PhD Entrance Examination
Physics and Chemistry of Biological Systems
September 2017

Solve **one** of the following problems (no extra credit is given for attempts to solve more than one problem). 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. Do not write your name on the problem sheet, but use extra envelope.

Problem n. 1 – Extensible polymer chain

Consider a linear polymer chain which is composed of N chemical units ("monomers"), each of which can be in one of two states, of different lengths a and b, with $b > a$. The total length of the molecule, L, therefore satisfies the inequalities $Na < L < Nb$. The energy of a monomer in the longer state is ϵ larger than a monomer in the shorter state. You may consider the thermodynamic limit $N \gg 1$ to simplify the calculations.

(a) Calculate the equilibrium length, $\langle L \rangle$, of the entire molecule as a function of temperature T.

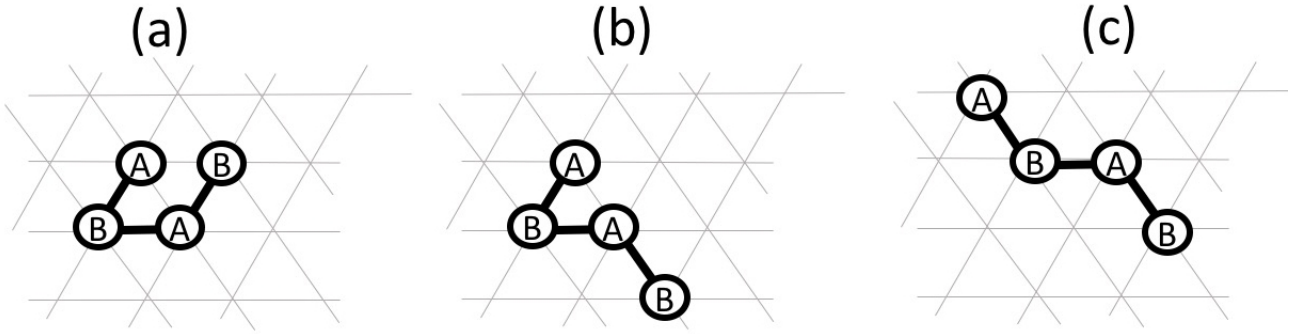
(b) Calculate the root-mean-square fluctuation in the length of the entire molecule as a function of temperature T.

(c) Now, suppose that the molecule is forced to have fixed length $L\,(Na < L < Nb)$. Find the internal energy $E(N, L)$ and the entropy $S(N, T, L)$.
Hint: Find first the total number of monomers in state b, N_b, as a function of L, a, b and N. Derive the other quantities in term of N_b.

(d) From (c) calculate the Helmholtz free energy $F(N, T, L)$, and finally the force needed to extend the molecule to length L at *fixed* temperature T.

Problem n. 2 – Inference of the parameters of a model protein

Consider a model protein composed by 4 residues on a triangular lattice. Each site cannot be occupied by more than one residue. Two residues interact only when they occupy neighboring sites. Consecutive residues do not interact. Some of the possible configurations of the protein are depicted in Figure



Assume first that the protein is a homopolimer of primary sequence AAAA. The interaction energy is $\varepsilon_{AA} = -1$.

1. Compute the probability that the two ends of the polymer are in contact at a temperature $T = 1$

2. Compute the entropy as a function of T. Draw a graph of the result.

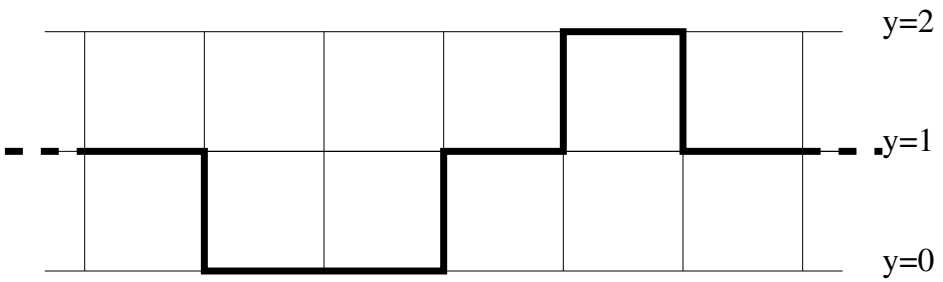
Assume now that the primary sequence is ABAB. Also in this case, two residues interact only when they occupy neighboring sites, with interaction energies ε_{AA} and ε_{AB}. We also assume $\varepsilon_{BB} = 0$, namely that B residues do not interact with each other. In an experiment one has observed the configuration (a) two times, the configuration (b) five times and the configuration (c) one time

3. Compute the partition function of the system.

4. Estimate the most likely values of the two parameters ε_{AA} and ε_{AB} (hint: maximize with respect to the parameters the probability of the experimental observations estimated with the model. Assume that the probabilities of the single observations are statistically independent).

