rotation in a weak magnetic field H is substantially higher than the energy kT of thermal fluctuations.

The magnetite particles found in the brain of many animals and human are of special interest. It was found that these particles are of biogenic origin (i.e., they form by crystallization occurring with time directly in the brain). The biogenic magnetite particles are often referred to as "magnetosomes;" such particles were observed for the first time in bacteria exhibiting magnetotaxis [6]. It has been found recently that magnetic nanoparticles can also form in DNA complexes [7]. The concentration of magnetosomes in human brain tissue is about $5 \cdot 10^6$ and in the brain tunic, more than 10^8 crystals per gram [8] (on average, 50 ng/g [9]).

The energy of a 100-nm magnetosome is approximately $24kT$. Consequently, regular variations of this energy in an additional alternating magnetic field h amount to $(h/H_{geo})24kT$. If such regular variations exceed random variations, which are of the order of $kT/2$, they may initiate a biological reaction. This sets a natural limit on the magnitude of the alternating MF capable of producing a noticeable effect on a biophysical or biochemical system: $h > 1$–2 μT. It was shown in [10] that the limit value of an MF detectable on a biological level may be still an order of magnitude lower in the case when magnetosomes move in a potential of the general form with two minima. In this case, thermal perturbations are not masked; on the contrary, such perturbations help weak magnetic forces to evoke a response from the organism.

The intrinsic MF of a particle is as high as 0.1 T in the vicinity of the particle itself and strongly depends on its orientation. Consequently, rotation of the particle may markedly change the rate of chemical reaction involving free radicals.

Obviously, in this case the kT problem in its conventional formulation simply does not apply since a primary act of magnetoreception occurs not on a molecular but on a submicrometer level, relatively large particles interacting with the MF. It has now been reliably established that such phenomena as precise orientation of many species of animals during their seasonal migration are due to the interaction of the geomagnetic field with magnetosomes [11]. We are interested in determining specific biophysical mechanisms of such magnetoreception and in ascertaining the thresholds of sensitivity to constant and varying MFs [12, 13].

MULTIQUANTUM NATURE OF INTERACTION OF A FIELD WITH A MOLECULAR TARGET

In accordance with the conventional formulation of the kT problem, atomic-molecular processes could theoretically be targets of an MF in magnetobiological effects. Are then the other postulates of the kT problem in such mechanisms (e.g., the single-quantum nature of the interaction between the field and the target) soundly substantiated? This question is closely related to the means of describing the electromagnetic field (classical or quantum-mechanical).

The criterion for applicability of the classical description is based on the requirement of a large quantum number for elementary oscillators of an EMF in the quantum-mechanical description. In [14], such a criterion obtained from general estimates connects frequency f with amplitude H of the magnetic component or E of the electric component of the varying field (in the Gaussian system of units, the dimension of E and H is the same):

$$H > \sqrt{\hbar c}\left(\frac{f}{c}\right)^2. \qquad (1)$$

According to numerical estimates, $H >> 10^{-29} f_2$. It follows hence that the classical description of EMF is applicable in the range of low-frequency magnetic fields down to vanishingly small amplitudes. Criterion (1) presumes isotropy and a broad radiation spectrum ($\Delta f - f$). The inclusion of the characteristics of field directionality for laboratory solenoids and of frequency stability of low-frequency (LF) oscillators only improves the applicability of the classical description of the LF MF.

Thus, for describing the state of a molecular target interacting with a LF MF, it is sufficient to use the so-called semiclassical approximation, in which quantum dynamics of particles is considered in the classical EMF. In this approximation, the dynamic equation for a particle has the form of a Schrödinger equation,

in which the EMF appears not in the form of field variables or *quanta*, but in the form of *parameters*, viz., vector potential **A** and scalar potential A_0 of the classical EMF.

It is well known that the states of the EMF close to classical ones are described in quantum electrodynamics with the help of so-called coherent states, which minimize quantum indeterminacy. Coherent states are multiquantum field excitations. For this reason, the processes of interaction with the classical field are also multiquantum processes. Consequently, we can speak about absorption of a single LF field quantum during the interaction with a molecular target only in a certain abstract sense; naturally, such a speculative process does not permit judgements on the possibility or impossibility of weak LF MFs causing biological effects.

The concept of EMF quanta (even if they are low-frequency quanta) is helpful if we are interested in the transmission of a weak EMF signal from the field to the target. It is natural to characterize this process of energy transfer by the number of quanta absorbed by the target per unit time. It is important to distinguish between a particular device or molecular target involved and the general principle of interaction between an LF EMF and a quantum system.

