The candidate should address one problem. No extra credit will be given for doing more than one problem.

Curriculum in drug discovery

PROBLEM A

Address three of the following issues:

A1) Describe the structure of chromatin and its dynamic changes in response to DNA transactions (transcription, repair).

A2) Secondary structures in RNA and their relation to function.

A3) Biophysical aspects of protein folding.

A4) Describe the main structural features of nucleic acid-binding proteins

A5) Discuss experimental methods (biophysical or genetic) to study protein-protein interactions.

A6) How may gene expression profiles help us in designing new drugs?

A7) The candidate is requested to provide examples of molecular diagnostics.

A8) What is personalized medicine?

A9) microRNA as drug target

PROBLEM B

Address one of the following points:

B1) Propose a synthetic approach to obtain the benzodiazepine scaffold and describe the mechanism of action for classical benzodiazepine anxiolitic agents.

B2) Describe the technique of virtual screening (both ligand- and target-based) applied to computational drug design.

B3) Describe the spectroscopic approaches for the characterization of newly synthesized chemical entities.

B4) Biology is undergoing a fundamental change with the application of modern computational methodologies that can manage huge amounts of information and can simulate highly complex processes.
In this context, describe a computational tool in biological sciences and discuss its possible connections to experiments.

PROBLEM C

Boundary effects on a chain of spins

Consider a one-dimensional chain of N ising spins, $s_i = \{+1, -1\}$, interacting through the following Hamiltonian:

$$\mathcal{H} = -\sum_{i=1}^{N-1} s_i \, s_{i+1} \tag{1}$$

1. Calculate (i) the partition function for the system; (ii) the free energy and (iii) the specific heat. Sketch and comment how the specific heat behaves as a function of the system temperature, T.

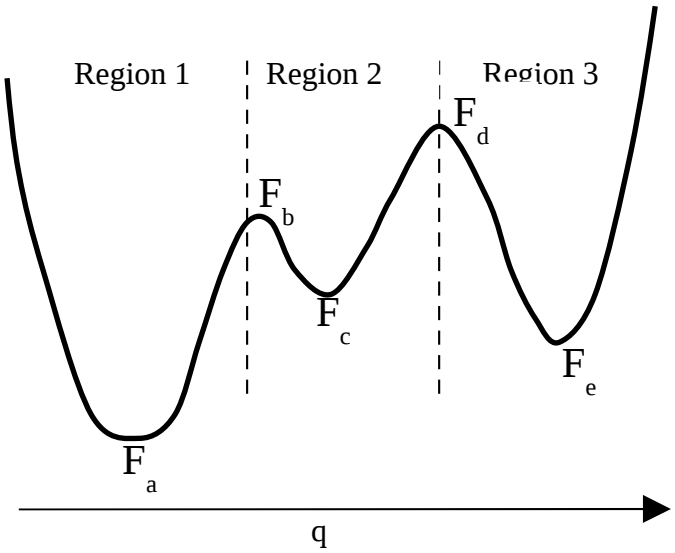
2. Repeat the above calculations for the case where the first and last spin are fixed to be up: $s_1 = s_N = +1$. Compare the answers with the previous case and comment on the differences.

3. Assume now that only the first spin is fixed and set to point up: $s_1 = +1$. Discuss how this choice of boundary conditions affects the subsequent spins along the chain. In particular, discuss how the (temperature-dependent) probability of the nth spin to be up, $P(s_n = +1)$, approaches its bulk limiting value as a function of n (assume $n << N$).

PROBLEM D

Rate model on a potential with three minima

The free energy as a function of a reaction coordinate q is the tristable potential depicted in figure:



The probability at time t to observe the reaction coordinate in the region 1, 2 or 3 is denoted as $c_1(t)$, $c_2(t)$ and $c_3(t)$, respectively. If the barriers separating the three regions are much higher than k_BT, the evolution of c_1, c_2 and c_3 can be approximately described by the rate equations

$$\frac{dc_1}{dt} = -k_{12}c_1 + k_{21}c_2$$
$$\frac{dc_2}{dt} = k_{12}c_1 - (k_{21} + k_{23})c_2 + k_{32}c_3 \qquad (1)$$
$$\frac{dc_3}{dt} = -k_{32}c_3 + k_{23}c_2$$

a) What is the equilibrium probability $< c_2 >$ to observe the system in the region 2?

b) How many time constants role the relaxation of the system towards equilibrium? Express these time constants as a function of the rates.

c) Find an approximate expression for the rate constants k_{ij} in Eq. 1 as a function of the free energies represented in figure and of the temperature. You can assume that the rate for crossing a barrier of k_BT is equal to one.

d) In the special case $F_a=F_c=F_e$ and $F_b=F_d$, use the kinetic model (1) to compute $c_2(t)$ for a system prepared at time t=0 in the region 2 and for a system prepared in the region 3.

Curriculum in Nanoscale Biophysics and Biotechnology

Describe in detail a recent experiment in any field of science or technology (physics , chemistry, biology, medicine) carried out at the nanoscale that you find particularly significant. Your paper should be divided into sections, each approx. one page long, as follow:

1) An introductory part to give some background information
2) Description of the experiment
3) Listing of the reasons why you find it significant

One of the goals we have in asking you to write your exam in this way is to define a ground on which you feel confortable to be examined in the oral part of the examination.