EVOLUTIONARY THEORY

The early origin of cooperation

The physical linkage of the first self-replicating molecules is likely to have been selected based on their capacity to perform cooperative catalysis.

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Few fields of biology are darker than the origin of life. We debate not only where and how life started, but also the origin of all major components of the cell, which of them came first, and even how to ask those questions[1]. One of the most contentious arguments is how to apply the evolutionary theory to the period before genes and genomes were available to be selected. On the one hand, the elegant simplicity of natural selection suggests a broad application, whenever inherited variation exists subject to environmental pressure. On the other hand, the traditionally narrow interpretation of Darwinism as competition selecting the fittest has often neglected that the fittest is a cooperative and dynamic unit. This unit can be an animal with a more efficient gut microbiome, or a multicellular organism with specialized cells that expand phenotypes, but also (particularly interesting for origins research) a single cell itself with millions of proteins and metabolites coordinated in enhancing growth and replication[2,3]. Darwin did highlight cooperation in his later work, but he could not in his time see any of the above; or the autocatalytic character of metabolic networks, the tight coordination of protein and RNA in a ribosome, and the profuse lateral gene transfer and metabolite exchange in microbial communities (Fig. 1). It is the responsibility of modern biology to tackle this complex interdependency, and beyond — to look for its origins. Writing in *Nature Ecology & Evolution*, Levin and colleagues[4] set the theoretical ground for the selection of cooperation at a very early stage, that of ancient replicative catalysis.

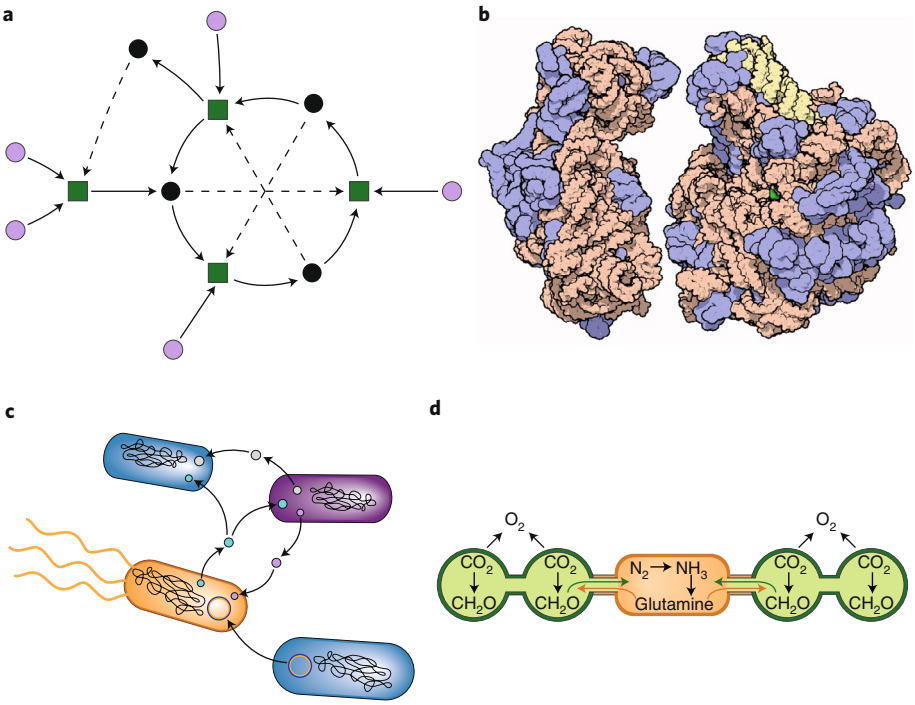

Fig. 1 | Molecular cooperation at different levels of complexity. a, An autocatalytic network of chemical reactions (green squares) forms spontaneously from starting food molecules (violet circles), creating new intermediates (black circles). Solid arrows indicate molecule consumption or production by reactions, dotted arrows denote catalysis exerted by molecules on reactions. **b**, RNA (orange and yellow), protein (blue) and ions are required to assemble and together form the active ribosomal complex. **c**, Prokaryotes (shown as rod-shaped cells) exchange metabolites (green, grey and violet circles) and genes (represented in plastids, as coloured circumferences) that promote collective fitness. **d**, Heterocysts (in orange) are cyanobacterial cells with differential gene expression and distinctive biochemical networks specialized in nitrogen fixation. Image in **b** courtesy of the RCSB PDB-101's Molecule of the Month and David S. Goodsell.