In the general case, to characterize the sensitivity of a detector, use is made of energy flux p, i.e., the number N of quanta $\hbar\Omega$ absorbed by the system in a certain time interval t during its interaction with the field:

$$p = n\hbar\Omega / t.$$

Thus, to determine the sensitivity, we must preset a certain time interval t and calculate the number of quanta absorbed during this time. We want to determine the limitations imposed on the sensitivity that follow from the most general laws of quantum physics; for this reason, we consider an idealized quantum system sufficiently isolated from the thermostat.

The time interval t must fully characterize the process of interaction as regards the sensitivity and permit in principle the counting of quanta. Naturally, the value of t cannot be arbitrarily large. The change in the energy of the system in a varying MF represents Rabi oscillations superimposed on an exponential approximation to a certain asymptotic level. With increasing observation time t, the average change in energy tends to zero. The value of t cannot be arbitrarily small either since the change in energy ε of the quantum system takes a certain time θ.

It is convenient to choose a time interval $t > \theta$, in which the energy of the quantum system does not acquire a quasi-stationary value. Obviously, this (coherent interaction) time is the shorter of two time periods, i.e., the lifetime of the quantum state and the time of self-correlation of the MF. The self-correlation time for the laboratory low-frequency MF normally amounts to at least several seconds; consequently, the time of coherent interaction is mainly determined by the lifetime τ of the quantum state. The latter is determined by the features of the interaction of the quantum system with the thermostat. In the subsequent analysis, we will assume that

$$p = n\hbar\Omega / \tau. \quad (2)$$

Limitations imposed on the value of p follow from the fundamental relation of quantum mechanics, which connects the change in the energy ε of the quantum system with time θ required for detecting this change [15]:

$$\varepsilon\theta > \hbar .$$

In the case of detecting n quanta, this relation can be written in the form $\theta > 1/n\theta$ since $\varepsilon \sim n\hbar\Omega$. However, in any case the time of detection of the change in energy cannot exceed the time of coherent interaction of the field with the atomic system. Consequently, we can write the inequality

$$\tau > \theta > \frac{1}{n\Omega};$$

i.e., $\tau > 1/n\Omega$. Substituting this inequality into expression (2), we obtain a simple estimate for the limit sensitivity:

$$p \sim \frac{\hbar}{\tau^2}. \quad (3)$$

Thus, the threshold of sensitivity to an LF EMF is determined by the lifetime of the quantum state of the target in the detector [16]. Energy fluxes smaller than the value given by expression (3) cannot be detected. This should be interpreted as follows. If n quanta of a varying field of frequency Ω are detected during time interval τ, which does not exceed the lifetime of the quantum states of the target, and $n > 1/\Omega\tau > 1$, the energy flux density through a target of size a must be

$$S \sim \frac{p}{a^2} \sim \left(\frac{n\Omega}{a}\right)^2.$$

In the plane-wave approximation, energy flux density S is equal to $cH^2/4\pi$; i.e., it is necessary that the MF be

$$H \sim \frac{2n\Omega}{a}\sqrt{\pi\frac{\pi\hbar}{c}}.$$

For example, for values of parameters $\tau = 10$ ms, $\Omega = 100$ rad/s, $n = 10^9$, and $a = 10^{-7}$ cm, the above-mentioned MF is 1 G in the order of magnitude.

This naturally does not imply that the target of this size necessarily absorbs 10^9 quanta during 10 ms in an MF of this amplitude. It should be recalled that limit (3) follows only from the fundamental quantum-mechanical relation. The sensitivity of devices (including biophysical targets) also depends on the probability of absorption of EMF quanta in these objects and is substantially lower than the sensitivity limit, while the sensitivity limit is accordingly substantially higher than the value given by expression (3). It is of fundamental importance, however, that the probability of absorption of EMF quanta is now determined by the specific structure of the targets. The nature of the target also determines the parameters that vary as a result of "summation" of MF quanta over the time of coherent interaction with the system and the extent of this variation.

Generally speaking, these arguments are conditional. The use of the concept of the number of EMF quanta and the energy states of a quantum system presumes that these states are isolated from one another (i.e., the energy of their interaction is smaller than the transition energies $\hbar\Omega$ and $\Delta\varepsilon$ in the states of the field and of the quantum system, respectively). For example, for the interaction of optical radiation from a commercial He–Ne laser with an atom, we have

$$\hbar\Omega \sim \Delta\varepsilon, \quad \frac{eEa}{\hbar\Omega} \sim 10^{-7}.$$

Here, eEa is the energy of interaction of charge e in the atom of size a with electric field E. For this reason, the language of field quanta and energy levels of the atom proves to be effective. In other words, the states of a complete system of an atom in an electromagnetic field can be reduced to a combination of states of isolated atom and field. A different situation takes place for the interaction of a weak LF MF with an atom-like system in the geomagnetic field: all three energies are of the same order of magnitude. The energy μH of interaction of magnetic field H with the magnetic moment $\mu = e\hbar/2mc$ of the orbital motion in fact coincides both with the Zeeman splitting $\hbar\Omega_c$ (Ω_c is the cyclotron frequency) and with the LF MF quantum $\hbar\Omega$.