Problem n. 3 – A polymer chain in a channel

As a simple model for a channel-confined polymer, consider a walk confined in a strip on a square lattice with unit spacing. The strip is unbound in the longitudinal direction (x Cartesian axis) while in the transverse direction (y Cartesian axis) it is bound by two impenetrable walls at positions $y = 0$ and $y = 2$, see Figure. For simplicity, let us assume the confined walk to be directed, meaning that there cannot be more than one step per lattice column (i.e. no longitudinal backfolds), and to be restricted too, meaning that vertical steps larger than one lattice spacing are not allowed, see Figure below where the walk is shown with a thick line.

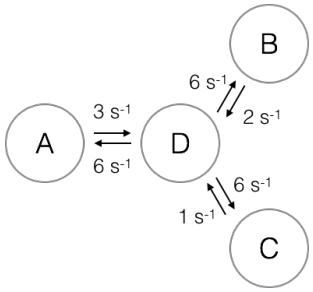


The step and wall fugacities are equal to z and w, respectively, so that the statistical weight of a chain configurations of n steps, of which m lie on the walls is given by: $z^n \cdot w^m$.
Consider the canonical ensemble of configurations that span N columns of the lattice, with $N \gg 1$.
After setting $w = 1$ compute:

1. the partition function of the system,
2. the average contour length of the chains,
3. the average number of steps touching the walls.
4. Discuss how the previous results change in more general case where w can take any non-negative value.

Problem n. 4 – equilibrium and out of equilibrium

A system has four metastable states labeled A, B, C, and D. The possible transitions among these states are shown in the Figure, where also the corresponding rates are indicated ($k_{A\to D} = 3s^{-1}$; $k_{B\to D} = 2s^{-1}$; $k_{C\to D} = 1s^{-1}$; $k_{D\to A} = k_{D\to B} = k_{D\to C} = 6s^{-1}$).

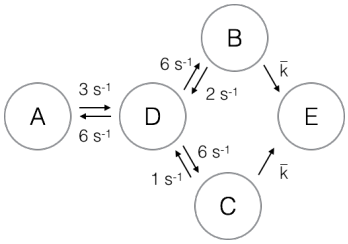


At equilibrium:

- Sort the four states from the most stable to the least stable.
- Find the equilibrium probability for each of the 4 states.

Now consider the following non equilibrium processes. In all these cases the system is initialized in A.

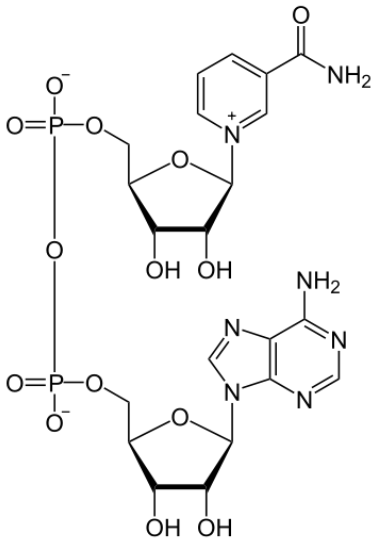
- Which is the probability that the system reaches B before C?



- Consider now an additional state (E) with can be reached both from B and from C with an irreversible transition such that $k_{B\to E} = k_{C\to E} = \bar{k}$. Which is the probability that the system reaches E passing through B rather than C? Does this probability depend on $\bar{k}$ and, if so, how?
- In the limit of $\bar{k} \ll 1$, compute the probability of finding the system in E as a function of time.
- In the limit of $\bar{k} \gg 1$, compute the first and second derivative with respect to time of the probability of finding the system in E.

Problem n. 5 - Biological Redox Reactions

The coenzyme Nicotinamide adenine dinucleotide (NAD) is involved in many biological redox reactions.
This coenzyme exists as oxidizing agents (NAD+, see Figure), which accepts electrons and a proton from a different molecule, becoming reduced (NADH). The biological standard potential for NAD+ reduction at 25° is -0.32 V.



1) Considering that C4 of the pyrimidine ring accepts a proton write the structure of NADH and the half reaction of the NAD+/NADH equilibrium.

2) Which is the change of oxidation state of the C4 atom?

3) Draw the possible resonance structures of NAD^+/NADH and comment on the stability of the molecules.

4) NAD^+/NADH participate to aerobic metabolism
Considering a biological standard potential for the reduction of O_2 (g) to H_2O_2 (aq) of 0.68 V, write the half reaction for the O_2 (g) to H_2O_2 reduction, and the overall reaction of the aerobic metabolism involving NAD^+/NADH and O_2/H_2O_2.
Calculate the standard potential of this reaction.

5) At standard conditions how would you expect the overall reaction to be affected by the pH?