Levin et al. model cooperation between autocatalytic replicators. Picture two independent populations of molecules, which we can call Cats and Stickers, which catalyse their own replication at distinct baseline rates. They can also bind, forming Cat–Sticker complexes. In complexes, Cats and Stickers replicate at a higher rate than they do alone, for example through an induced conformational change or a beneficial waste product. Moreover, Cat and Sticker can mutate, and gain new features: a mutant Cat can catalyse the replication of Stickers as well, and a mutant Sticker binds tighter to a Cat than a wildtype Sticker would. Given these assumptions, Levin et al. simulate the replication of Cats, Stickers and their mutants, and ask: who survives? The model considers several parameters, such as rates of self-replication, destruction, complex formation, by-product benefits, proximity and dissociation. The answers are forthright: starting with Cats and Stickers, if only Cats mutate they will die; if only Stickers mutate, they can thrive, but only if their benefits to the pair are sufficiently large. But if both Cats and Stickers mutate, a new winning combination emerges: both mutants will thrive and no longer be rare.

Levin et al. explore the dynamics of the very beginnings of a type of collective (or network) autocatalysis, which has been familiar to origins studies for quite some time[5,6]. But collective autocatalysis — and especially, as done by Levin et al., the investigation of its emergence — still

brings much-required fresh air and new insights to heated debates on the origin of life. This is because it applies equally well to RNA or peptide worlds and metabolism-first theories. Cells are autocatalytic, for they require themselves to emerge anew, so it is most parsimonious to assume that the precursors of cells were also collective autocatalytic systems with mutually catalytic subcomponents[7] involving universal biomolecules.

Two features of the model by Levin et al. are less familiar. First, they demonstrate that physical association can lead to both fitness and complexity, by returning the benefits of cooperative catalysis to cooperators and their copies. Second, the model takes the focus away from the environment and onto the individual molecules in the search for the origin of cooperation. Although some of the above-mentioned model parameters must relate to, and reflect environmental conditions, these can now be circumvented by properties of the individual molecules, if they are powerful enough. This fits with known properties of molecules that can be mechanistic causes for chemical selection, such as in the preferential oligomerization of proteinaceous amino acids[8] and the spontaneous emergence of self-replicators[9].

Levin et al. suggest that their model is also relevant for the origin of a primitive genome. The coevolution of physical linkage and catalytic cooperation is required for the origin of numerous actors in the cell, such as in potential 'selfish cooperatives' forming protogenomic ensembles[10], but also non-encoded heteromeric proteins and holoenzymes that associate with cofactors. However, the origin of the genome also requires the evolution of the genetic code, which is a layer of complexity extending beyond the genome's structural features. The largest basic research science prize in history is still on offer for the demonstration of a natural origin of genetic code from chemical organization[11].

These are exciting times for those peeking into the dark. One must consider that at the origin of genomes, and life, molecules cooperated as they do now in metabolic networks, ribosomes, cells and multicellular ensembles of increasing complexity (Fig. 1). And why did molecules cooperate? Because by doing so they become a more successful whole, one that is naturally selected. ❐

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References

1. Scharf, C. et al. *Astrobiology* **15**, 1031–1042 (2015).
2. Gould, S. J. *The Structure of Evolutionary Theory* (Harvard Univ. Press, 2002).
3. Penny, D. *Biol. Direct* **10**, 26 (2014).
4. Levin, S. R., Gandon, S. & West, S. A. *Nat. Ecol. Evol.* https://doi.org/10.1038/s41559-019-1039-3 (2019).
5. Dyson, F. J. *J. Mol. Evol.* **18**, 344–350 (1982).
6. Kauffman, S. A. *Life* **1**, 34–48 (2011).
7. Markovitch, O. & Lancet, D. *Artif. Life* **18**, 243–266 (2012).
8. Frenkel-Pinter, M. et al. *Proc. Natl Acad. Sci. USA* **116**, 16338–16346 (2019).
9. Malakoutikhah, M. et al. *J. Am. Chem. Soc.* **135**, 18406–18417 (2013).
10. Koonin, E. V. & Martin, W. *Trends Genet.* **21**, 647–654 (2005).
11. Origin Of Life: $10 Million Prize at the Royal Society. *Voices from Oxford* https://go.nature.com/2RiOwdq (July 2019).

Competing interests

The author declares no competing interests.