BIOPHYSICAL INSIGHTS FROM IN VITRO EVOLUTION OF RNA: APTAMER-TARGET BINDING.

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Introduction: Protein-RNA interactions are particularly important as they can shed some light on the origin and early evolution of the primordial forms of life. How proteins selectively bind specific sites on nucleic acids has been a challenging and interesting problem since the earliest days of molecular biology [1], and during the last couple of decades, the use of high-resolution structures has provided new insights to the study of protein-RNA interactions [2-7]. However, our understanding of these interactions have been so far limited to the study of protein-RNA complexes in biological systems, which have been subjected to evolutionary constraints unrelated to RNA binding.

Approach: Protein-RNA complexes that arose by in vitro selection - that is, that are evolutionarily independent from one another – are ideal candidates to study the interaction between proteins and nucleic acids in the absence of any evolutionary pressure other than RNA binding, and characteristics shared among them can be assumed to be solely related to the underlying biophysics of protein-RNA interactions. Thus, understanding the biophysical rules that govern protein-RNA interactions in complexes that arose by in vitro selection can give us a better understanding on which amino acids could have been critical for prebiotic interactions between peptides or proteins and primordial RNA-like polymers.

Methods: We analyze different subsets of protein-RNA complexes that arose by in vitro selection and look for common biophysical trends among them. We compare the biophysical properties of aptamer-binding regions of a given protein against the non-binding regions of the same protein. We also identify the protein residues at the interface that lower the energy of solvation and compare the biophysical properties of these solvating residues against the rest of the protein.

Results: We find unique biophysical trends for proteins binding RNA through in vitro selection. We also find strong correlations between the biophysical properties of binding areas and non-binding binding. In particular, we find positively charged residues to be generally over-represented at the protein-RNA interfaces, playing an essential role on RNA binding.

Discussion: The fact that certain amino acids seem to be required for RNA-binding suggests that their presence might have been critical for prebiotic interactions between peptides and nucleic acids -that is, their presence must have been a must by the time the genetic code was invented-. This implication, although speculative, can be used to assess the prebiotic availability of certain amino acids even in the absence of prebiotically plausible routes for their synthesis.

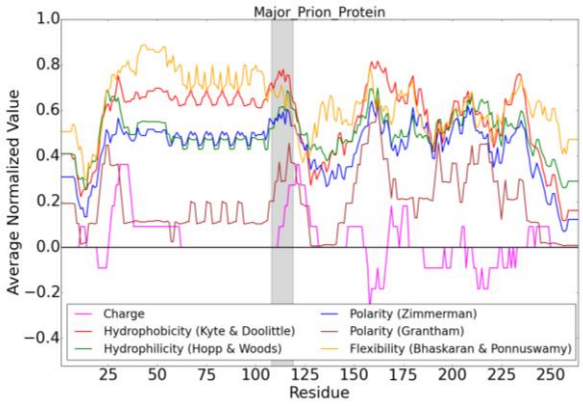

Fig. 1. Computed profile for different biophysical properties (charge, hydrophobicity, hydrophilicity, polarity and flexibility) along the protein sequence. The gray area corresponds to the protein-RNA interface.

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