Review of: "Systematically Challenging Three Prevailing Notions About Entropy and Life"

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This is an interesting collaboration, yet different, containing some strongly worded views. Within this 'strong statement paradigm,' I will offer some comments:

The first notion, challenged by the authors, is the concept of entropy as a measure of disorder. The underlying problem is, of course, the seemingly contradictory issues that concern the fundamental understanding of certain deep-seated properties of micro-macro correlates, in particular the relations between thermodynamical laws and statistical mechanics. In general, these theories have a solid deductive/axiomatic origin, which combined yields very general conclusions on a purely macroscopic level of description from original statistical postulates.

This understanding has evolved to such a concrete experimental stage that fundamental constants, such as Boltzmann's constant *k* or Avogadro's number, NA, have currently been exactly defined, see Norden, Mol. Front. J. 2021, 5, 1-13. It is indeed surprising that such a simple notion as entropy, as defined by the founding fathers, has today continued to remain at center stage, despite more than 150 years of scientific enterprise. The authors confront the *J*/*k* unit of entropy as revealing an analogy with energy rather than its foremost underlying relation to statistics, as presently promoted by the exact definition of *k*.

A related challenge concerns the extensions of the entropy concept to quantum mechanics and further to life sciences. We are all familiar with von Neumann's ensemble theory and his celebrated entropy formula, see e.g., a consistent axiomatic trace algebra formulation of statistical mechanics including modern reductionism, the genetic code, and hereditary information, Löwdin, Found. Phys. 1992, 22, 41-105. I do not see here that the present challenge of the entropy concept will be intemperate, even as applicable to both equilibrium and more general situations, see e.g., the work of the Brussel-Austin School, founded by Ilya Prigogine.

The second difficult question concerns life processes and the concept of negative entropy, which also relates intimately to the third and final challenge, the increasing disorder of systems due to the second law of thermodynamics, including a number of examples from chemistry and biology, where tentative interpretations of inconsistency are implied and concluded. Let us start with the list 'five types of changes,' where the last two demonstrate uneven energy distributions due to an increase of its entropy seemingly contradicting the third example of even energy distribution in an isolated system according to the second law. This conclusion, including some other examples mentioned in the paper (plants, dissipation from humans, see later below), is incorrect and misleading.

Take, for instance, the process of photosynthesis in plants. Modern classical-quantum formulations on subdynamics and correlations (consistent with the 2nd law) say that the total entropy change per unit time, dS, of a system subject to a steady flow of energy-entropy entails a decomposition of the form $dS = dSi + dSp$, where dSi is the entropic gain due to the work performed in the process (photosynthesis) and dSp is the associated entropy production, due to irreversible processes in the plant. The associated energy changes are similarly given from the associated changes in the free energy $F = U – ST$. These problems, including temperature (and time), call for an analysis beyond the canonical ensemble. This view can straightforwardly be extended to handle biological systems, including the genetic code, etc., without violating the second law. This includes, in particular, the seven examples given in section 3.4. As a representative example, let us take number 7, a thirsty human man drinking cold water. The man is hot, and the water is cold, so the temperature of the man is higher than the system of water molecules. Note that the entropy of the separate systems, water-man, is lower than the mixed system, water and man, coming into equilibrium after a certain time. From an analysis of the whole cooling process, we can deduce the following energy-entropy exchanges: energy in terms of water enters the man. After the biological cooling process, i.e., the work carried out by the system, the water leaves the man. First law: the energy coming into the body equals the (cooling) work plus the energy of the excreted water.

Second law: the entropy difference between the cooling water (at a temperature lower than the man) and the excreted water (hotter than the original water particles) will, in a steady-state scenario (OBS! this is not an equilibrium situation), equal the entropic gain that presumably ‘made the man well at ease’. Similarly, the developmental process from a fertilized egg into a prenatal baby is commensurate with a substantial entropy production matching a corresponding entropy gain, all within the second law of thermodynamics. The simplified narratives above can be made more detailed by introducing the time scales for each chemical/biological process, etc., also generalizing Schrödinger’s concept of negentropy to consider a non-contradictory concept of information as well as the notion of free energy in complex enough biological systems.

It is obvious that the present arguments, not violating the second law, are commensurate with Schrödinger’s three viewpoints: (i) entropy represents disorder and is detrimental to animals, (ii) animals rely on food to reduce their entropy and generate order, and (iii) that animal food contains less entropy than animal excreta. The inherited genes accumulating through long-term evolution through natural selection belong naturally in this scientific paradigm. Obviously, this motivates a significant modification in the colors and arrows in Fig. 2.