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

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Potential competing interests: No potential competing interests to declare.

The paper presents a compelling and controversial narrative that questions foundational concepts in genetics and evolution. By emphasizing thermodynamics as the primary evolutionary driver, it challenges the reductionist gene-centric view of life. However, the universality of these conclusions and their implications for broader biological systems remain to be thoroughly tested. While it may not dismantle the Modern Synthesis entirely, the work invites deeper integration of physical principles into evolutionary biology and inspires a reevaluation of long-held assumptions. Further research should aim to reconcile thermodynamics with molecular and genetic insights rather than replace one framework with another.

Strengths:

1. The paper courageously challenges entrenched scientific paradigms, sparking necessary debates in evolutionary biology.
2. Findings from the LTEE provide a robust experimental foundation, though interpretations are contentious.
3. Linking evolution to thermodynamic principles offers a novel perspective that could unify biology with physics.

Weaknesses and Areas for Improvement:

1. The leap from *E. coli* observations to universal evolutionary laws requires broader empirical evidence.
2. The dismissal of genetic explanations like epistasis may overlook nuances in their application and evidence.
3. While the principle of least action is invoked, the specific biochemical or physical mechanisms driving this process in *E. coli* evolution remain underexplored.