Review of: "The evolution of E. coli is NOT driven by genetic variance but by thermodynamics."

Shokhan M. Al-Barzinji[1]

1 University of Anbar, Iraq

Potential competing interests: No potential competing interests to declare.

The paper presents a radical challenge not just to evolutionary biology, but also to modern genetics, including GWAS, which depend on the premise that genetic mutations directly cause disease and traits. By rejecting the role of genetic mutations in driving evolution, the paper calls into question the validity of much contemporary research in genetics and human health. In conclusion, Baverstock and Annila's paper posits a novel, thermodynamics-based theory of evolution, suggesting that the evolutionary process is much more about systems seeking to minimize energy and achieve thermodynamic equilibrium than about genetic variation and mutation. The implications are profound, potentially changing how scientists view the very mechanisms of evolution, inheritance, and adaptation across biological and non-biological systems alike.

To improve the paper "The evolution of E. coli is NOT driven by genetic variance but by thermodynamics," several aspects can be strengthened in terms of clarity, argumentation, empirical support, and engagement with existing literature. Below are specific suggestions for improvement:

1. While the paper emphasizes the principle of least action and the Second Law of Thermodynamics, it does not fully explain how these laws specifically translate to the evolutionary dynamics of *E. coli*. The authors should offer a more detailed mechanistic model linking thermodynamic principles to biological processes. For example, they could explore how the concept of entropy and energy dissipation could be applied to molecular evolution, gene expression, or metabolic networks in the bacterial populations.
2. The current paper underplays the role of genetic processes. A clearer explanation of how thermodynamics might complement genetic processes (rather than entirely replace them) could make the argument more robust. For example, they could consider how genetic variation interacts with thermodynamic principles to shape evolutionary trajectories.
3. The paper relies on the LTEE data, but the connection between thermodynamic laws and the observed data is not empirically validated. The authors should consider conducting additional experiments or simulations that directly link thermodynamic efficiency or entropy changes with fitness or population dynamics in the LTEE or other experimental systems.
4. While the paper criticizes Fisher's Genetical Theory of Natural Selection, it could benefit from a more thorough engagement with modern genetic theories, such as epistasis, pleiotropy, and trade-offs. These mechanisms could potentially reconcile the authors' thermodynamic argument with the genetic variance observed in the LTEE. The

authors should address how these concepts might fit into their thermodynamic framework or why they do not.

5. The paper critiques the Modern Synthesis without sufficiently engaging with counterarguments or responses that might attempt to reconcile genetic variation with thermodynamic processes. A deeper review of the literature on how thermodynamic principles have been applied in evolutionary biology could strengthen the paper's position. This might include discussing works that apply non-equilibrium thermodynamics to biological systems or evolutionary processes.
6. The critique of Genome-Wide Association Studies (GWAS) seems only partially developed. A more comprehensive review of the limitations of GWAS in the context of evolutionary theory would strengthen the argument. The authors could address why GWAS has not contributed significantly to understanding complex traits and how this relates to their broader claim that genetic mutations do not drive evolution.