

Peer Review

Review of: "Mechanisms of Glycolysis and Fermentation: A Non-Equilibrium Thermodynamics Perspective"

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The manuscript has been improved significantly, but it could still be enhanced in some areas. Many biologists who have not followed the discussions of “Maxwell zombies” would find it difficult to follow the logic of the manuscript. For example, here is a quote from one of the citations early in the manuscript that lays out the argument clearly:

“Unlike the original Maxwell demon, many contemporary challenges are big (macroscopic, hence not prone to failure via thermal fluctuations); dumb (do not carry out calculations, making information erasure irrelevant); and durable (more difficult to dispel than Maxwell’s demon), hence their name: Maxwell zombies”.

The authors may want to make their description of Maxwell zombies more detailed, as in the above quotation.

Other examples where confusion may arise include the following sentence:

“This review builds on a scientific concept of metabolism by introducing that glycolytically generated energy is either transformed into ATP or drives a biological process.”

The current understanding of glycolysis is that it generates two net ATP molecules and that it also drives the conversion of glucose to pyruvate, which is a biological process. The authors should make it clear how their interpretation is substantively different from the classical thermodynamic view. This also relates to their focus on protons and MCT; the current thinking is that proton translocation is merely intended to maintain pH balance, whereas the authors are suggesting that the proton is a critical aspect of energy derivation and use in maintaining the non-equilibrium condition.

Minor points: in Figure 3, the right side of the figure is labeled “Energy particledynamics” rather than “Energy particle dynamics”. In Pathway 3, Pyruvatehydrogenase should be two words.

As noted, the manuscript has been substantially improved, but minor modifications are recommended.

Declarations

Potential competing interests: No potential competing interests to declare.