PhD Entrance Examination
Physics and Chemistry of Biological Systems
September 2022

IMPORTANT GUIDELINES

- Solve **three** of the following problems.
- No extra credit is given for attempts to solve more than three problems.
- Do not write your name on the problem sheet nor use any mark that can identify you, as this would invalidate your exam.
- Write out solutions clearly and concisely. State each approximation used. Diagrams welcome.
- Number page, problem, and question clearly.
- All essays/solutions should be written in English.

Exercise 1

A molecule at thermal equilibrium can be found in three states, A, B, and C, with energy 0 kJ/mol, 2.5 kJ/mol, and 5 kJ/mol, respectively. Assume k_B=0.0083 kJ/mol/K, and answer the following questions:

- Find the population of the three states at temperature T=300K.
- Find at which temperature the population of state A is twice the population of state C.
- Find at which temperature the population of state B is twice the population of state C.
- Find at which temperature the population of state C is 1/7.

Exercise 2

A polymer chain of $N + 1$ monomers is modeled as a N-step random-walk on the cubic lattice in d spatial dimensions. The initial monomer of the chain is assumed fixed at the origin of the lattice.

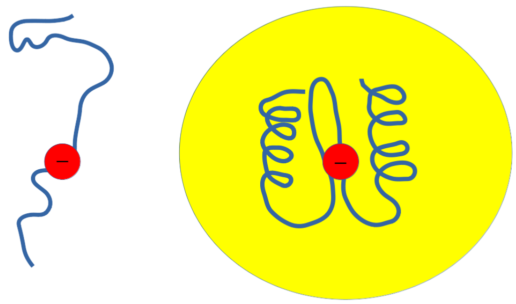
(1) Find the expression of the conformational entropy of the polymer as a function of N and d.

Assume that the polymer may either fluctuate freely in $d = 3$ or become fully absorbed on the $d = 2$ xy-plane (*i.e.*, such that all the monomers are on the plane) with absorption *energy per monomer* $= -|\epsilon|$.

(2) Find the transition temperature T_s between these two states.

Exercise 3

The ionization of the acidic side-chain (A^-) of an amino acid of an unfolded protein in solution of pure water (dielectric constant at 310K $\epsilon_w = 74.5$) is modeled as charging the surface of a particle (say, radius $= r_p$) at the center of a low dielectric ($\epsilon_p = 20$) sphere of radius 6 Å.
The ionization of the same amino acid in the folded protein structure is modeled as charging the surface of a particle (again radius $= r_p$) at the center of a larger low dielectric ($\epsilon_p = 20$) sphere of radius 30 Å.



The pKa ($-\log_{10}(K_a)$, $K_a = \frac{[H^+][A^-]}{[AH]}$) of the ionizable group in the unfolded protein is 4.4.
1) Provide an estimate of the pKa in the folded protein at 310 K using a pure electrostatic model.
Hint: The free energy of charging a sphere of radius r_p in a medium with dielectric constant ϵ is given by the Born formula:

$$\frac{1}{4\pi\epsilon_0}\frac{q^2}{2\epsilon r_p}$$

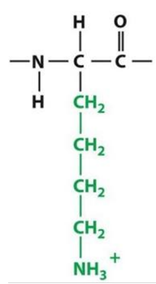
Hint: Use differences in free energy to compute differences in pKa.
Useful quantities:
$k_B = 1.380649 \text{ x } 10^{-23}$ m^2 kg s^{-2} K^{-1} – Boltzmann constant
$q = 1.6022 \text{ x } 10^{-19}$C elementary charge
$N_{Av} = 6.022 \text{ x } 10^23$ Avogadro's number
$\epsilon_0 = 8.8542 \text{ x } 10^{-12}$ C^2 N^{-1} m^{-2} – Vacuum dielectric constant.
2) The dielectric constant of water may be approximated in the range of temperature (T) 280 K to 340 K by the equation:

$$\log_{10}\epsilon = 1.94315 - 0.001972 * (T - 273.15\text{K})$$

Can you discuss possible effects of temperature on the pKa?

Exercise 4

The following question considers the molecular interactions associated with the thermodynamics of the amino acid Lysine in biological settings. Lysine consists of a side chain that has both a hydrophobic tail made up of hydrocarbons as well as a positively charged group at pH=7 illustrated below:



Answer the following questions showing as much of your work/thinking:

1. What types of molecular interactions occur between the CH2 groups and the surrounding water? Compare the strength of these interactions to thermal energy k_BT.

2. What types of molecular interactions occur between the positively charged NH_3+ group and surrounding water? Compare the strength of these interactions to thermal energy k_BT.

