QCB Trainee-Sponsored Seminar Series

Protein dynamics, entropy and function

Molecular recognition by proteins is fundamental to the molecular basis of biology. Dissection of the thermodynamic landscape governing protein-ligand interactions has proven difficult because determination of various entropic contributions is quite challenging. NMR relaxation measurements, theory and simulations suggest that conformational entropy can be accessed through a dynamical proxy. The construction and validation of a robust and relatively model independent relationship between measures of fast side chain motion and the underlying conformational entropy will be presented. The dynamical proxy reveals that the contribution of conformational entropy can range from highly favorable to highly unfavorable and demonstrates the potential of this key thermodynamic variable to modulate protein-ligand interactions. The dynamical "entropy meter" also refines the role of solvent entropy and directly determines the loss in rotational-translational entropy that occurs upon formation of high affinity complexes. The ability to quantify the roles of entropy through an "entropy meter" based on measurable dynamical properties promises to highlight its role in protein function. Several examples will be presented including the importance of dynamics over several timescales, and the entropy it represents, to allosteric regulation in the Lac repressor. Finally, it is shown that the purposeful manipulation of conformational entropy can be used to create a protein-protein complex with an unprecedented affinity. Supported by the NIH and the G. Harold & Leila Y. Mathers Charitable Foundation.

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Quantitative and Chemical Biology
Indiana University

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Department of Chemistry and the Graduate Program in Biochemistry

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For further details, contact Mr. Steven Watkins at 5-9749