Final Exam
(Date: Tuesday, 2009/12/08, 1:00 PM–3:00 PM, Room: 12-919)

1. Hydrogen Bonds.

(a) Draw a schematic picture of a water molecule and identify the hydrogen bond donors and acceptors. How many hydrogen bonds can one water molecule form with other water molecules?

(b) Draw a schematic picture of a protein and identify the hydrogen bond donors and acceptors on the protein backbone. How many backbone hydrogen bonds can one amino acid form? Are there any exceptions?

2. Kinetics of β-Sheet Formation. The nucleus of a β-sheet protein contains M^* residues and m_{opt} β-strands. Nucleus formation is a rate limiting step of the β-sheet formation associated with a free energy barrier $F^{\#}$. The free energy barrier $F^{\#}$ depends on the free energies of (1) a bend between two adjacent β-strands, U, (2) a β-strand edge, Δf_β, and (3) a residue in the center of a β-sheet f_β,

$$F^{\#} = 2\frac{U\Delta f_\beta}{-f_\beta}\,.$$

(a) Draw a dependence of the free energy F on the number of residues M participating in the β-sheet formation for the β-sheet protein, for which $f_\beta < 0$. Mark the number of residues corresponding to the nucleus size, M^*, and the free energy barrier, $F^{\#}$.

(b) The β-sheet protein we are investigating has a nucleus made of 4 β-strands ($m_{opt} = 4$) and the free energies $U = 2$ kcal/mol and $\Delta f_\beta = 1$ kcal/mol. Calculate the number of residues M^* in the nucleus, f_β, and the free energy barrier $F^{\#}$.

3. The Photosynthetic Reaction Center. This center consists of cytochrome with four hemes and small, cyclic molecules, pigments. The center spans the 40 Å–thick membrane.

(a) What is the function of the photosynthetic reaction center? What are the roles of the protein and the pigments? What triggers the reaction?

(b) Describe the quantum mechanical process involved in the reaction. How many steps are involved in the reaction? What would happen if the number of steps was reduced to only a single step? What mechanisms ensure that the reaction will be conducted in only one direction?

4. Energy and Entropy Defects in Water-Soluble Globular Proteins. Quasi-random pattern of amino acid sequences of globular proteins allows us to apply statistical physics principles to study the occurrence of all possible folded structures. The multitude principle states that the more sequences fit the given folded structure (without disturbing the stability of the fold), the higher the occurrence of this structure is in native proteins. Rarely observed structural patterns are thus associated with energy or entropy defects.

(a) Name two different energy/entropy defects that occur in proteins in only rare cases. Knowing the free energy of the defect, how can you estimate the probability of occurrence of this defect? Is this probability affected by the free energy of the native state?

(b) Consider a protein with two types of secondary structure domains: (1) α-helical and (2) β-sheet. Which of the two is more likely to be found in the core of the folded protein? Provide a quantitative explanation.

5. Protein Sequence → Structure & pH Effects Consider a protein with a sequence repeat (-H-V-H-V-H-V-H-)$_n$. Note that H (His) with $pK_a = 6.08$ is a ionizable, polar (hydrophilic) amino acid and V (Val) is a non-polar (hydrophobic) amino acid.

(a) At pH¿7.5, the above protein sequence folds into a regular secondary structure. Which secondary structure do you expect to observe, based on the protein sequence?

(b) Would you expect this structure to be more or less stable at pH=4? What is the factor that will affect the stability of this structure at low pH?

6. Protein Denaturation. Protein can lose its native structure and thus its function due to heat or cold denaturation as well as due to the presence of a strong denaturant, such as urea, guanidine dihydrochloride, or SDS.
(For honors undergraduate and graduate students.)

(a) What is the experimental evidence for the existence of cold denaturation in some proteins? What is the main physical reason for occurrence of cold denaturation?

(b) You wish to induce a random coil state in your protein. Which of the two mechanisms: (1) cold denaturation or (2) high concentration of a strong denaturant would you use to achieve that?

7. Molten Globule (MG) State.
(For honors undergraduate and graduate students.)

(a) Draw a graph of free energy versus reaction coordinate and identify (1) the completely unfolded (random coil) state, (2) the MG state, and (3) the native state. Does the MG state correspond to a free energy minimum or maximum?

(b) Identify one characteristic of the MG state that is similar to the native state and another that is different from the native state. Do you expect the protein in the MG state to perform the same physiological function as when it is in its native state?

8. Protein Folding & Unfolding as "All-Or-None" Transitions. Consider a protein that can be either unfolded or folded but does not adopt any intermediate state. *(Extra Credit Problem.)*

(a) Express the folding and unfolding rates with the free energies of the unfolded, folded, and transition states. Which of the two processes is faster, folding or unfolding? Why?

(b) What feature on the density of states, $S(E)$, ensures that the protein melting from the native to the unfolded state is "all-or-none" transition? Why is the existence of "all-or-none" transition physiologically important?