3. In a salt solution, negatively charged chloride ions (Cl-) would be attracted to the positively charged NH_3+. At what distance between the NH_3+ and Cl- ions do you expect the interaction energy between them to be equal to thermal energy (k_BT)? It is not so important to get the exact numerical value but the process of how you got to your answer.

   Hint 1: How does the electrostatic interaction energy between a positive and a negative charge change when in vacuum vs in water?

   Hint 2: Try and relate the information from Hint 1 to thermal energy (k_BT).

Exercise 5

Consider a system with two states, A and B. The dynamics of the system is described by the rate equation

$$\frac{d\,P_A(t)}{dt} = -k_{AB}P_A(t) + k_{BA}P_B(t)$$

$$\frac{d\,P_B(t)}{dt} = k_{AB}P_A(t) - k_{BA}P_B(t)$$

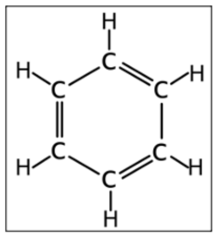
where P_A is the probability of observing state A, P_B is the probability of observing state B, $k_{AB} = 3\,\mathrm{sec}^{-1}$ and $k_{BA} = 1\,\mathrm{sec}^{-1}$.

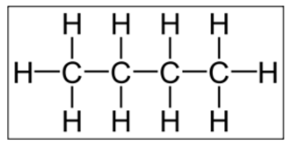
1. What is the equilibrium probability of observing the system in A and B?

2. Imagine to prepare the system in state A (namely $P_A(0) = 1$ and $P_B(0) = 0$). Find the time t at which it is equally probable observing the system in state A or B (namely $P_A(t) = 0.5$).

Exercise 6

The following question will explore your understanding of the electronic properties of different types of chemical moieties and how this changes their interactions with light. Consider the two molecules shown below namely, Benzene (on the left) and Butane (on the right).





Answer the following questions showing as much of your work/thinking:

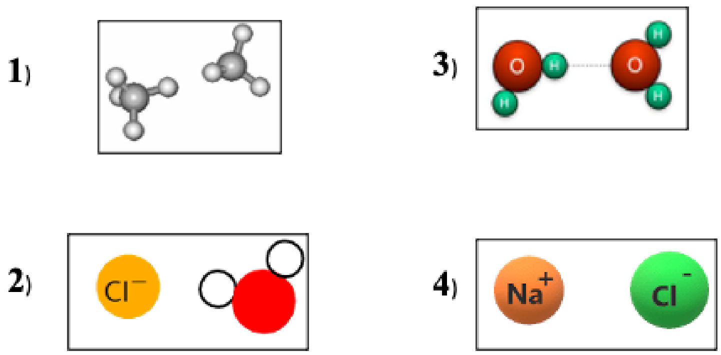
1. In benzene, some of the carbon atoms have two lines between them, while in butane there are only single lines shown connecting the carbon atoms. Can you comment on the physical origin of these differences?

2. Is it possible to arrange the single and double lines connecting the carbon atoms in benzene in a different manner? Explain your rationale.

3. Imagine a photon interacting with benzene separately and butane separately. Do you think it is energetically easier/harder to excite electrons in benzene or butane? Explain your rationale.

Exercise 7

The following question explores interactions in common molecules studied in chemistry. The picture below shows 4 different types of *pairs of molecules*: 1) two methane molecules, 2) Chloride ion and a water molecule, 3) two water molecules and finally 4) a sodium and chloride ion.



Answer the following questions showing as much of your work/thinking:

1. Rank the 4 *pairs of molecules* shown in order of their interaction strength from strongest to weakest.
2. For the interaction you have classified as weakest, sketch a curve showing the interaction energy between the two molecules as a function of distance between them.
3. For the interaction you have classified as the strongest, sketch a curve showing the interaction energy between the two molecules as a function of distance between them. Plot this curve on the same graph the previous question.

Exercise 8

Consider a chain of 3 Ising spins, σ_1, σ_2, σ_3, with $\sigma_i \in \{-1, 1\}$. The nearest neighbours interact via exchange interaction $J > 0$, favouring parallel orientation, and the system is in equilibrium at temperature T.

1. Write down the expression for the total magnetization of the system, M, when the leftmost spin is fixed in the "up" state, $\sigma_1 = 1$. Draw a sketch M as a function of T.

2. Write down the expression of the probability that the rightmost spin, σ_3, is up, too. Sketch this probability as a function of T.

3. Write the expression for the average energy of the system when both σ_1 and σ_3 are kept fixed n the "up" state. Draw a sketch of the heat capacity of the system as a function of T.