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.

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1. Overall Impression:

The article presents a comprehensive review of the long-term evolution experiment (LTEE) of E. coli, drawing significant conclusions regarding the relationship between genetic variation and the observed fitness trajectories. The manuscript is well-referenced, suggesting a thorough literature survey.

2. Strengths:

Data Presentation: The presented data, especially from the LTEE, is compelling and has been detailed extensively. This foundation provides a strong base for the subsequent arguments made in the manuscript.

Literature Review: The manuscript cites several reputable sources, suggesting a comprehensive survey of current and past literature.

Scope: The implications of the LTEE results are extensively discussed, providing a broad perspective on the topic of evolution, thermodynamics, and genetics.

3. Concerns and Recommendations:

Bold Claims: The paper makes strong claims, like the overturning of Johannsen’s genotype conception and Fisher’s Genetical Theory of Natural Selection. While the evidence is intriguing, further studies might be needed to validate such overarching conclusions.

Overemphasis on LTEE: The heavy reliance on the LTEE results might introduce bias. While the LTEE is a unique and remarkable experiment, incorporating additional independent studies could bolster the article's claims.

Clarity in Definitions: The article occasionally delves into terminologies and concepts without adequate introductions, like the principle of least action and the 2nd Law of Thermodynamics. For readers unfamiliar with these concepts, a concise introduction or a brief explanation might be beneficial.

Discussion on GWAS: The conclusion on the ineffectiveness of Genome-Wide Association Studies (GWAS) seems slightly off-topic. While the argument is understood within the context of the paper, delving deeper into this topic might

detract from the main focus. The authors could consider streamlining this section or providing more evidence to directly link it