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LETTERS TO THE EDITORS

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A few remarks evoked by Binhi and Savin's review on magnetobiology

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1. Introduction

Magnetobiology is the study of magnetic field effects on biological living systems. It is about as old as the study of magnetism itself. Recently, an important event occurred for this field — a review article on this subject was published in one of the most highly reputed physics journals, *Physics – Uspekhi* [1]. There was hope that the clarity of real physics is finally reaching this complicated field, entangled in controversies. The goal of the present letter is to express the opinion that the clarification was not achieved, and more likely the field has become even more confusing than before.

To appreciate the degree of confusion in the field, it is enough to consider two facts. On the one hand, magnetic bracelets, as well as pieces designed for various other body parts, are sold in many countries. Producers and sellers of this merchandise state that magnetism cures many human sufferings (and a lot of people believe that). On the other hand, there is a constantly recurring idea (which is also mentioned in [1]), that the magnetic fields of electric transmission lines, electric transport, and industrial equipment 'pollute the environment,' cause cancer, or increase the chances of cancer, particularly leukemia. Of course, it is in principle possible that a permanent constant magnetic field has therapeutic effects, while an alternating field at a frequency of about 50 Hertz is terribly detrimental. However, if this is true, then something like "Do not shake to avoid a deadly hazard!" should be written on every supposedly therapeutic magnet, and it should be written in a very large script. This is not the case, as we know: nothing like that appears on any of the 'medical' magnets. It is, therefore, not surprising that magnetobiology appears on the not so honorable list of 'voodoo' scientific disciplines [2].

The situation gets even worse due to the attempts by some physicists, sometimes even good ones, to prove that magnetic effects on biological systems are impossible. Attempts at such proofs are unlikely to succeed, as the authors of the review [1] point out correctly. Indeed, it is always tricky to prove the impossibility or non-existence of anything. More importantly, in the rare cases when such 'theorems of impossibility' are proven, this is achieved at the expense of a very clear and usually very restrictive definition of whatever the subject of the proof is. This is, of course, the case with two of the most prominent theorems of non-existence. The fifth power equation is impossible to 'solve' if and only if we mean the solution in terms of the algebraic radicals. And the heat engine cannot outperform the Carnot limit if it satisfies all the conditions, for instance, does not interact with anything colder than its 'own' heat drain. The subject of magnetobiology is not defined accurately enough to allow any theorems to be proven, and this is likely an advantage rather than disadvantage, as it indicates that the field remains open, ready to accept experimental observations, whatever they might be.

What we just said testifies to the complicated experimental situation in the field of magnetobiology. What do the authors of the review [1] write about that?

2. Experiments

The authors of the work [1] make no attempt to conceal from the reader the unpleasant scene of controversial, irreproducible experiments in magnetobiology. Surprisingly, they do not even attempt to clarify the matter. Instead, they offer an explanation to the reader, that the requirement of reproducibility should be relaxed for experiments in the field of magnetobiology. This is because, in the authors' jargon, observation of magnetobiological effects depends on 'simultaneously getting into electromagnetic and physiological windows.' In other words, all the conditions of the experiment should simultaneously meet all the criteria imposed by both electromagnetic and physiological constraints. It goes without saying that there is nothing unusual in this situation. Every serious experiment always necessitates meeting a number, and frequently of a large number, of mutually frustrating requirements. This has always been the case in the history of science, starting from the Cavendish experiment

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measuring the gravity constant, and finishing with countless experiments in present day physics or biology. Everyone would agree that it is extremely difficult to design and perform a reliable reproducible experiment, but it seems that there is no way around it. No? The authors of the review [1] state that there is a shortcut: instead of the incredibly laborious experimental work, it is suggested to select "common features in the manifestations of magnetobiological effects in a number of experimental setups with a variety of biological substances," and then to subject these 'common features' to some kind of theoretical generalization. In plain words, instead of one high quality reproducible experiment (which so far does not exist, according to the opinion of the authors) it is suggested to approach the problem 'democratically': take many irreproducible experiments of not-so-high quality, and see if there is anything common in their results. Would this novel approach to science work? Although we are tempted to answer negatively to this general question, let us look at how the authors of the review [1] apply their method in the specific context of magnetobiology.

There are a total of four figures with experimental data in the review [1]. A characteristic case is Figure 5, which presents the dependence of mobility of diatom seaweed on the frequency of the applied magnetic field. It is highly doubtful that all readers of *Physics – Uspekhi* know what these diatom seaweeds are (the author of the present letter, for instance, does not know). More importantly, what is mobility in this context? Is it the quantity related by Einstein to the diffusion coefficient? Or, alternatively, maybe it has to do with some life activity of the organism? Which kind of activity, then? And why should we look at this seaweed? There are no answers to all these simple questions.

Figure 12 presents the data on viscosity measurements for the suspension of *E. Coli*. What these words mean, remains, once again, completely unclear. Are we speaking about a dilute suspension, in which case changing viscosity tells us something about sizes and shapes of particles (e.g., bacteria in this case)? Or, alternatively, maybe we are speaking about a concentrated suspension, in which case viscosity is determined by the interactions between particles? There is no answer.

