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LETTERS TO THE EDITORS

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First principles of probability theory and some paradoxes in modern biology (comment on "21st century: what is life from the perspective of physics?" by G R Ivanitskii)

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Abstract. It is argued that a discussion of two paradoxes in the commented paper is at odds with some points of probability theory and well-known optimization theorems.

In the recent article "21st century: what is life from the perspective of physics?" published in *Physics Uspekhi* by G R Ivanitskii [1], the author addresses a few biological paradoxes and proposes their solution from the standpoint of modern physics.

After reading the article, one cannot escape from the impression that no more paradoxes central to the understanding of life remain. The facts are indeed very much otherwise. In order to demonstrate that the solutions to certain paradoxes suggested in Ref. [1] are incorrect, let us first consider some principles of probability theory. What can be regarded as the first principles of this theory in the context of the problem in question?

To begin with, it is the definition of probability itself. The probability of any event A is equal to the ratio of the number of outcomes of experiment Ω favoring realization of this event to the total number of all elementary outcomes. This means that if a state of a system is not forbidden by physical laws, it must be taken into account in the calculation of probabilities. In this case, a key notion is that of 'experiment', i.e., any action that allows finding the value of the sought quantity.

A priori probability (and related *a priori* information) is also of importance in probability theory. Indeed, suppose we have a key and m doors that should be unlocked with the key. Then, the mean number of attempts needed to open a door essentially depends on the available *a priori* information. In the absence of such information, the number of attempts is m. The more *a priori* information we have, the fewer the attempts that are needed. Of course, this observation fully refers to molecules as well and constitutes the foundation of statistical physics.

On the other hand, the proof of several theorems in the 1990s provided a basis for rather general conclusions concerning the processes of search and optimization. First and foremost is the No Free Lunch Theorem [2, 3] stating that there are no algorithms optimal for all problems. In this context, *a priori* information about a problem is of crucial importance. Evolution and behavior being actually search processes based on specific algorithms, the conclusions following from this theorem have fundamental significance.

The most debatable issue is the analysis of two paradoxes among those considered in article [1]: paradox 6 (paradox of time deficit), and paradox 10 (Buridan's ass paradox). They are discussed below.

Paradox 6 (paradox of time deficit). F Hoyle and N C Wickramasinghe compared the probability of the origin of life with that of assembling the aircraft from bits of junk. G R Ivanitskii believes this paradox is easily refuted by the fact that "the assembly of a whole from constituent elements is possible by means of the *bottom-up* strategy passing successively from small to larger blocks, i.e., from atoms and molecules to the integral organism." The author of Ref. [1] argues that it is in this way that the complication and development of living systems proceeded (block-hierarchical selection). At the same time, he does not call into question the Darwinian principle of natural selection.

However, there is a logical error in this reasoning: who (or what) should determine block composition if neither organisms nor their environment has any goal? Then, all possible blocks need to be sorted out! (This was shown in paper [4].) If it is assumed that the building-block concept is applied (i.e., evolution proceeded through self-assembling of building blocks), the key Darwinian paradigm (undirectedness of evolution) should be rejected. It will be necessary then to admit that some structures contain information on what blocks may be suitable for further assembly. In the absence of such information, a breaking down into blocks is equivalent to the complete sorting of all variants.

From the standpoint of probability theory, understanding the mechanism of evolution requires that each step be described based on a certain principle (e.g., a physical law). Therefore, an argument like 'since this block produced a good result before it may do the same now' cannot be taken as a basis of the evolution process without regard for the probability of such a process. However, the probability is essentially dependent on the availability of *a priori* information for each step. Molecular motion is governed by the laws of probability theory. This means that whatever state is not forbidden by physical laws it should be taken into account in calculations. It other words, if other block combinations are not forbidden by these laws (the modern paradigm admits no such laws), the probability that evolution will proceed by sorting out the '*right*' blocks turns out to be exponentially small because the total number of blocks is exponentially large.

