

27-4 Oral

THE MISSING LINK BETWEEN PREBIOTIC AMINO ACIDS AND EARLY PROTEINS

Peter Van der Gulik¹, Serge Massar², Dimitri Gilis³, Harry Buhrman^{1,4}, Marianne Rooman³

¹*Centrum Wiskunde & Informatica, Amsterdam, Netherlands*

²*Université Libre de Bruxelles, Laboratoire d'Information quantique, Brussels, Belgium*

³*Université Libre de Bruxelles, Unité de Bioinformatique génomique et structurale, Brussels, Belgium*

⁴*Universiteit of Amsterdam, Amsterdam, Netherlands*

Peter.van.der.Gulik@cwi.nl

One of the big open questions in evolutionary biology is the character of the first coded peptides. Two competing hypotheses concerning this question can be formulated. According to the first hypothesis, the first coded peptides were structural elements, functioning in RNA-peptide complexes, much like polyamines are nowadays functioning in complexes with, among other molecules, tRNAs. From this early, short molecules the evolutionary development would go on towards the first protein domains, which would have played a role as a kind of RNA chaperones. The next stage would be independent proteins, with their own function, developing active sites as a last step. According to the second hypothesis, the first coded peptides were autonomous active sites. Short peptides with a metal ion, bound by carboxyl groups, would have had a fixed conformation, and have provided a rough, chemical activity. The metal-binding active sites would have been the heart of the first protein domains, which would develop when an evolving biochemistry became progressively more complex. As a last step, multi-domain proteins would emerge. To accumulate evidence to support the second hypothesis, a computer program was developed with which short, metal-binding amino acid sequences were extracted from the Protein Data Bank. The sequences which were searched for, are composed of prebiotic amino acids (including the negatively charged Asp) and are bound to a positive metal ion. This program extracted sequences representing the active sites from proteins like kinases, mutases and polymerases. Remarkably, these activities of proteins, all involving the manipulation of phosphate groups, are very much like the activities of ribozymes, which also manipulate phosphate groups with the participation of metal ions. When comparing ribozyme activities with very primitive protein activities (the active site of the mRNA producing polymerase is universally conserved, and thus probably about four billion years old), the two kind of macromolecules seem to converge to a same kind of catalytic repertoire! Considering recent results about the potential of montmorillonite clay to catalyze the production of random oligomers of both RNA and peptide (starting with nucleotides and amino acids), the question can be posed if a role was played by amino acids, dipeptides and short, coded oligopeptides in the RNA world. In other words: did RNA ever exist without protein around?