# Protein-like structures from the primordial soup

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Current scientific theory postulates that the precursors of life originated in shallow lagoons. Credit: Science Photo Library / Richard Bizely

Experiments performed by ETH scientists have shown that it is remarkably easy for protein-like, two-dimensional structures—amyloids—to form from basic building blocks. This discovery supports the researchers' hypothesis that primal life could have evolved from amyloids such as these.

The story starts at least four billion years ago, when there was no living matter on the planet. Sometime around then, smaller chemical compounds formed into larger organised structures capable of self-

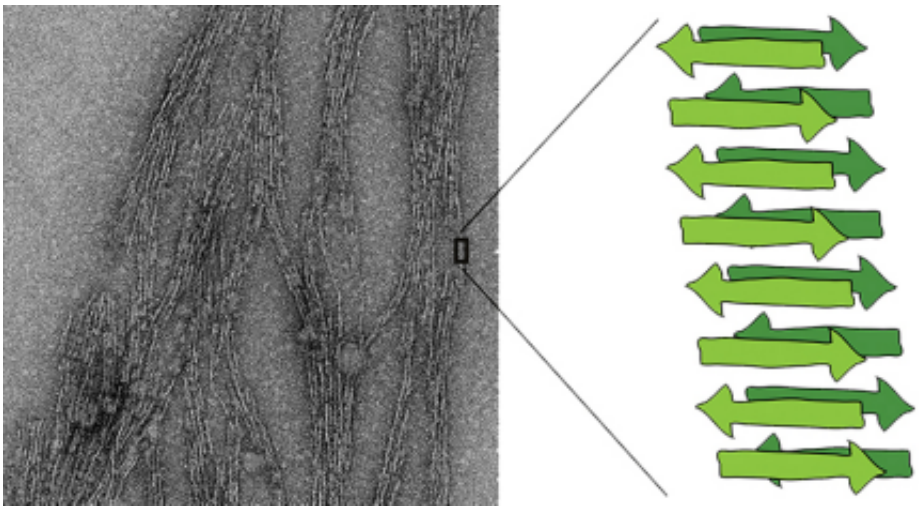
reproduction. And so the early precursors of life were born. Exactly which molecules were involved, and what they were made of, is the biggest puzzle in evolutionary history.

However, ETH Professor Roland Riek and his senior scientist Jason Greenwald have a compelling idea: these primordial lifelike structures could well have been proteinaceous aggregates, or amyloids. The latest results of their laboratory research now lend weight to their hypothesis.

The scientists performed an experiment to demonstrate that it is remarkably easy for such amyloid structures to assemble spontaneously from building blocks that existed on the prebiotic Earth, and under reaction conditions that also seem plausible for the primeval era. The scientists used four simple amino acids as starting materials: glycine, alanine, aspartate and valine. In addition, they used carbonyl sulphide as a catalyst for the reaction. This volcanic gas is also likely to have existed in the atmosphere billions of years ago.

## Long sheet structures

In the laboratory experiment, the amino acid molecules spontaneously assembled, with the help the carbonyl sulphide, into short chains (peptides) comprising between 5 and 14 building blocks. These chains in turn arranged themselves in parallel into amyloid structures known as beta sheets. In the experiment, these sheet structures took the form of fibres and typically comprised thousands of adjoining peptide chains which the scientists were able to identify using an electron microscope.



The schema of a sheet structure comprising several shorter peptide chains is shown in green. During their experiments, scientists discovered these structures in the form of long fibres (left: electron microscope image). Credit: ETH Zurich / Jason Greenwald

To make sure the amino acid molecules formed into sufficiently long peptide chains, the scientists had to use a clever trick. "Simply mixing amino acids with carbonyl sulphide in a test tube only produces very short peptide chains which do not assemble into a sheet structure", Greenwald explains. The scientists therefore slowly dripped amino acid molecules activated with carbonyl sulphide into a test tube in a procedure lasting several hours. "It is conceivable that an equally slow process - possibly taking several years - with a steady flow of new chemical compounds may well have taken place in the Earth's primeval history", says Greenwald.

## Catalytic effect

Scientists have already proposed amyloids as candidates for the very first lifelike structures on Earth, as even simple amyloids are capable of

performing certain chemical functions. Last year, for example, Professor Riek and his team discovered amyloid structures able to split esters.

The ETH scientists stress, however, that there is still an important piece of the puzzle missing from their argument in support of the "amyloid hypothesis": Are amyloids also capable of self-replication, just like RNA molecules? This is conceivable, claim Riek and Greenwald, but there is still no experimental evidence to support it. The professor and his team are working on it.

## Amyloids more likely than exclusively RNA

Even so, the researchers already describe their hypothesis as being much more plausible than the decades-old scientific assumption that the precursors of life were made up solely of RNA molecules. The scientists' main contention: RNA molecules with a biological function are comparatively large and complex. "They are so big that it would have been difficult for them to form spontaneously. Even with far simpler structures, amyloids exhibit certain chemical functions", says Greenwald. On top of that, the building blocks of RNA are more complex than those of amyloids and proteins. Furthermore, the latter are more stable even under harsh environmental conditions. "All this makes it plausible that the first functional molecules were amyloids", concludes Professor Riek.

**More information:** Jason Greenwald et al, Amyloid Aggregates Arise from Amino Acid Condensations under Prebiotic Conditions, *Angewandte Chemie International Edition* (2016). DOI: 10.1002/anie.201605321

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