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

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I must first state that I appreciate thoughts out of the established scientific concepts as they stimulate discussion and innovation and I will support their publication.

On the other end these innovative opinions should be based on solid scientific bases. The paper by Baverstock and Annila appears rather innovative, however, for me, it is little based on scientific data. In addition, concerning innovation, it seems that the paper does not add too much to what was already more extensively published by Baverstock in 2021, on the contrary, the very short presentation, with little analysis and detailed reasoning, make it difficult to appreciate its originality.

I will try to discuss the paper following its progress.

Frontispiece, “Critics to Modern synthesis”: Authors should be aware that Modern synthesis is now widely considered no more modern, as extensively reported in the 2010 collective book " The extended synthesis" by Pigliucci and Muller, and this too is by now in part outdated. So I don’t see the point in challenging modern synthesis. The author should recognize that evolutionary theories update continuously with new findings, and also that different versions of the theory fit better into different biological systems, there isn’t one true evolutionary theory explaining all.

Introduction,

“the evolution of E. coli is NOT driven by genetic variance but by thermodynamics”: Authors should explain why should mutation and thermodynamics be in contrast, biology does not exclude thermodynamics laws. In addition, mutations do not "drive" (whatever drive means) evolution, mutations generate variation on which natural selection (environment, in the broadest definition) acts to select the fit varieties.

Evidence,

“Unique trajectory”, “identical power law trajectories”: this seems not completely true, the cited paper by Lenski and Trevisano emphasizes diversification of the different evolving cultures and in fact they mention the J. Monod book on “Chance and necessity” as both participating in that evolutionary experiment.

“the rate of fitness increase was at a maximum when the accrual of mutations was at a minimum”. Here the author should discuss the fact that the contribution of each mutation to the increase of fitness can be very high or very low (down to zero

for neutral mutations) depending on which DNA sequence is mutated then, trying to correlate the accrual of mutations to increase in fitness has little meaning without defining the effect of these particular mutations on the fitness.

Conclusion 1,

“identical fitness trajectories” the authors should appreciate that the trajectory could be identical but the outcome of the cultures are different, see above.

“the E. coli evolve independently of the mutations”, however, it should be considered that mutations are necessary, there is no evolution (and no life) without mutations.

Conclusion 2

“the power law characteristic…” I agree that laws of thermodynamic apply to natural world, however this seems too generic, how this apply to biology across scales, scopes etc. should be proved, or solid references given.

Conclusion 3

“mutations do not functionally influence the evolution of E.coli”: Authors should clarify where does this conclusion come from? Actually we don't know what function each mutation can affect in that particular environment and genetic background, then we cannot infer their effect on fitness.

“genes cannot be Mendel’s units of inheritance” Authors should explain what Mendel unit of inheritance have to do with adaptation?

“Instead, the phenotypes of the gametes that fuse into the zygote must be accountable” Authors should consider that gametes are single cell and try to define what they mean mentioning their phenotype. In addition, gametes belong to sexually reproducing organisms, their biology does not apply to E.coli.

Discussion

“this experiment falsifies Fisher’s Genetical Theory of Natural Selection”. Authors surely know that Fisher theory is outdated anyway and is based on sexual reproduction which does not occur in E.coli.

“The fitness is increasing at its maximum rate while the accrued mutations (genetic

variance) are very low, next to zero” As stated by the authors of the referred paper, fitness is measured as relative to another genotype (in this case the ancestral), so it is expected that at the beginning the fitness grows very fast and slow down as the adaptation of the cultures to the environment increases, while mutations continue to occur with less appreciable effect on fitness. In addition, mutation can have very different effects on fitness and deleterious mutations can become neutral as the genotype of the cell change (see table 2 of Barrick, Yu et al 2009).

“12 independent cultures have identical fitness trajectories despite diverse spectra of mutations” The cultures were not identical, the trajectory is the same (all tend to increase adaptation to the environment) but there are variations depending

on which mutation occurred in each particular culture.

"..It says a system will minimize free energy…" This, if true, but I am not sure really proven for biological systems, does not exclude the role of mutation as, without mutations evolution does not occur.

"Despite this extensive use, no clear mechanism has been identified…" this is untrue, epistasis have been widely demonstrated by thousands of experimental evidences. Moore 2003 appears as a misleading citation, first, the paper is a strong contribution to considering epistasis in genetics; second, it list different successful methods to detect epistasis, I think the sentence mentioned is put out of the context.

"Early studies (Elena and Lenski 1997) with E. coli…" This also appears as a misleading reference as the paper deals with the hypothesis that gene interaction is involved in the evolution of sex, while there is plenty of evidence of the effect of gene interaction on fitness.

"we ask why epistasis would produce identical profiles for fitness but not for cell size" the simple answer in my opinion is that in this particular experiment fitness and cell size are the outcome of different genetic and physiological processes.

"genetic variation does NOT drive evolution" authors can see above on the role of selection. I think that a possible mistake is considering genetic variations, mutations, as all identical in term of evolution.

"evolution is a thermodynamic process," I agree with the authors that stating that evolution is a thermodynamic process is possibly true, as it is true for many natural processes, but I think is of little use and definitely not heuristic; it seems to me as to say that evolution is a natural process.

"genes cannot be Mendel's units of inheritance follow conclusion 1 and 2" I cannot see why conclusion 1 and 2 are related to inheritance? As far as I understood, conclusion 1 is about fitness, conclusion 2 is about power low and thermodynamics.

"although the gene sequence change is inherited, it does not influence the cellular phenotype" authors must recognize that mutations can change the color in plants and animals, the phenotype, and these are selectable traits which can influence evolution.

"GWA studies have not contributed to measurable public health advances" I advise the authors that this reference is not a trustworthy one, the authors being clinical virologists with no experience in medical genetics and the journal is one reporting opinions and ranked among "history and philosophy of science". In addition, it seems to me an incongruous statement, why should we measure the role of genes in inheritance by the success of a particular kind of genetic test?

Overall conclusion

"The LTEE has overturned Johannsen's genotype…" As I said above, this only means that theories develop with scientific progress, not that mutations are not necessary for evolution.