

Abstract Submitted  
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**The Evolutionary Design of Proteins** FRANK J. POELWIJK, Green Center for Systems Biology, UT Southwestern Medical Center, Dallas. Laboratory of Living Matter, Rockefeller University, New York, ARJUN S. RAMAN, Green Center for Systems Biology, UT Southwestern Medical Center, Dallas, STANISLAS LEIBLER, Laboratory of Living Matter, Rockefeller University, New York, RAMA RANGANATHAN, Green Center for Systems Biology, UT Southwestern Medical Center, Dallas — Proteins fold spontaneously into precise, well-packed 3D structures, and execute complex functions such as specificity in molecular recognition, and efficient catalysis. Despite this, many studies show that proteins are robust to random mutagenesis. Additionally, proteins are evolvable. What principles underlying the design of natural proteins explain these properties? Recent work examining correlated evolution of amino acid positions shows that many positions in proteins are nearly statistically independent while 10-20% are organized into groups of co-evolving positions – termed “protein sectors” – that underlie conserved, independently varying biological activities. These findings suggest that the basic design of natural proteins is fundamentally tied to the nature of fluctuations in the selection pressures during evolution. We propose to test this hypothesis using a system for high-speed laboratory evolution and determine how variation in selection pressures influences the architecture of amino acid interactions within a protein.

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