Homework Assignment H2
(Due: Friday, 2009/10/16, 4:00 PM)

H2.1. Protein Structure and Interactions

(a) Draw a *cis* peptide bond and identify the groups that experience steric interference. Explain why the conformational freedom of peptide bonds is limited.

(b) Why can't proteins have mirror symmetry?

(c) Consider a molten globule. Which of the two amino acids is more likely to be on the protein surface (as opposed to the interior of the molten globule), serine (Ser) or isoleucine (Ile)? Explain.

(d) In the Fersht experiment, an enzyme in water at a physiological temperature $T_1 = 310$ K was found to be characterized by a pH-optimum shift of $\Delta \mathrm{pH}_1 = 1.6$, upon a substitution of the active site by a charged amino acid. What would be the pH-optimum shift, $\Delta \mathrm{pH}_2$, at a higher temperature $T_2 = 360$ K? Assume that the effective permittivity ϵ_{eff} of water linearly decreases from 88 at $T = 273$ K to 55 at $T = 373$ K.

H1.2. Selected Questions on the Study: A. Sali, E. Shakhnovich, and M. Karplus, "How does a protein fold?" Nature **369**, 248-251 (1994). (*For Honors Undergraduate & Graduate Students*).

(a) A protein sequence is represented by a self–avoiding chain of 27 monomers. How are different random protein sequences modeled? How is the native state in the model defined?

(b) How is the folding tendency defined? What model parameters does the folding tendency depend on?

(c) What is the density of states $\omega(Q_0, \epsilon)$? How is it used to calculate the entropy and free energy in dependence on the reaction coordinate Q_0?

(d) How do the results of this study help explain the Levinthal paradox?