

Viewpoint

RNA in cycles

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Theoretical analysis of periodic RNA modifications in a simple biochemical reactor reveals emergent evolutionary properties.

Subject Areas: **Biological Physics, Chemical Physics**

A Viewpoint on:

Emergence of Information Transmission in a Prebiotic RNA Reactor

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In the 1950s, Miller showed that organic biomolecules may spontaneously form [1] from inorganic matter by running electricity through a mixture of gases. Since then, many experiments have shown that molecules that play vital roles in today's organisms, such as amino acids or the building blocks of DNA and RNA, are likely to have arisen soon after the formation of Earth. However, how a primordial molecular soup of organic building blocks gave rise to self-sustaining reproduction or early forms of life remains unexplained. Writing in *Physical Review Letters*, Benedikt Obermayer and colleagues at Ludwig Maximilian University of Munich, Germany, report their theoretical efforts to make progress on aspects of this question [2].

The “RNA world” hypothesis [3] proposes that life based on RNA biopolymers predated our current life based on DNA, RNA, and protein. Single-stranded RNA consists of a succession of different bases joined by a backbone. The bases are named adenine (A), guanine (G), cytosine (C) and uracil (U) (see Fig. 1). At moderately elevated temperatures, an RNA molecule may bind to a second strand that is complementary in sequence, in such a way that AU and CG base pairs are formed. This process is called hybridization. Besides carrying the genetic information stored in the succession of bases of an RNA strand through a cell, RNA has other astonishing functions. It can form aptamers, strands that bind very specifically to proteins (just as antibodies can). Special sequences of RNA, called ribozymes, can catalyze other biochemical reactions in a way similar to the action of enzyme proteins. A designed sequence of RNA has been shown to catalyze its own reproduction from other strands [4].

In an RNA world, it is assumed that RNA fulfilled some of the functions that were taken over at a later evolutionary stage by proteins (catalysis) and DNA (information storage). How an accumulation and selection of useful RNA macromolecules on the prebiotic Earth

could have occurred has been an object of debate. Accumulation of biological macromolecules may have been driven by temperature gradients, through thermophoresis [5]. Strong temperature gradients exist at the sea floor level, where hydrothermal vents emit many of the suspected building blocks of future biomolecules through porous rocks at high temperatures. In the porous rocks, the temperature gradients produce thermal convection, and molecules transported by the convective flow experience periodic temperature variations.

In their paper [2], Obermayer *et al.* ask how RNA would behave if it was subject to such periodic conditions in an open reactor. This may be reminiscent of Schuster and Eigen's famous work on hypercycles [6] considering the evolution, in competition, of multiple, self-reproducing, cyclic, mainly deterministic reactions of RNA and enzymes. In this case, RNA contains the information for the production of enzymes, which in turn multiply the RNA and, at the same time, read the stored information to produce more enzyme. However, Schuster and Eigen introduced molecular self-reproduction by hand from the beginning—unlike Obermayer *et al.*, who consider a real situation: randomly generated RNA folds and hybridizes before it is degraded, and then the process is repeated periodically without self-reproduction. Accordingly, the hypothetical reactor is fed by an influx of the four different RNA building blocks (bases) that will bind (ligate) randomly to produce single-stranded RNA polymers. An imposed condition of length-dependent outflux makes the reaction volume always contain different sequences of various lengths.

In the reactor, the RNA strands produced by ligation will hybridize in a second step (this occurs when a lower temperature of the convection path is reached). Hybridization can lead to two complementary strands forming a double strand, but also to folded single strands that have undergone self-hybridization. Much more complex objects may form when strands of suitable sequences oc-

the emergence of self-organizing, self-reproductive molecular dynamics that constituted the first forms of life. Concerning the RNA world hypothesis, the paper shows that a suitable molecular toolbox may have occurred spontaneously, in fast and simple ways. This is a strong argument in favor of the theory. Now it remains to be demonstrated that functional ribozymes can form from these elements spontaneously.

References

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About the Author

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Albrecht Ott has held a chair of experimental biological physics at the University of Saarland, Germany, since 2007. After graduating in 1987 and gaining his Ph.D. in 1990 from the University Pierre et Marie Curie (Paris VI), he carried out research at the Ecole Normale Supérieure in Paris, France, as a permanent staff member of the French national research body, CNRS. In 1991 he became a consultant at the NEC Research Institute, Princeton, and at the same time a visiting postdoctoral fellow at Princeton University, US. He spent the following eight years developing research at the physics department of the Institut Curie, Paris, France, until he moved to Bayreuth University in Germany in 2001, where he was appointed as a full professor. His current research interests are DNA molecular recognition and the investigation of driven biochemical systems.