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Speaker: Debora Marks , Harvard Medical School

Title: Evolutionary couplings: causal relationships for discovery and design

Abstract:

There is a now major opportunity to link genomic sequence information to phenotype and to apply this to concrete engineering and health problems. Attributes of living systems are constrained in evolution. An alternative to the analysis of conserved attributes ('characters') is analysis of functional interactions ('couplings') that cause conservation. Collections of sequence homologs record the outcomes of millions of evolutionary experiments in which the protein evolves according to functional constraints. This record of evolutionary constraints can in principle be exploited for predictive and engineering purposes. My previous work demonstrated that sequence co-evolution in proteins in the form of amino acid pairwise co-variation across a protein family, given sufficiently diverse sequence information, can be used to fold proteins, to predict oligomerization, identify functional sites and determine protein interactions. I will present new aspects of this work including the theoretical foundation, how that can be improved and used to address critical open questions in biology such as protein plasticity, fibrils formation and the quantitative effect of genetic variation.