

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

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Modern Synthesis clearly needs further developments to constitute a complete theory for organic evolution. However, this paper attacks Modern Synthesis in wrong ways by cherry-picking evidence and misinterpreting the data to come to wrong conclusions.

For conclusion 1, shared fitness trajectories do not violate Fisher's theory. The seeming lack of correlation between growth rate increase and the amount of mutations can be explained by the emergence of mutator strains (Sniegowski 1997). Many of the 12 populations evolved to be hypermutagenic so that they accumulate mutations at rates one to two orders of magnitude higher than the ancestor.

For conclusion 2, I agree with the authors that thermodynamics plays a role in LTEE experiments. The simple environment, in which sufficient nutrients are provided for bacteria to grow, and stresses are absent, selects for optimization of growth rate. Increasing growth rate in the face of a fixed amount of nutrients boils down to the stream-lining of biochemistry of the metabolic networks, essentially improving thermodynamic economy. However, this thermodynamic change does not contradict growth rate increase by adaptive mutations. Indeed, the thermodynamic change is caused by mutations. Such examples abound in literature.

For conclusion 3, a major discovery from LTEE experiments is the innovation of citrate metabolism, which changed the course of evolution and is clearly a case of adaptation. A hall mark E. coli as a bacterial species is its inability to use citric acid as carbon source. However, citrate-eating mutants emerged from LTEE experiments and took over several populations. Their genetic and molecular mechanisms have been elucidated (Blount 2008).

In summary, the authors' attack on Modern Synthesis based on their interpretation of LTEE experiments is unfounded. Instead of overthrowing Modern Synthesis, a more fruitful way forward is to incorporate functional components into the framework of Modern Synthesis. For instance, what are the molecular and biochemical mechanisms of fitness at a given environment? and how to formulate these mechanisms into the language of change in allele frequencies in a population?

Blount ZD et al PNAS 2008

Sniegowski PD et al Nature 1997

