Stable majorities

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Rifted rocks riddled with water-filled pores and steep temperature gradients: Prebiotic informational biomolecules could have been formed in such a setting at the dawn of life. Credit: Dieter Braun

How could prebiotic information-bearing DNA sequences survive in the face of competition from a vast excess of shorter molecules with random sequences? LMU scientists now show that a relatively simple mechanism could have done the trick.

Life is a matter of energy and information—lots of information—more specifically, the hereditary information stored in the DNA that is present in all living cells. Thus the coding capacity of the nuclear DNA found in every mammalian cell is equivalent to some 700 Mbytes. This information has accumulated and been successfully transmitted over billions of years of evolution. For researchers like Dieter Braun (Professor of Systems Biophysics at LMU) who are interested in understanding how life on Earth originated, one of the many questions this raises is how the very first informational molecules that were formed under prebiotic conditions could have outcompeted their many rivals with much smaller information content.

In collaboration with his colleague Professor Shoichi Toyabe of Tohoku University in Sendai (Japan), who has already made many working visits to his laboratory, Braun now reports a set of experiments and simulations which suggests that quite a simple mechanism can in principle resolve the paradox, and could have enabled primordial informational sequences to survive. That in turn implies that any useful genetic information which happened to be encoded in such sequences need not have vanished (like the myriads of random sequences) back into the chaos from which they arose, or been progressively fragmented into shorter and shorter molecules (which most models of the primordial soup indicate were most likely to be replicated) and essentially diluted out.

The templated ligation mechanism proposed by Braun and Toyabe is a well-known molecular genetic process in modern-day cells. When two single-stranded DNA molecules bind to adjacent regions of a longer strand (the template), the two can easily be connected to one another (ligated) by the same kind of mechanism that first gave rise to them. "As long as this simple mechanism is available under the prevailing reaction conditions, compatible DNA segments can be selected from a random mixture of sequences and brought into a position which allows them to be linked together to create a longer strand," Braun explains.

In this way, depending on the relative concentrations of the complementary sequences, the stage is set for intermolecular cooperation. Higher temperatures and steep temperature gradients—like those that are thought to have characterized the narrow, water-filled pores in volcanic rocks in which primordial DNA synthesis may have occurred—promote the stringing together of shorter molecules into longer sequences. This would allow faster selection, elongation and subsequent replication of longer molecules. In other words, templated ligation can create stable majorities by promoting the assembly and replication of sequences that are complex enough to encode the first genetic information. For the authors of the new paper, "these cooperative ligation networks provide an example of symmetry breaking, a well-known mechanism of structure formation in physics," says Braun.

In the 1970s, Manfred Eigen (Nobel Prize for Chemistry 1967) and Peter Schuster developed their 'hypercycle' model as a theoretically feasible pathway from the earliest prebiotic DNA sequences to the stable transmission of genetic information. However, they lacked an experimentally tractable system that would allow them to mimic prebiotic conditions in a more-or-less realistic fashion. "Our experimental contributions demonstrate, that it is possible to obtain the required stable majorities of informational sequences in the primordial soup using the simplest of methods," Braun concludes.

More information: Shoichi Toyabe et al. Cooperative Ligation Breaks Sequence Symmetry and Stabilizes Early Molecular Replication, *Physical Review X* (2019). DOI: 10.1103/PhysRevX.9.011056

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