

PhD Entrance Examination
Physics and Chemistry of Biological Systems
April 2023

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.
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Exercise 1

Consider a system of N Ising spins, $S_{1,\dots,N} = \pm 1$, on a d -dimensional hypercubic lattice with interactions between nearest neighbours, $\mathcal{H} = -J \sum_{\langle ij \rangle} S_i S_j$. The interactions are ferromagnetic, $J > 0$, so that all spins are aligned in the same direction at $T = 0$.

Consider first $d = 1$, where the N spins are arranged in a one-dimensional chain with periodic boundary conditions.

1. What is the energy gap between the ground state and first excited state? How does the degeneracy of the first excited state scale with N ?

Consider now $d = 2$, with the N spins arranged in a square of side \sqrt{N} , again with periodic boundary conditions.

2. Repeat the same analysis of point 1, and discuss the differences
3. What are the implications for the expected behaviour of the two systems at small temperatures?

Support your arguments with graphs and calculations as appropriate.

Exercise 2

In a mean-field approximation, excluded-volume interactions in a polymer chain of N monomers, at temperature T and in \mathcal{D} -spatial dimensions are described by the expression:

$$\frac{U}{k_B T} = \frac{b^{\mathcal{D}}}{2} \int d^{\mathcal{D}}r \rho(\vec{r})^2, \quad (1)$$

where $\rho(\vec{r})$ is the distribution of the monomers' spatial distances \vec{r} from the center of mass of the chain and b is the bond length.

1. Justify Eq. (1) by simple physical arguments.

A good approximation for $\rho(\vec{r})$ is the Gaussian function:

$$\rho(\vec{r}) = N \left(\frac{\mathcal{D}}{2\pi R_g^2} \right)^{\mathcal{D}/2} \exp \left(-\frac{\mathcal{D}r^2}{2R_g^2} \right), \quad (2)$$

where R_g^2 is the mean-square distance of the monomers from the chain centre of mass (*i.e.*, the chain mean-square gyration radius).

2. By using Eq. (2), compute U (Eq. (1)) as a function¹ of b , N , \mathcal{D} and R_g .
3. Use the exact expression valid for a polymer chain *without* excluded-volume

$$R_g^2 = \frac{b^2 N}{6} \quad (3)$$

together with the expression derived at point (2), to derive for which spatial dimensions Eq. (3) is still valid *even in the presence* of excluded-volume interactions.

¹Useful expressions: $\int d^{\mathcal{D}}x e^{-x^2} = \pi^{\mathcal{D}/2}$.

Exercise 3

Consider a molecular system which can exist in three states: a Dissociated state (D), a product state with Left chiral symmetry (L) and a product state with a Right chiral symmetry (R). The three states can perform transitions among each other according to the rate model

$$\begin{aligned}\frac{dP_D}{dt} &= -(k_{DL} + k_{DR})P_D + k_{LD}P_L + k_{RD}P_R \\ \frac{dP_R}{dt} &= -(k_{RL} + k_{RD})P_R + k_{LR}P_L + k_{DR}P_D \\ \frac{dP_L}{dt} &= -(k_{LD} + k_{LR})P_L + k_{DL}P_D + k_{RL}P_R\end{aligned}$$

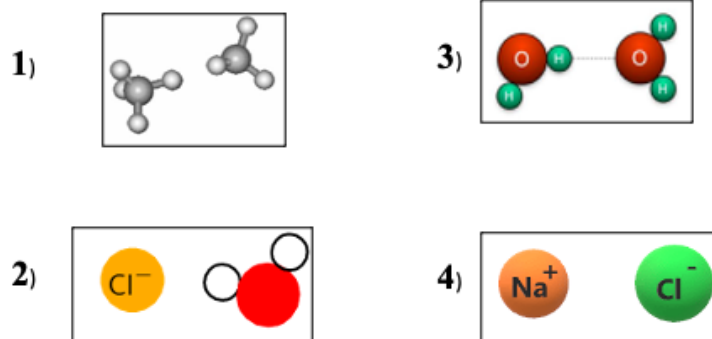
where P_D , P_R and P_L are the probabilities to observe the system in the D, R and L state.

Assume that in an experiment one is able to measure the stationary probabilities of observing the three states: $P_D = 0.5$, $P_R = P_L = 0.25$. Moreover, one is able to measure three of the rate constants: $k_{LR} = k_{DL} = k_{DR} = 0.01s^{-1}$

1. Estimate the three rate constants which are not measured.
2. Assume now that the left chirality state is cleaved by an enzyme as soon as it appears (namely assume that the state L behaves as a probability sink) Compute the stationary probabilities to observe R and D in these conditions.
3. Assume now that also the the right chirality state is cleaved (namely assume that both L and R behave as probability sinks). Assume that the system is prepared at $t = 0$ in state D (namely $P_D(0) = 1$). What is the value of P_D after 5 minutes?

Exercise 4

Donald, Arieh, Martina and Sanna are debating about the strength and length-scale of different molecular interactions. The picture below shows 4 different types of *pairs of molecules* that they are studying: 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 that will help them obtain the correct ranking.

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 5

A molecule at equilibrium can exist in 2 states (A and B) with two different values of the gyration radius ($R_A=2$ nm and $R_B=3$ nm). An experiment reports an average value of the squared gyration radius equal to 2.4^2 nm². Compute the population of the two states.

