

Metabolism before enzymes?

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Little is known about the evolutionary origins of biological metabolism. Is it simply a tool evolved to provide nutrients to the cell, or something even more fundamental? Several lines of evidence now support the idea that a self-organized, non-enzymatic form of metabolism predated the rise of RNA, enzymes and biology altogether. Like other self-organized dynamic processes in nature, such a reaction network would have been driven into existence by the far from-equilibrium nature of its environment, directed in its chemical release of energy by naturally occurring catalysts such as minerals and metal ions. We do not know to what extent this primitive metabolism would have changed due to Darwinian evolution, but there are good reasons to think it should still resemble the metabolism we know today in key aspects. We are attempting to identify the conditions for self-organization by discovering non-enzymatic fragments of ancient metabolic processes, and then triangulating from these. This talk will summarize my group's published efforts to discover non-enzymatic chemistry that resembles the acetyl CoA pathway, the reverse Krebs cycle, the Krebs cycle, the glyoxylate cycle, and reductive amination. I will also briefly describe ongoing work, including non-enzymatic transamination, gluconeogenesis and ribonucleotide biosynthesis. The talk will conclude with a call to re-evaluate the common conception of the fundamental nature of life.