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The mechanism of evolution by means of block-hierarchical selection could have been practicable only if *a priori* information had been available about what would be good for a given species in the future. A universal mechanism of this type is nonexistent because it would be at variance with the above No Free Lunch Theorem.

Had such a mechanism existed, it could have been used to easily resolve all NP (nondeterministic polynomial time)-hard (requiring an exponentially large number of steps) problems, e.g. computer password hacking.

The situation is not saved by the fact that the problem of evolution, unlike the password problem, implies more than one solution. Such a problem was considered in paper [5], taking account of real inter- and intraspecies differences; it was shown that the problem remains NP-hard in the absence of *a priori* information and cannot be realized within real times.

In other words, one has either to admit the *a priori* undirectedness of evolutionary processes as a basic principle of Darwinism implying exponentially large times of evolution (to recall, Darwin's theory was proposed in opposition to religious beliefs that by definition recognize *a priori* directedness) or to utilize certain algorithms substantially reducing the time of evolution (in accordance with experimental data). In the latter case, one has to renounce the idea of *a priori* undirectedness as a basis of evolution theory, i.e., to assume that evolution is somehow *a priori* directed.

***Paradox 10* (*Buridan's ass paradox or the problem of knowledge acquisition*).** According to G R Ivanitskii, this paradox merely reduces to a system of two equivalent states choosing either of them; its resolution implies a noise that makes such transition inevitable. In such a formulation of the problem, the substitution of notions and the problem itself takes place (accordingly, the name of the paradox does not reflect the essence of the problem). The problem is not how a system comes to one of its equivalent states (that it does occur via noise was shown long ago for physical systems). The problem is actually where new knowledge comes from. This is quite a different matter! Why should a state adequate to the altered environment arise in a system, e.g., the human brain? If such an event is algorithmically (unambiguously) determined, no knowledge is gained; if such a state was not inherent in the system, the question is raised: What may be the mechanism of its origin [6]? G R Ivanitskii advocates randomness as a mechanism of cognizing. However, the question arises how high the probability of the *random* acquisition of knowledge is? In all likelihood, such a probability is negligibly small because the total number of possible variants of synaptic connections between neurons is exponentially large. This brings us back to sorting out a large number of quantities that would take an exponentially great amount of time.

Further, the author of review [1] simply postulates that the subjects of set X are capable of learning (see page 348) but provide no definition (either mathematical or logical) of such an ability — that is, the author postulates what he then tries to prove.

He cites publications that in his opinion describe self-learning neurocomputers [7, 8]. However, the fact that a system is called self-learning does not mean that it actually has a learning ability of its own. The self-learning of neurocomputers is just a conventional term, as is clear from the article by D S Chernavskii [7], where a paragraph reads as follows: "A neurocomputer begins to operate after being presented with a standard pattern... Presentation of the pattern — or, which is the same, input of the primary set of attributes — is performed in the following manner. At the initial instant, the external links are used to send signals that switch certain elements into the active state. The pattern is applied for some time, during which the links are 'taught' (the conductivity of links that carry a current decreases)... After teaching, the processor will be able to recognize the presented (examined) objects, relating them to one of the classes (from those that it has been taught)." It is humans who use external links to send signals and thereby feed new information into the neurocomputer (i.e., prepare it). Evidently, no neurocomputer would work, if left to its own devices, without such preparation.

In a word, neurocomputers cannot gain knowledge by themselves.

If a certain universal algorithm of acquiring new useful information existed, it would once again violate the No Free Lunch Theorem. This means that such an algorithm could only operate when the information to be acquired was known *a priori*. In this case, however, the information is not new and contains nothing beyond what is already embedded in the system.

Thus, there are currently no simple solutions to the paradoxes under consideration. Further theoretical and experimental studies are needed to clarify whether a shift of the paradigm might be helpful in understanding living systems.

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