Physical and Chemical Biology Seminar

Tuesday, January 25, 2011 | **11:00 a.m.** | **Room 1315 Chemistry Building**

Sharing the Energy Landscape for Folding and Function: From Small Proteins to Large Machines.

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Globally the energy landscape of a folding protein resembles a partially rough funnel with reduced energetic frustration. A consequence of minimizing energetic frustration is that the topology of the native fold also plays a major role in the folding mechanism. Some folding motifs are easier to design than others suggesting the possibility that evolution not only selected sequences with sufficiently small energetic frustration but also selected more easily designable native structures. The overall structures of the on-route and off-route (traps) intermediates for the folding of more complex proteins are also strongly influenced by topology.

Going beyond folding, the power of reduced models to study the physics of protein assembly has also proven powerful. Since energetic frustration is sufficiently small, native structure-based models, which correspond to perfectly unfrustrated energy landscapes, have shown that binding mechanisms are robust and governed primarily by the protein's native topology. These structure-based models impressively capture many of the binding characteristics found in experiments and highlight the fundamental role of flexibility in binding. Deciphering and quantifying the key ingredients for biological self-assembly is invaluable to reading out genomic sequences and understanding cellular interaction networks. This conceptual framework is also allowing us to envisage the dynamics of molecular motors from the structural perspective and it provides the means to make several quantitative predictions that can be tested by experiments. For the kinesin motor, a prototype of the biological machines in the cell, structure-based molecular simulations of an explicit kinesin and microtubule structures were used to glean a number of salient features that supplement the current experimental findings.

Refreshments will be available prior to the seminar at 10:45 a.m. outside room 1315

Graduate Students may meet with the speaker at 1:00 p.m. in Room 8335