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Sorting the wheat from the chaff

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Physicists from Ludwig-Maximilians-Universitaet (LMU) in Munich report that temperature gradients within pores in rock could have separated primitive biopolymers on the basis of their sequences—a vital precondition for the formation of self-replicating systems in the primordial ocean.

The earliest phase in the process that gave rise to living organisms on our planet is thought to have involved selective interactions between simple prebiotic molecules that enabled them to form progressively more complex chemical structures. These metastable structures eventually became capable of storing genetic information and transmitting it by selfreplication. The most likely candidates for such self-replicating systems are polymeric molecules made up of subunits called ribonucleotides. These RNA molecules in turn could have provided the starting point for biological evolution, which led to the first cell and everything that followed. Christof Mast and Dieter Braun (Professor of Systems Biophysics at LMU) have been exploring how precursor molecules such as ribonucleotides (and the deoxyribonucleotides of the hereditary material DNA) present in Earth's primordial ocean could have accumulated locally in concentrations high enough to permit them to interact.

But how was the wheat separated from the chaff in such systems? In other words, what mechanism could have separated 'useful' from 'useless' RNA molecules, and concentrated the former sufficiently to give them a chance to interact with other RNA chains and be elongated? New work by Braun, who is also a member of the Nanosystems Initiative Munich (NIM) and the Center for NanoScience (CeNS), together with Christof Mast and Matthias Morasch, points to a possible answer. In earlier laboratory experiments, Braun and his colleagues have shown that temperature differences in tiny water-filled channels, such as those found at hydrothermal vents and in the igneous rock extruded at mid-ocean ridges, are able to partition DNA molecules based on their lengths. Now they demonstrate that the same mechanism can also sort DNA strands that differ in their nucleotide sequences from each other. Their findings appear in the latest issue of the journal *Angewandte Chemie*.

Sequence-dependent partitioning

Instead of samples of porous rock, the LMU researchers used glass capillary tubes filled with an aqueous solution containing mixtures of two DNA fragments with slightly different nucleotide sequences for their experiments. "DNA is chemically closely related to RNA and behaves in a similar way under our experimental conditions. But it is more stable and therefore easier to handle," says Matthias Morasch, first author of the new study. The DNA-containing glass "pores" were then heated from one side, generating a gradient of approximately 17°C within the capillary, and the distribution of the DNA molecules was analyzed. Under these conditions, the different DNA molecules were found to separate into homogeneous, highly concentrated assemblies, depending on their sequences and their ability to interact with each other via complementary base-pairing. Thus in addition to sorting molecules according to their lengths, temperature differences can also drive sequence-dependent sorting. Both effects are based on the phenomenon of thermophoresis, the differential response of components of molecular mixtures to temperature gradients.

"The separation is so effective that certain types of fragments actually condense into gels when they hybridize with complementary partner molecules.—Even more strikingly, sequences that differ by only a few bases are partitioned into different gels," Mast explains. This degree of specificity was a big surprise, for DNA gels formed by drying show no evidence of sequence-dependent differentiation. This argues that it is the temperature gradient within the pores that makes the crucial difference. "Settings in which pores in volcanic rock were exposed to directional heat flow were probably very common on the young Earth," says Braun. So temperature-driven sorting may well have provided an important mechanism for the partitioning and concentration of biomolecules that could readily interact with each other, thus allowing them to form longer and longer polymer chains—the essential prerequisite for the origin of life.

More information: Matthias Morasch et al. Heat-Flow-Driven Oligonucleotide Gelation Separates Single-Base Differences, *Angewandte Chemie* (2016). DOI: 10.1002/ange.201601886