In this case, the small parameter (interaction) is missing and the representation of the state of the complete system in the form of a combination of the states of the atom and of the field is not quite substantiated. A more reliable description can be obtained using quantum electrodynamics. However, it is clear a priori that the conclusion on the multiquantum nature of the interaction corresponds to a quite adequate description of the situation in conventional terms.

Thus, the interaction of an LF MF with a quantum target is a multiquantum process; the conventional formulation of the kT problem and its corollaries are invalid for such processes. The first principles do not impose serious limitations on the threshold sensitivity. The microscopic structure of a biological receptor and the lifetime of its states determine the sensitivity limit in each specific case. It is important to note that the lifetime can be long enough owing to the state of the elements of biophysical structures, which is far from thermal equilibrium.

NONEQUILIBRIUM STATES AS THE BASIS OF MOLECULAR MECHANISMS OF MAGNETORECEPTION

The conventional formulation of the kT problem is negative by nature. It reflects a skeptical attitude to the likelihood of magnetobiological effects and does not carry any impetus for resolving the paradox. It is thus reasonable to use another (more constructive) formulation of the problem, which refines the following two aspects: (1) what is the mechanism of transformation of a weak MF signal into a (bio)chemical signal? and (2) why is this mechanism operative against the background of thermal perturbations of the medium?

It is expedient to take into account the following circumstance. First, the very concept of kT originates from statistical physics. It is meaningful for systems close to thermal equilibrium. In such systems, neither a single quantum $\hbar W$, nor even many quanta corresponding to a weak LF MF substantially change the mean energy of the degrees of freedom. However, in

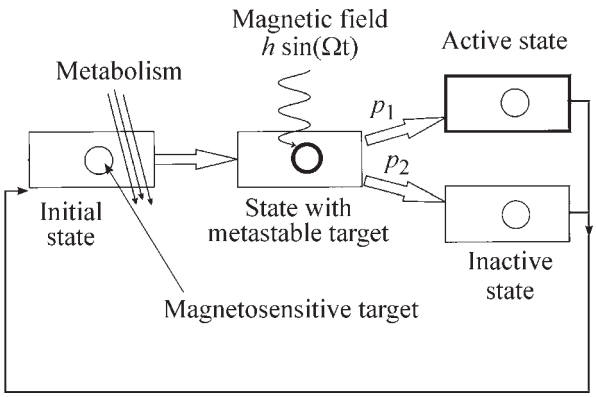

Fig. 1. Evolution of states of a protein complex with a magnetosensitive molecular target.

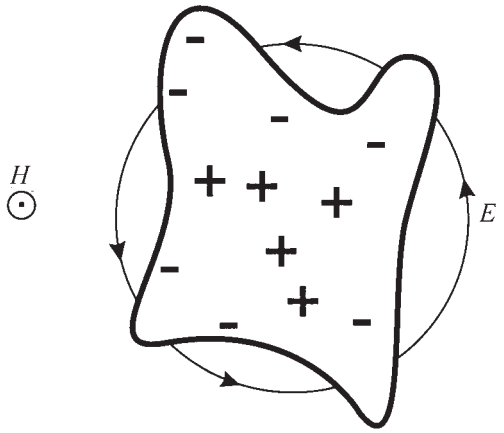

Fig. 2. A vortex electric field generated by a varying MF affects the rotation of a molecule with a nonuniform charge density distribution.

systems weakly coupled with the thermostat, thermalization is a relatively slow process and such systems can be far from equilibrium conditions for a long time. In this case, an MF may cause a large relative change in energy of some dynamic variables, whose energy is small for some reason or other. In other words, if the thermalization time of some degrees of freedom interacting with the MF is longer than the characteristic lifetime of the system itself, the concept of temperature in the conventional thermodynamic sense is inapplicable to such degrees of freedom, and the comparison of the changes in their energy with kT upon the absorption of field quanta becomes meaningless.

