Review of: "A Law for Irreversible Thermodynamics? Synergy Increases Free Energy by Decreasing Entropy"

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Potential competing interests: No potential competing interests to declare.

1. Synergy is purely an information theoretic concept and derives from entropy only. The exact definition of bivariate synergy is clearly given as follows: (See for example Anastassiou, Dimitris. "Computational analysis of the synergy among multiple interacting genes." Molecular systems biology 3.1 (2007): 83.)

Given two factors G1, G2 and a phenotype C:

• The information that G1 provides about C is equal to I(G1;C)

• The information that G2 provides about C is equal to I(G2;C)

• The information that G1 and G2 jointly provide about C is equal to I(G1,G2;C)

The synergy between G1 and G2 with respect to C is then defined as

Syn(G1,G2;C)=I(G1,G2;C)-[I(G1;C)+I(G2;C)]

The right hand side is a function of entropy only (See . Therefore synergy is purely an entropic variable. When we look at the equation which the author as well cites in words:

deltaG=deltaU-TdeltaS

we conclude that entropy, therefore synergy, may change independently of energy. Therefore it is difficult to understand the whole point of the paper which reads as ‘Synergy Increases Free Energy by Decreasing Entropy’. This sentence will be true only if certain constraints are imposed on energy changes.

2. Comment on ‘With advances in irreversible thermodynamics applied to open systems, as contrasted with classical equilibrium thermodynamics that apply to closed systems.’

Equilibrium thermodynamics applies to open systems as well.See for example Callen, Herbert B. "Thermodynamics and an Introduction to Thermostatistics." (1998)

3. I would feel more confident if there were no typing and language errors in the present form of the manuscript.