

# 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.

This paper seems to be based on confusion between the rate at which mutations appear and the fitness effects of each mutation, as well as the difference between the rate at which mutations appear and the rate at which they fix.

The authors say that "it is clear that the rate of fitness increase was at a maximum when the accrual of mutations was at a minimum" and say that this is a contradiction of classical evolutionary theory. However, it makes perfect sense from that perspective. When adapting to a new environment, the availability of mutations with a large fitness increase is higher, and therefore few mutations are needed for a large increase in fitness. The main process then is the fixation of those mutations. As time progresses, the big-fitness-increase mutations run out and the lower ones have a chance to fix. Note that they could appear earlier, but they would simply get outcompeted by the higher ones and not fix. As there are more of these lower-fitness -increase mutations, the rate at which mutations fix increases.

They say that "the improbability of all 12 LTEE cultures having identical fitness trajectories ..." is an argument. But fitness is a really macro-scale variable, so it is quite unsurprising that the trajectories are similar, as they are selected from the same distribution of available mutations.

They say that the appearance of power laws is proof that the effect is thermodynamic, but power laws appear in multiple contexts, and invoke the second law of thermodynamics. Living systems are far from equilibrium, and therefore there is no basis for affirming that in them "free energy is invariably consumed in the least time". A very nice discussion of the relationship between entropy and life is given in *What is life?* by Erwin Schrödinger. To summarize, cells decrease their entropy by increasing external entropy and that increases the total entropy. But it is implicit in the entropy inside the cell is decreasing.

Their confusion about the basic definitions is clear from their statement "Furthermore, geneticists widely assume that the majority of mutations are deleterious, not beneficial, by a large margin, even 1,000,000 to 1 (Elena and Lenski 1998). Accordingly, one would expect that, initially, fitness would *decrease* with each generation." Indeed, most mutations *that appear* are deleterious, but they don't fix. Most mutations *that fix* are neutral or positive.

