

PREBIOTIC CHEMISTRY

Systematic soup sampling

“I feel we are very close to understanding how informational and functional (bio)polymers emerged from the primordial soup”

At some point in the history of the Earth, amino acids coupled into peptides, which further developed into proteins, eventually enabling life as we know it. But how did individual molecules combine to become functional sequences with secondary structures? Chemical evolution theories generally agree that condensations of amino acids played a crucial part in the proto-peptide world. Chemical analyses of meteorites and model prebiotic reactions have suggested that ancient peptides were built not only from amino acids but also from α -hydroxy acids; the two species can indeed form co-oligomers. What did these proto-peptidic molecules look like? As they are different from today's proteins, current databases are not helpful here. In a study published in the *Proceedings of the National Academy of Sciences, USA*, a team led by Facundo M.

Fernández presents a workflow based on an array of separation methods as well as mass spectrometry to analyse the diverse content of such a prebiotic peptide soup.

Fernández and his colleagues had previously shown that peptide-like structures can emerge from solutions of α -amino and α -hydroxy acids during repeated hot-dry/cool-wet cycles. The resulting oligomers — so-called depsipeptides — contain both amide and ester linkages. As ester bonds are more reactive towards nucleophiles such as amino acids, they are gradually exchanged for amide bonds upon extended cycling. “The attack of the NH_2 group of the amino acid on the ester bond would produce a peptide bond. The free carboxylic acid group of this newly formed (depsi)peptide can react further with an α -hydroxy acid to form another ester bond, which would be attacked again by an amino acid, etc. Repeating this process in cyclic steps would lead to longer oligo(depsi)peptides enriched in peptide bonds,” Fernández explains.

Oligo(depsi)peptides are by any measure unusual compounds, but the team subjected them to structural elucidation by mass spectrometry, a technique that has been useful in the study of peptides. However, as data for depsipeptides are not part of any current database, things were not that easy. The team devised their own algorithm to generate possible sequences, correlating these with experimental data. Their workflow to analyse a proto-peptide mixture consisted of ultra-performance liquid chromatography followed by travelling-wave ion mobility spectrometry and, finally, data-dependent MS/MS acquisition.

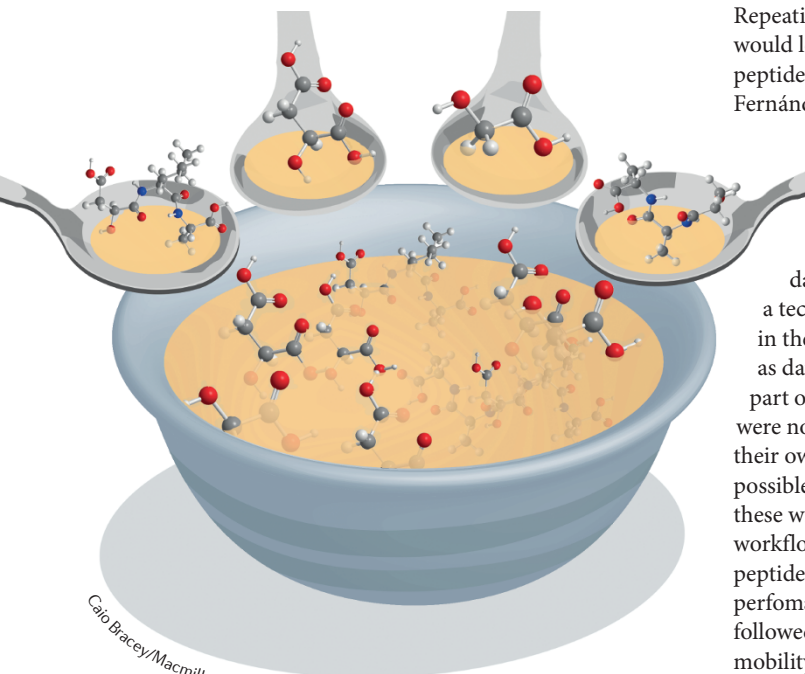
“Overall, it was an analytical tour de force,” notes Fernández.

To test their methodology, the team sampled the contents of three different peptide soups that were formed by mixing glycine, leucine and alanine with glycolic, lactic or malic acid and letting them cycle for up to three times over the period of 4 days. Hundreds of oligomers were found to be present in the mixtures and subjected to the analysis setup. Apart from demonstrating the utility of their workflow, Fernández's team discovered new information relevant to the origin of life. For example, the diversity and peptide character of the depsipeptides increased with each cycling round. Interestingly, the incorporation of amino acids was not random. For instance, in the mixtures containing glycolic or lactic acid, glycine and alanine were appended to the emerging depsipeptides earlier than was leucine.

The great diversity of the new molecules resulted from combinations of only three amino acids and one α -hydroxy acid. What is going to be revealed when more amino acids, alternative monomers (such as proto-glycans) or even inorganic species are added to the soup? The workflow presented by the team has the scope to allow for such experiments, which would more closely mimic the conditions at the origin of life. “I feel we are very close to understanding how informational and functional (bio)polymers emerged from the primordial soup,” rejoices Fernández.

Julia Eckhoff, Associate Editor,
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