Figures 3 and 4 present data on the PC-12 cells, with the same sort of problems, starting from the simplest issue, what these RC-12 cells are.

A general comment is worthy of emphasis here. It often happens in biological systems, even in relatively simple ones, that one and the same responce is caused by opposite stimuli. For instance, many proteins denature both upon heating up and upon cooling down. But it also happens, about as frequently, that one and the same action causes opposite reactions. A good example is positive and negative chemotaxis, when some bacteria swim down the concentration gradient of certain molecules, while others swim up against this same gradient. Clearly, *Physics – Uspekhi* is not the proper place to discuss technical subtleties of biological experiments. Nevertheless, there is a necessary minimum; below this minimum the discussion becomes meaningless. Consider, for example, a classical subject of biophysics: the description by telegraph equation of the nerve impulse propagation along the axon. When talking about corresponding experiments (by the way, perfectly reproducible ones) to physicists, it would be meaningless to concentrate on the fact that these experiments are usually performed on the axons of squid. Instead, we should concentrate on the fact that the physics is the same in axons of squid or any other organism, and the advantage of squid is only the fact that its neurons are big. By contrast, if the story is told about some special seaweed, and about some vaguely characterized suspension of ambiguously described bacteria, and when the data are not reproducible and, therefore, are different for other organisms — then physicists are at a loss to understand. Moreover, usually physicists are not interested in such material, assuming, with good reason, that this kind of data is not appropriate for physics.

To make a long story short, we can summarize that the review [1] does not contribute to clarification of the experimental situation in magnetobiology. To be fair, the review [1] is mostly about theory, so experiments are discussed more in their connection to the theory than on their own. Let us therefore look at what is said about the theory.

3. Theories

The central theoretical idea of the review article [1] is that of the molecular gyroscope. By molecular gyroscope authors understand a molecular group that rotates in a vacuum cavity in such a way that thermalization does not occur and the quantum rotational state remains coherent for milliseconds or even seconds. To justify the possibility of a molecular gyroscope, the authors postulate the existence of vacuum cavities inside protein molecules as big as 30 angstroms, or even bigger. They also postulate the possibility that a molecular group spins around a couple of exactly co-axial σ-bonds, practically without dissipation.

To begin with, if such a coherent molecular object could be found or artificially created, it would have found many applications far more exciting than a magnetic effect in seaweed. Using such a system, we could have attempted to build a quantum computer or, for instance, to address the question of whether our brain represents a kind of quantum computer.

Thus, we should address the question: is a molecular gyroscope possible? It would be hard to imagine. First, let us discuss the vacuum-filled cavity. The authors mention that no cavities of a size anywhere near 30 angstroms are found in the X-ray determined protein structures, but they also state correctly that this fact itself, logically, leaves open the possibility that the cavities exist in proteins in solution. However, no evidence to support such a hypothesis is presented. At the same time, whether this is a strong argument or a weak one, vacuum cavities are not expected based on the modern theoretical concepts of protein structures. Second, let us look at the issue of the lack of friction or extremely small friction. If we take the ethane molecule C_2H_6, we know that rotation is possible around the C – C bond, and there are potential barriers, due to hydrogen atoms, every 120 degrees of angle, and these barriers fluctuate along with valence angles. Moreover, the barriers themselves and their fluctuations get stronger if we replace hydrogen atoms with more bulky chemical groups typical for the molecules in biology. There was even a discussion in polymer physics some time ago on what is the leading mechanism of dissipation in polymer systems, and one of the contenders was the 'friction' between side groups during the rotational isomerization of the polymer chains. In the end this mechanism of losses was found to be a non-dominant one, but it does contribute to losses to a noticeable degree (see, for instance, [3]). In light of this fact, it is totally unclear how it might be possible to shield a molecular gyroscope from dissipation for a macroscopic time.

Can we prove the impossibility of the molecular gyroscope? Most likely — no, we cannot, for the reasons already discussed. However, we are not even facing the problem to prove the impossibility. Just as jurisprudence is impossible without the presumption of innocence, which relegates the burden of proof entirely to the prosecution, similarly science requires positive proof from the author or the inventor that his/her suggestion is possible. We, therefore, simply notice here that the possibility of the molecular gyroscope has not been proven so far. As a matter of course we leave aside here the idea (which is unlikely to be taken seriously by the *Physics – Uspekhi* readership) that the magnetic properties of diatom seaweed, or even our inability to understand them, present the desirable proof of quantum coherence.

