Midterm Exam
(Date: Thursday, 2009/11/05, 11:00 AM–12:20 PM)

1. Each residue in a peptide chain can adopt a range of conformations described by the Ψ and Φ angles in the Ramachandran plot. Of the 20 naturally occurring amino acids, identify the amino acid that can adopt the largest range of (Ψ, Φ) values. Which amino acid is characterized by the most restricted range of (Ψ, Φ) values? Explain both choices.

2. The hydrogen bond between two water molecules in isolation is about ten times stronger energetically than a van der Waals contact between two xenon atoms, yet water molecules dimerize in the gas phase only about 30% more frequently than xenon atoms. Explain why.

3. The temperature at which the protein unfolds *increases* by 40°C when the water is removed either by dehydration or by transferring the protein to a non-aqueous solvent. What are the implications of this for the stability of protein folded conformations? Explain what happens to the free energy of a protein-protein hydrogen bond upon water removal.

4. Folding of a hypothetical protein is associated with a formation of a crucial metastable intermediate state I. What is the effect of an increased stability of this intermediate state, $F_I \rightarrow F_I - \Delta F_I$, on the folding rate? See the schematic figure. Express the transition time from unfolded to folded state in terms of the free energies in unfolded (F_U), intermediate (F_I or $F_I - \Delta F_I$), and folded (F_F) states as well as the two free energy values at the top of the two barriers, $F^{\#1}$ and $F^{\#2}$.

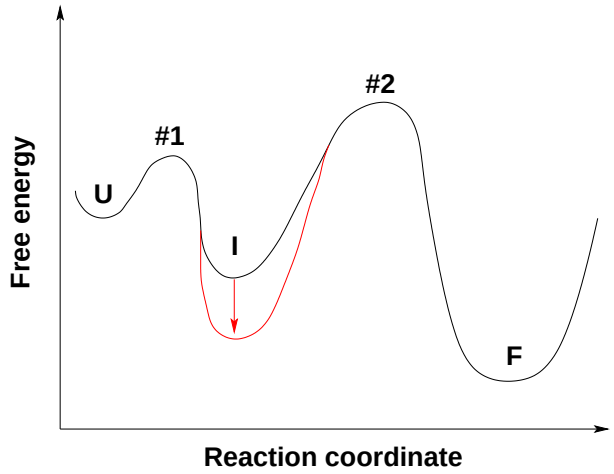

FIG. 1: *Schematic picture of unfolded (U), intermediate (I), and folded (F) state (Problem 4.)*

5. A Mg^{2+} ion and a Cl^{-} ion are 6Å apart in water at 25°C. What is their electrostatic interaction energy in units of k_BT? Debye-Hückel radius in water at physiological conditions is 8Å, $\epsilon_{eff} = 79$, and $\epsilon_0 = 8.85 \times 10^{-12}$ As/Vm. How much stronger would this interaction be if the ions were two-times closer to each other?

6. A hypothetical protein is in unfolded state with the free energy F_U. Suppose that upon folding, the protein can adopt any of 5 transition states characterized by free energy values: $F_1 < F_2 < F_3 < F_4 < F_5$, where $F_i > F_U$ for all $i \in 1, 2, .., 5$. Which of these states will contribute the most to the protein folding rate? Express the folding rate by the dominant term.
(For honors undergraduate and graduate students.)

7. Explain the origin of the change of the Gibbs free energy ΔG of a hydrophobic molecule upon a transfer from vapor to water. Take into consideration that ΔG consists of two contributions, (i) enthaphy change ΔH and (ii) change in the entropic part TΔS, $\Delta G = \Delta H - T\Delta S$.
(For honors undergraduate and graduate students.)