Now consider that the diffusion constant of the molecule is inversely proportional to the gyration radius. In an experiment performed on a timescale in which the molecule can interconvert between the two states, the diffusion constant is measured to be $100 \mu\text{m}^2/\text{s}$. Find which is the diffusion constant corresponding to each of the two states.

Finally, imagine that the interconversion rate is significantly longer than the experimental time scale, so that a single molecule will remain in the same state for the entire duration of the experiment. Based on the points above, describe an experiment that could be used to separate molecules in state A from molecules in state B.

Exercise 6

A butane molecule ($\text{CH}_3 - \text{CH}_2 - \text{CH}_2 - \text{CH}_3$) is studied by molecular dynamics simulations at equilibrium at 310 K in the gas phase at constant pressure.

The analysis of 10000 snapshots of a single butane molecule shows that the torsion angle Φ defined by the four carbon atoms adopts, as expected, three main rotamers:

c1 roughly centered at $\Phi = -60^\circ$

c2 roughly centered at $\Phi = 60^\circ$

c3 roughly centered at $\Phi = 180^\circ$

where the c3 conformer is referred to as the *anti* conformer and the ensemble of c1, c2 conformers as the *gauche* conformer.

The populations of c1, c2, c3 conformers are: 1629, 1679, 6692, respectively.

The distributions of the angles within each conformers may be approximated by a gaussian with the following mean (μ) and standard deviation (σ):

c1: $\mu = -76.74$ $\mu = 16.4$

c2: $\mu = 76.2$ $\mu = 16.6$

c3: $\mu = 170.2$ $\mu = 18.9$

The observed average energy of the conformers is:

c1: 11.16 kJ/mol

c2: 10.57 kJ/mol

c3: 7.48 kJ/mol

1) estimate the Gibbs' free energy change for the conformational transition *gauche* \rightarrow *anti*.

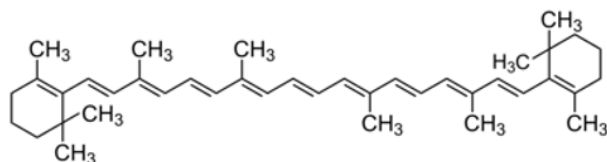
2) estimate the enthalpy and entropy change for the conformational transition *gauche* \rightarrow *anti*.

3) knowing that the distribution of the angle Φ within each conformer is not uniform but similar, can you provide an independent estimate of the conformational entropy?

HyBop applicants can also pick exercises 7, 8 and 9.

Exercise 7 (HyBOP Applicants)

Beta-Carotene is a molecule that is found in carrots and gives it its orange colour.



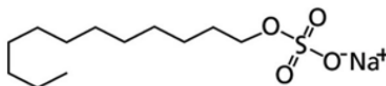
Answer the following questions showing as much of your work/thinking:

1. In the Beta-Carotene structure shown above, some of the carbon atoms are shown being connected with single lines while others are shown with double lines. 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 Beta-Carotene in a different manner? Explain your rationale.
3. Imagine you have been assigned the task of engineering a purple colored carrot. How would you go about changing Beta Carotene so that its color becomes purple? (Hint: 1) Think about what causes the orange color of normal carrot and 2) Think about what controls the energy required to excite an electron in Beta-Carotene with light).

Exercise 8 (HyBOP Applicants)

DT Industries is a newly formed company founded after the recent Covid pandemic. Their specialty is in manufacturing special Soap bars that are claimed to be able to work much better at the spreading of viruses. Below you will find a recent press release that has been published on their website coming from their science team:

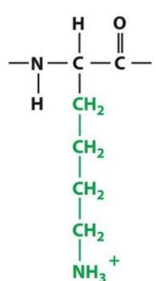
Our team of scientists have synthesized a new soap molecule called SODS-2023 which has a chemical structure shown below. This molecule has an end-to-end length of about 100 nanometers. Tests in our lab have recently demonstrated that the SODS-2023 molecule when mixed with the Corona virus, binds strongly to DNA inside the virus and leads to the modification of the DNA bases. The microscopic origins of this phenomena is due to the fact that SODS-2023 is able to exert forces as large as 5 Newtons that can break the covalent bonds of DNA.



You have been invited as part of an external scientific review panel to evaluate these claims of DT Industries on SODS-2023. Please provide your critique. (Note: Make sure to clearly state what you agree with in the arguments above and why).

Exercise 9 (HyBOP Applicants)

Imraan is taking a Biochemistry course at the University of Beirut and is trying to understand why amino acids such as Lysine (a positively charged amino acid with a structure shown below) are typically found on the surface of proteins and not in the interior. Your task is to rationalize this using the Born Solvation model.



The Born Solvation model allows one to understand the electrostatic contribution to the solvation energy of ions. It states that the free energy of solvation associated with transferring an ion of charge q with radius a from a medium of dielectric constant ϵ_1 to ϵ_2 where $\epsilon_1 < \epsilon_2$ is given by: $\Delta G = -\frac{q^2}{8a\pi\epsilon_0}(\frac{1}{\epsilon_1} - \frac{1}{\epsilon_2})$.

1. Use the Born Solvation model to help Imraan explain why a positively charged amino acid like Lysine is unlikely to be found in the interior of a protein.
2. Can you think about how Lysine could be stabilized inside the center of a protein? (Hint: what types of interactions can Lysine form inside a protein.).