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Computational protein design: exploring the link between sequence and function

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Abstract:

Proteins are naturally self-assembling materials, fundamental for all living organisms. Their structure and function are univocally determined by the sequence of amino acids along the backbone. The process of searching for the sequence that gives rise to a stable fold into a selected target structure is known as protein design.

Protein design has been extensively investigated and is of paramount importance since its applications range from material science to medicine. I apply computational protein design, through Monte Carlo simulations, to gain insights into the origin of the protein alphabet, locate functional regions in natural protein domains, and rationalise naturally occurring contact areas in protein-protein binding.

I present a protein design framework that models the competition for the availability of the amino acids. The system spontaneously identifies the minimal optimum alphabet for the protein design among all possible ones.

Furthermore, I developed a strategy to identify functional regions in natural domains, by comparing the natural and artificial site conservation and co-evolution signals, generated with statistical analysis of different sequences.

Finally, I apply protein design to a simplified protein-protein system, reducing it to an artificial protein-binding site, evaluating the binding affinity between the partners and rationalising the range of experimentally determined binding site areas.