

Ghost in the protein: how do new proteins come about?

Initiative: "Leben?" - Ein neuer Blick der Naturwissenschaften auf die grundlegenden Prinzipien des Lebens

(beendet)

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Proteins are ubiquitous biopolymers which carry out almost all essential functions of life. But where did proteins come from and how do new proteins emerge? It is widely assumed that new proteins derive from old proteins, via duplication and adaptation of one of the copies or by combining smaller, already viable fragments with a well-defined structure. However, it recently became clear that (i) many functional proteins do not assume well-defined structures, (ii) proteins from random sequences can adapt and assume novel functions too, and (iii) in modern organisms many functional proteins emerge de-novo, i.e. from previously non-coding DNA regions lacking prior selection. These observations suggest that alternative trajectories of protein emergence exist and the goal of this project is to explore these by combining modern approaches of synthetic biology and biocomputing. The research team will investigate how nature overcomes these obstacles in using de-novo proteins as starting points for further adaptation. Here, it will be tested whether de-novo proteins are more evolvable than random sequences and differences in their sequence parameters will be looked for. Specifically, the capacities to form viable proteins will be compared using protein libraries of: (i) de-novo proteins which the team has determined in various species using comparative genomics and phylogenetics (ii) random sequences, (iii) random sequences optimized for soluble expression through machine learning. Through this project, it will be learned how nature crosses the boundary of protein sequence viability, allowing the team to formulate principles for directed evolution and protein design.

Projektbeteiligte

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Structure and function of naturally evolved de novo proteins.

Heterologous expression of naturally evolved putative de novo proteins with chaperones.