It is well known that the metabolism of living systems is a combination of predominantly nonequilibrium processes. Generation and decay of biophysical structures, which occur over time intervals shorter than the time of the thermalization of some of the degrees of freedom of such structures, are examples of nonequilibrium systems in which weak MFs can manifest themselves in the variables of the structure.

Another circumstance is associated with the fact that the energy of interaction of an MF with any molecular target is low. For example, several years are required to change the energy of an ideal molecular or ionic oscillator by kT with the help of a varying MF under resonance conditions [16]. It follows hence that the MF can only play the role of a controlling signal rather than an energy factor like kT. It is expedient to look for the mechanisms in which the MF controls not the processes, but the probabilities of development of processes in a certain direction.

In short, the nonequilibrium nature or metastability of a target and the probabilistic nature of transformation of a weak MF signal into a biochemical response are two indispensable properties of the molecular mechanism of magnetoreception. Let us consider in greater detail how these properties might be realized in magnetoreception involving a protein complex with a magnetosensitive target (Fig. 1).

As a result of conformational rearrangements initiated by metabolism, specially organized molecular groups occur in some proteins. These groups "live" for some time, after which they decay so that the protein transforms into modified states, active or inactive relative to some other biochemical processes. The structure of a molecular group is such that some of its degrees of freedom are sensitive to an MF (i.e., this group is a target for the MF). On the other hand, such a target affects the probability of protein evolution from an intermediate state to the final (active or inactive) state. Then the protein returns to the initial state, and the cycle is repeated. The amount of protein in the active state depends on the MF in this case. The MF controls the state of the target since the lifetime of the target is shorter than the time of its thermalization and the target is in a nonequilibrium state. Thus, the MF determines the probability of a certain path of protein evolution.

Within the framework of this generalized concept, we can represent various mechanisms of magnetoreception according to nature of the metastable molecular target controlling the reaction probability.

An example of a metastable target is described in [17]: a molecular rotator for which the probability

of reaction with the environment depends on the MF. The essence of this example is as follows. A varying MF produces a vortex electric field. The charge density of a molecule is usually distributed nonuniformly; for this reason, the electric field generates a torque accelerating or decelerating the random thermal rotation of the molecule (Fig. 2). If the molecule is fixed by a pair of covalent bonds (supports) in the protein matrix, and the space around this molecule is sufficient for more or less free rotation or rotational oscillations, thermal vibrations do not produce a torque relative to the rotational axis of the rotator. This degree of freedom is thermalized slowly through van der Waals interactions, and the circular electric field effectively controls the rotation of the molecule.

For some special combinations of MF frequencies and amplitudes, a specific mode of nonuniform rotation of the molecule is attained: the molecule is nearly stationary during almost the entire period of MF variation, then rapidly rotates through the complete angle, and so on. In this mode, the probability of reaction of side groups of the molecule with the surroundings increases. Since the de Broglie wavelength in the angular variable is on the order of π even at room temperature, the rotations of molecules are described quantum-mechanically in [17] as the interference of angular molecular states. It should be noted that rotations partly insulated from the thermostat are quite realistic (spectral manifestations of such degrees of freedom are known [18]).

In this case, two problems concerning the structural form of the *kT* problem are solved as follows: (1) the mechanism of MF transformation is associated with the control of the reaction probability; (2) the mechanism of the transformation stability is associated with the metastability of the target.

Another example of a molecular target is the generalized coordinate of the reaction for processes with proton or electron transfer in a two-well potential controlled by a magnetosensitive aqueous medium. Many researchers noted the fact that an aqueous medium may play the role of a "mediator" in the transmission of an MF signal to the level of biological reactions. This idea was confirmed theoretically and experimentally [19].

In our case, the target is not in the bulk of a protein, but surrounds it (which naturally does not change the gist of the matter). The state of water surrounding the protein surface affects its conformational ability, and hence it affects the height of the potential barrier along the generalized coordinate of charge transfer reaction. Most plausibly, elementary targets in the aqueous matrix are the magnetic moments of protons forming hydrogen bonds. Concerted simultaneous action on the magnetic moments and, hence, on the spin states of protons may affect the realization of the spin exclusion principle in rearrangement of hydrogen bonds and, hence, the conformational mobility. In this model, the MF controls the probability of charge transfer reaction, and in place of a metastable localized target we have an equilibrium but distributed target (the aggregate of elementary magnetic moments of protons).

CONCLUSIONS

The *kT* problem in its conventional formulation is invalid as an argument against the possibility of magnetobiological effects. The fallacy of this problem follows from (i) the contradictory nature of its implicit postulates and (ii) counterexamples of envisaging magnetoreception mechanisms that are consistent with physical laws.

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