Another realization of a similar idea is used by the authors to explain the data on diatom seaweed in terms of cyclotron resonance of certain ions. To avoid repetition, let us leave aside here the question of why the rotation of these ions is shielded from friction and dissipation; authors give an unconvincing answer to this, just as in the case of the gyroscope. Let us concentrate on the other side of the problem, namely, the fact that agreement in terms of a single parameter (in this case, the frequency) cannot serve as a proof of the theory, particularly for systems of so high a degree of complexity. For instance, what do we learn from the approximate coincidence of the average heartbeat period with the relaxation time of the slowest folding proteins? Most likely, nothing. Thus, the hypothesis of the cyclotron resonance of ions in a biological cell remains baseless experimentally and implausible theoretically.

A significant part of the review article [1] addresses what the authors call 'the kT problem': the fact that typical energies of interactions with a magnetic field are usually several orders of magnitude smaller than the thermal energy kT. To discuss this issue, the authors point out that biological systems are not equilibrium ones. This is undoubtedly true. At the same time, it is worth emphasizing that molecular biological systems are non-equilibrium in a very peculiar sense. These systems are frequently called partially-non-equilibrium, which means that there are relatively very few degrees of freedom which determine the system design, construction [4], and use for recording information and for similar purposes, while in terms of the vast majority of other degrees of freedom the system is in, or very close to, thermodynamic equilibrium. Of course, although there are few of these 'special' degrees of freedom, they are extremely important; to avoid misunderstanding, let us repeat that the system as a whole is very far from equilibrium. However, the peculiarity is that although the system is far from equilibrium, it does have a well defined temperature. Everyone who has suffered at least once from a common cold and has used a thermometer knows this fact. In this sense, the value of kT remains to play the role of a universal energetic currency, although, once again, one has to stay very much alert, because special degrees of freedom exist, they are important, and some of the 'springs' exchange energy with the thermostat incredibly slow. Moreover, it would be a mistake to think that a change of energy by a quantity smaller than kT is never of any importance. A good counterexample is the swap of two nucleotides in DNA: although the difference in energies (before the swap and after it) is totally negligible, the consequences for the organism might be grandiose and truly devastating (of course, apart from the energy change, there is also a barrier, which is usually larger than kT).

4. Conclusion

Here, a few more comments are given by way of a conclusion.

The authors of the review [1] presented a diagram showing exponential growth of magnetobiological publications over the years. The point is that every science-measuring criterion, such as the number of journals, or the number of publications, or the number of scientists, exhibits exponential growth. In all cases, the doubling period is about 10 years. Therefore, there are no grounds to state that we have witnessed an explosion of interest in magnetobiology.

It is hard to avoid mentioning the comparison of situations in such fields as magnetobiology and high temperature superconductivity. The authors of the review [1] write correctly that both fields lack satisfactory theories. However, there is also a dramatic difference in the quality and the level of experiment. The very fact of high T_c superconductivity in certain materials is perfectly reproducible, and, of course, many properties of the phenomenon are also well established. Judging by the review [1], magnetobiology is currently nowhere near this level.

The authors of the review [1] also touch on the scary issue of medical statistics. If, they say, a magnetic field increases the "probability of oncological diseases by just 1%, then the death toll in a country of 50 million people can total up to 1000 per year." To begin with, the estimate of 1% is taken literally from nowhere (just as 50 million). Even worse, this consideration brings us to the very special field of medical statistics. To appreciate how delicate this issue may be, it is enough to mention the following surprising (although understandable) fact. Massive use of antibiotics has led to a significant increase in the 'probability of oncological diseases' (to remain with the author's terminology). This is, of course, simply because in the era of antibiotics there are many people who live long enough to get cancer instead of dying earlier from tuberculosis, pneumonia, or meningitis. What we see from this example is the fact that references to medical statistics remain unconvincing as long as one does not go deep enough into the specific medical problems, which is hardly suitable in *Physics – Uspekhi* Besides, to establish reliable facts for medical statistics it is imperative that the experiments be double blind [1], and this brings us again to the issue of insufficient quality of experiments in magnetobiology.

So, what is the conclusion? The conclusion is that the review [1] failed to shed clear light on the field of magnetobiology. As before, the field is waiting for convincing experiments with the same standards of quality that are universally accepted in other fields of physics and biophysics.

Last but not least, a critical note on the magnetobiological review is likely to cause counter-critique, saying that traditional science does not like to yield to innovations. To this, it

[1] In medical experiment, to test the action of some factor (say a new pharmacological substance) on the organism, it is necessary to have two groups of patients, experimental and control. People in the former group receive the real tested substance, people in the latter group receive an inert harmless replacement, called placebo. To avoid psychological effects, which can completely mar the results, the patients should not be told whether they are receiving the real substance or the placebo (single blind experiment). But this is insufficient, and the doctor administering the pills should not know whether he/she is giving the real substance or the placebo to any given patient (double blind experiment).

is possible to reply with the words of Jean Baptiste de la Marck (1744 – 1829), commonly known as Lamarck, the real scientific revolutionary who knew well what he was speaking about: "It is better if the truth, once understood, was left for a long fight for survival, meeting less attention than merited, than if every fruit of unbound imagination was taken for granted." (inverse translation from Russian, taken from the book [5]).

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