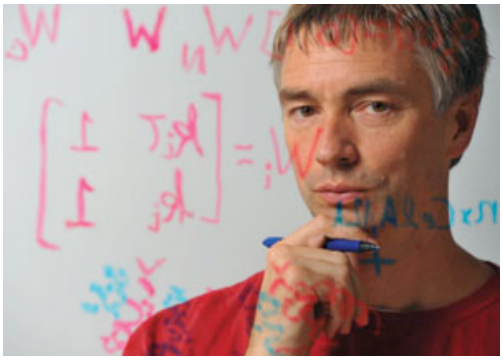
Joint ChemBio/Physical Chemistry Seminar

Tuesday, February 25, 2014 | **11:00 am** | **Room 1315 Chemistry Building**

Measuring coupling energies in and folding pathways in simple repeat proteins



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Host: Professor Silvia Cavagnero

One of the most striking features of the protein folding process is cooperativity. Although the structures of the native states of proteins are built from pieces that might appear to be independent (in a thermodynamic sense), these units highly coupled, and to good approximation populate in an all-or-none transition. Cooperativity in folding is likely to use the same underlying interactions, and thus, have the same thermodynamic features as functional properties such as allostery and assembly. Despite the importance of cooperativity in folding, our analysis of it remains largely at the "yes" or "no" (i.e., two-state versus multistate) level. We have been using linear repeat proteins to extend this qualitative picture of cooperativity in folding to a quantitative (thermodynamic) level. By constructing an array of 33-residue ankyrin repeats that have varying length but identical (consensus) sequence, we have resolved the high cooperativity of unfolding into local versus nearest-neighbor energy, entropy, and heat capacity. This approach has revealed an extremely strong coupling free energy between repeats. We find this coupling to be entropically driven at low temperatures, consistent with hydrophobic desolvation, and to be highly sensitive to histidine protonation state and to salt concentration, suggesting an electrostatic contribution to interface formation. This high level of coupling is considerably stronger than that seen in a set of consensus TPR helical repeats. Recent results with a novel, naturally occurring 42 residue TPR-like polypeptide (that shows nearly identical sequence from unit to unit) is of lower stability than the 34 residue TPR motifs, perhaps resulting from weaker coupling between repeats. For β-sheet leucine-rich repeat proteins, we find that a high level of cooperativity and stability can also be achieved with consensus repeats, although stability contributions are also made from variable capping motifs.

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