Green functions of correlated genes and the mechanical evolution of protein

Tsvi Tlusty

Center for Soft and Living Matter, Institute of Basic Science, South Korea

Growing evidence suggests that cooperative interactions and motions underpin protein functions. But in spite of vast data, the information-dense, heterogeneous nature of protein has held back the progress in understanding the underlying principles. We will outline a general theory of protein that quantitatively links sequence, dynamics and function: The protein is a strongly-coupled amino acid network whose interactions and large-scale motions are captured by the mechanical propagator (the Green function). The propagator relates the gene to the connectivity of the amino acid network and the transmission of forces through the protein. Mutations introduce localized perturbations to the propagator which scatter the force field. The emergence of function is manifested by a topological transition when a band of perturbations divides the protein into subdomains. Epistasis quantifies how much the combined effect of multiple mutations departs from additivity. We show that epistasis is the nonlinearity of the Green function, which corresponds to a sum over multiple scattering paths passing through the localized perturbations. Our model lays the foundation for understanding the protein as an evolved state of matter and may be a prototype for other strongly-correlated living systems.