Green functions of correlated genes and the mechanical evolution of protein

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The function of proteins arises from cooperative interactions and rearrangements of their amino acids, which exhibit large-scale dynamical modes. Long-range correlations have also been revealed in protein sequences, and this has motivated the search for physical links between the observed genetic and dynamic cooperativity. We will discuss a theory of protein, which relates sequence correlations to physical interactions and to the emergence of mechanical function. The protein is modeled as an amino acid network whose interactions and motions are captured by the mechanical propagator, the Green function. The propagator describes how the gene determines the connectivity of the amino acids, and thereby the transmission of forces. 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 such perturbations divides the protein into subdomains. We find that epistasis -- the interaction among mutations in the gene -- is related to the nonlinearity of the Green function, which can be interpreted as a sum over multiple scattering paths. We apply this mechanical framework to simulations of protein evolution, and observe long-range epistasis that facilitates collective functional modes. The model may be a prototype for other strongly-correlated living systems. (Dutta, Eckmann, Libchaber et al., PNAS 2018)