Free Energies by Regularizing Binding Energies: Application to Modeling Hydration of Proteins using All-Atom Simulations

Dilip Asthagiri [C, S]
Chemical and Biomolecular Engineering, Rice University, Houston, TX, U.S.A.
dna6@rice.edu

Dheeraj Tomar
Chemical and Biomolecular Engg., Johns Hopkins University, Baltimore, MD, U.S.A.

Valery Weber
IBM, Switzerland

B. Montgomery Pettitt
Sealy Center for Structural Biology and Molecular Biophysics, University of Texas Medical Branch, Galveston, TX, U.S.A.

The interaction of a hydrated solute with the solvent spans a wide range of energies. Traditionally, in computing the thermodynamic properties of hydration, the problem of disparate energy scales is dealt by alchemically transforming the solute from a non-interacting solute to a fully interacting solute. But at the scale of a globular protein such approaches can prove challenging. Here, guided by the quasichemical organization of the potential distribution theorem, we present an approach that readily applies to systems ranging in complexity from those described by first principles (ab initio) potentials to large molecular solutes such as a protein in water described using empirical (classical) potentials. In this presentation, we will sketch the regularization approach and present results on the hydration thermodynamics in the coil-to-helix transition and in helix-helix pairing of a deca-alanine peptide using classical (empirical) potentials. On this basis, and in contrast to the extant ideas on the role of hydrophobicity in protein folding, we will show that in both the coil-to-helix transformation and in helix-helix pairing, changes in protein intramolecular interactions are decisive in favoring the ordered structure.