PhD Entrance Examination
Physics and Chemistry of Biological Systems
September 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.

Exercise 1

Consider N, non-interacting point particles in one-dimension and at temperature T. The particles are subject to the following potential,

$$V(x) = \begin{cases} V_0 > 0\,, & 0 \leq x \leq a \\ 0\,, & a < x \leq L \\ +\infty\,, & \text{otherwise} \end{cases} \tag{1}$$

By neglecting the momentum of the particles:

1. Compute the free energy, $\mathcal{F}$, of the system.

2. Compute the mean internal energy, $\mathcal{U}$, of the system.

3. Compute the entropy, $\mathcal{S}$, of the system. Discuss its behavior in the limits of low ($T \to 0$) and high ($T \to \infty$) temperature.

Exercise 2

Consider a particle of mass m that is in canonical equilibrium at temperature T in a one-dimensional confining potential $U(x)$, where

$$U(x) = \begin{cases} \frac{1}{x} + \frac{1}{1-x} & \text{for } 0 < x < 1 \\ \infty & \text{otherwise} \end{cases}$$

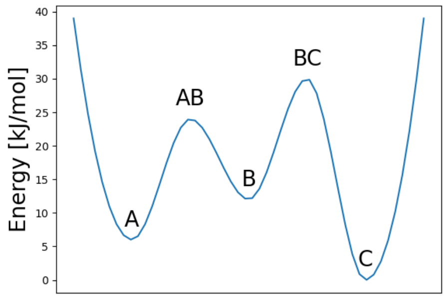
1. Sketch the probability distribution for the position of the particle, $p_T(x)$, for a generic finite temperature T.

2. Consider the mean square fluctuation of the particle around its average position, σ_T^2. How does σ_T^2 depend on T for $T \to 0$? How does the result depend on the particle mass, m?

3. Calculate the asymptotic value of σ_T^2 in the limit $T \to \infty$, σ_∞^2.

4. Estimate the power law with which $\Delta_T \equiv (\sigma_\infty^2 - \sigma_T^2)$ scales with T as $T \to \infty$.

Exercise 3



A system is diffusing on the energy profile represented in the figure. Energies of the minima and saddle points labeled in the figure are:

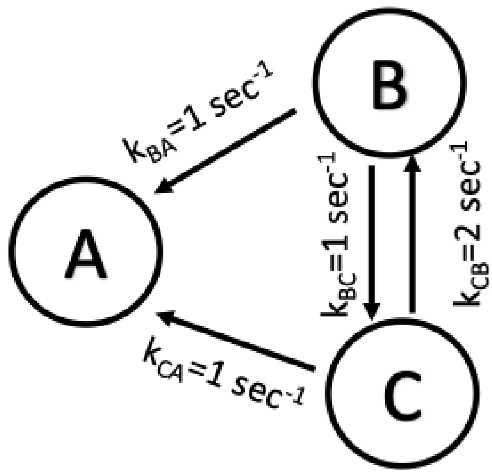
- E_A=6 kJ/mol
- E_{AB}=24 kJ/mol
- E_B=12 kJ/mol
- E_{BC}=30 kJ/mol
- E_C=0 kJ/mol

The thermal energy is $k_B T = 2.5$ kJ/mol. The rates for going from state A to state B and from state B to state C are identical and equal to $k_{A\to B} = k_{B\to C} = 1$ s^{-1}. The system is initialized in state B. Answer the following questions:

1. In which state is the system most probably located after a time $\gg 1$ s?
2. On which timescale is the system expected to arrive to this state?
3. Assume the system has arrived to the most probable state. On average, how long will it take for the system to leave it?
4. Consider again the system as initialized in state B, and imagine to repeat the experiment a large number of times. Is the system more likely visiting state A or C first? With which relative probability?
5. On average, how much time will the first transition, to either A or C, take to happen? Which is the probability distribution of such transition time?

Exercise 4

A molecule can exist in three conformations, labeled A, B, and C. The rate constants for the transitions between these states are represented in figure.



1. Assuming that at time zero the molecule is in state B, in which state will the molecule be at infinite time?
2. Write a differential equation describing the dynamics of the probability of observing the molecule in the three states, p_A, p_B and p_C.
3. The probability of observing the molecule in state B relaxes to equilibrium with the following law:

$$p_B(t) = a_1 \exp\left(-\frac{t}{\tau_1}\right) + a_2 \exp\left(-\frac{t}{\tau_2}\right) + a_3$$

   where a_1, a_2 and a_3 are constants. By using the equation written in the second point find the values of τ_1 and τ_2.

Exercise 5

Consider a one-dimensional harmonic model of a molecule, where a linear succession of N beads are connected by $(N-1)$ harmonic springs of stiffness k. No excluded volume interaction is present among the beads, which can cross through each other. One of the terminal beads is kept fixed while a pulling force is applied to the other. Each spring has rest length L.

Answer the following questions:

1. Consider the system at temperature $T = 0$. How does the energy of the system depend on its signed elongation?
2. Consider the system at finite temperature. How does the free energy of the system depend on its signed elongation and on the temperature T?

Now consider replacing each spring with a square well potential so that the absolute value of the distance between two consecutive beads ranges from 0 to L.

Answer the following questions:

1. Consider the system at temperature $T = 0$. How does the energy of the system depend on its signed elongation?
2. Consider the system at finite temperature. How does the free energy of the system depend on its signed elongation and on the temperature T for $N = 2$ and for $N = 3$? For a generic value of N, how do the average and the standard deviation of the elongation depend on N?

Exercise 6

In many docking programs the binding free energy between two molecules is computed as the sum of different contributions from a single docking pose.

1. try to figure out what are such contributions;
2. comment on the kind of approximations involved in this approach;
3. comment on the kind of approximations involved, for each term you listed;
4. comment on pros and cons of the approach.