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Comment

Living systems do not minimize free energy
Comment on "Answering Schrödinger's question: A free-energy formulation" by Maxwell James Dèsormeau Ramstead et al.

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The paper [1] is certainly very useful and important for understanding living systems (e.g. brain) as adaptive, self-organizing patterns. There is no need to enumerate all advantages of the paper, they are obvious. The purpose of my brief comment is to discuss one issue which, as I see it, was not thought out by the authors well enough. As a consequence, their ideas do not find as wide distribution as they otherwise could have found. This issue is related to the name selected for the principle forming the basis of their approach: free-energy principle (FEP). According to the sec. 2.1 [1]: "It asserts that all biological systems maintain their integrity by actively reducing the disorder or dispersion (i.e., entropy) of their sensory and physiological states by minimizing their variational free energy." Let us note that the authors suggested different names for the principle in their earlier works (an objective function, a function of the ensemble density encoded by the organism's configuration and the sensory data to which it is exposed, etc.), and explicitly and correctly mentioned that the free energy and entropy considered by them had nothing in common with the quantities employed in physics [2,3]. It is also obvious that a purely information-theoretic approach used by the authors with regard to the problems under study allows many other wordings and interpretations. However, in spite of this fact, in their last papers as well as in the present paper, the authors choose specifically FEP. Apparently, it may be explained by the intent to additionally base their approach on the foundation of statistical thermodynamics and therefore to demonstrate the universality of the described method. However, this is exactly what might cause misunderstandings specifically among physicists and consequently in their rejection and ignoring of FEP. The physical analogy employed by the authors has the following fundamental inconsistencies:

1. In physics, free energy is used to describe processes occurring at constant temperatures and volumes. In physics, the minimum free energy corresponds to an equilibrium state to which an isochoric–isothermal system relaxes [4,5]. It is obvious that the biological systems considered by the authors are fundamentally non-equilibrium, do not seek equilibrium, and, in most cases, do not retain their volumes as they develop. For a biological system, the equilibrium means death, decay. Therefore, to base the idea of life on FEP is the same as to state that the pursuit

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of death is the purpose and meaning of life. In order to consider processes addressed by the authors, one needs functionals employed in non-equilibrium rather than equilibrium thermodynamics [6–8]. Specifically, I would like to draw their attention to the rate of change of the Gibbs energy with time, or entropy production (the maximum entropy production principle can be useful here [7,9–12]).
2. There is a persistent misunderstanding among non-physicists that physical entropy is related to disorder. This analogy can also be found in the author's paper [1]. Nevertheless, there is no direct connection between a value of physical entropy and a system's degree of order. This question has been repeatedly discussed in the literature (see, e.g. [10] and references therein). Depending of the method of introduction, informational entropy can be directly related to some order. However, informational entropy has no connection to the second law of thermodynamics, i.e. to the statement that processes in an isolated system are accompanied by an increase of physical entropy. That is why an extreme cautiousness is necessary when dealing with the concept of entropy and principles related thereto.

The comments given herein are important because this journal requires a special degree of rigor as it mainly seeks to explain the physics of living systems. Another reason is that Schrödinger's question used in the title of the paper under discussion and forming its main subject represents only the first half of the name of the famous book by E. Schrödinger [13]. The second part of this book's name is "The Physical Aspect of the Living Cell." The renowned physicist strove to understand life specifically from the viewpoint of physics. And he tried to use the concept of physical entropy as one of his tools. If readers want to understand life from the perspective of physics, the recommended papers are [10,14]. The paper at hand [1] considers life from the viewpoint of neuroscience, system and informational theory. This is very important; however, in order to evoke interest among physicists and attract them, the authors need to take the above recommendations into account.

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