Homework Assignment H3
(Due: Monday, 2009/11/02, 4:00 PM)

H3.1. A Two-Dimensional (2D) Lattice Protein Model. Consider a 2D square lattice of 4×4 nodes with lattice spacing a. A peptide of four amino acids is modeled as a chain of four nodes (one amino acid per node) separated by "peptide bonds" of length a. Peptide conformations are characterized by either zero, one, or two kinks. A kink occurs when the (i+1)-th peptide bond is at the 90° angle with respect to i-th peptide bond. Potential energy E of each conformation consists of two parts, elastic and hydrophobic. Each kink contributes a positive elastic energy $\delta > 0$ to E. An attractive interaction due to effective hydrophobicity between those amino acids i and j that are at a distance a but are not peptide bonded $|i - j| > 1$ contributes to E a negative value $-\epsilon$, where $\epsilon >> 2\delta$.

(a) Identify all *different* (non-equivalent) conformations of the 4–residue peptide on a 2D lattice. Take into account the directionality (N→C) of the peptide chain. Suggestion: Classify conformation based on the number of kinks. Important consideration: Two conformations are equivalent if they can be overlapped by using a translation within the lattice plane and rotation around the axis perpendicular to the lattice plane.

(b) For each conformation, count the number of possible conformational states Ω, i.e. placements of a given conformation on the 4×4 square lattice.

(c) For each conformation, identified in (a), calculate the potential energy E. Identify the conformation classes with the lowest and the highest potential energy.

(d) Use the results of (b) and (c) to find for each conformation the free energy, $F = E - Tk_B \ln \Omega$. Identify the conformation(s) that will have the lowest free energy at low temperatures.

(e) Find the values of δ, for which conformations with no kinks will have the highest free energy.

(f) Identify conformations with the largest entropy. Find the temperature T^*, above which these conformations will have the lowest free energy.

H3.2. Selected Questions on the Study: K. W. Plaxco, Kim T. Simons and David Baker, "Contact Order, Transition State Placement and the Refolding Rates of Single Domain Proteins," J. Mol. Biol. **277**, 985-994 (1998). (*For Honors Undergraduate & Graduate Students*).

(a) What is a contact order? Is there a correlation between the high contact order of the native state and the loss of entropy upon folding? Is the contact order correlated with the free energy barrier associated with the folding transition? Explain your answers.

(b) Do proteins with a high contact order fold faster or slower than the proteins with a low contact order? Use the results of this study to explain.

(c) Do long proteins need a significantly longer folding time than short proteins? Use the results of this study to answer this question.

(d) How is a transition state placement, θ_m, defined? What range of values can θ_m adopt? Explain the correlation between θ_m and contact order as observed in this study.