The chemical evolution of DNA and RNA on early Earth

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The basic constituents of the earliest RNA molecules may have formed in a geothermal environment, such that seen here in Yellowstone National Park in Wyoming. Photo: picture alliance / Mint Images

RNA was probably the first informational molecule. Now, chemists from Ludwig-Maximilians-Universitaet (LMU) in Munich have demonstrated that alternation of wet and dry conditions could have

sufficed to drive the prebiotic synthesis of the RNA nucleosides found in all domains of life.

How might the chemical structures that provide the basic subunits of RNA and DNA have formed from simpler starting materials some 4 billion years ago? Under what conditions could these building blocks have then been linked into long chains encoding information and propagating it by self-reproduction? Many possible scenarios have been proposed for the phase of chemical evolution that preceded the emergence of the first biological cells. Now, researchers led by LMU chemist Professor Thomas Carell have extended these models by demonstrating a plausible route for the prebiotic synthesis of the nucleosides that constitute the informational components of RNA.

Specifically, Carell and his colleagues have shown that nucleosides can be formed in a continuous process by exposing simple chemicals to the kinds of fluctuating physical conditions that would have prevailed in geothermally active areas characterized by volcanic activity on the early Earth. They begin with a mixture of formic acid, acetic acid, sodium nitrite and a few nitrogen-containing compounds, all of which have previously been shown to form from even simpler precursors under prebiotic conditions. The reaction mixture also contained nickel and iron, which are found in large amounts in the Earth's crust. The driving force for the chemical reactions is supplied by fluctuations in temperature and pH, together with wet/dry cycles, such as those that occur in the vicinity of periodically active hot springs or in strongly seasonal climates with alternating periods of precipitation and evaporation.

The core of the process is a series of reactions that gives rise to compounds called formamidopyrimidines, which can in turn be converted into the canonical purines (adenosine and guanosine) found in RNA. In a paper published last year, Carell and his team first described

this FaPy pathway as a possible chemical scenario for the prebiotic synthesis of nucleosides. "This time around, we not only began with simpler precursor compounds, but chose conditions that would be expected to prevail in a plausible geological setting, such as hydrothermal springs on land," explains Sidney Becker, a Ph.D. student in Carell's group and first author of the study. The paper has now appeared in *Nature Communications*.

The canonical purine nucleosides found in RNA were synthesized in the new experiments, along with a whole series of closely related molecules. Even more strikingly, all of the modifications observed are known to occur in RNAs in all three domains of life—eukaryota (animals and plants), bacteria and archaea—and are therefore essential components of functional genetic systems. Hence, they were most probably already present in the last common ancestor of all life forms. This suggests that these compounds must have been available on early Earth when biological evolution began. Indeed, the authors of the new study suggest that the non-canonical nucleosides could have played a crucial role in the phase of chemical evolution that preceded the emergence of the RNA world, a term referring to a hypothetical period during which RNA molecules are thought to have served as chemical catalysts in addition to storing genetic information in primordial cells. Seen in this light, the RNA modifications found in today's organisms represent molecular fossils that have continued to participate in vital biological functions for billions of years.

More information: Sidney Becker et al, Wet-dry cycles enable the parallel origin of canonical and non-canonical nucleosides by continuous synthesis, *Nature Communications* (2018). DOI: 10.1038/s41467-017-02639-1