October 2010 - Entrance Examination
Physics and Chemistry of Biological Systems

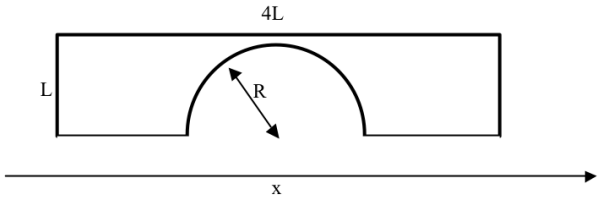
Solve **one** of the following problems (no extra credit is given for attempts to solve more than one problem). Write out solutions clearly and concisely. State each approximation used. Diagrams welcome. Number page, problem, and question clearly. All essays/solutions should be written in English. Do not write your name on the problem sheet, but use extra envelope.

Exercise 1 - Dragged harmonic oscillator

A point of mass m hangs at a rest height x_0 from a vertical spring whose elastic constant is k. The top point of the spring, $\boldsymbol{O}$, is held fixed in $\boldsymbol{O_0}$. The horizontal movements of the point are negligible. At time $t = t_0$ the spring attachment point, $\boldsymbol{O}$, is moved vertically (no horizontal displacements) and reaches height $\boldsymbol{O_1}$ at time $t = t_1$. During the movement the point mass moves only vertically.

1. Write the coupled differential equations satisfied by the vertical position $x(t)$ and velocitiy $v(t)$ of the point in the three situations:
    a. $t < t_0$
    b. $t_0 < t < t_1$
    c. $t > t_1$.
2. Assuming that the point start at its rest height $x(t_0) = x_0$ and with initial velocity $v(t_0) = v_0$, provide an explicit expression for the trajectory $[x(t), v(t)]$ for:
    a. $t < t_0$
    b. $t_0 < t < t_1$
3. Calculate the total work W made to move the spring attachment point from $\boldsymbol{O_0}$ to $\boldsymbol{O_1}$. At fixed $\Delta t = t_1 - t_0$, and assuming that initially the point mass is at rest, $v_0 = 0$, plot W as a function the movement amplitude $\boldsymbol{\Delta O} = \boldsymbol{O_1} - \boldsymbol{O_0}$.
4. Imagine to repeat the experiment for an ensemble of Gaussian-distributed initial velocities v_0. Given the standard gravity g, is the average work larger or smaller than $mg\boldsymbol{\Delta O}$? Can the work be exactly equal to $mg\boldsymbol{\Delta O}$? Motivate your answers.
5. How do you expect the above results to be affected if the experiment is performed in a viscous medium?

Exercise 2 - A particle confined in a two-chamber container
Consider a particle of mass *M* and charge *q* confined in the two-dimensional box represented in figure.



The particle is held at a temperature *T* by a thermostat and its radius is very small compared to the dimension of the container.

1. Compute the probability density, *P(x),* to observe the particle at position *x*.
2. Compute the average energy *E(x)* and the free energy *F(x)* as a function of *x*. Sketch *F(x)* for *R=L/2* and *R=L-ε*, where *ε<< L*
3. Apply now a constant electric field V along the x direction. Repeat the calculation of *P(x)*, *E(x)* and *F(x)*.
4. For *R=L-ε*, discuss how the rate for a transition between the left and the right chamber depends on *V* and *T* (hint: to estimate the transition rate use transition state theory, in which the rate depends only on the free energy difference between the barrier and the free energy minimum corresponding to the initial state).

Exercise 3 - Classical molecular dynamics
Describe the theoretical foundations of classical molecular dynamics (MD). Next discuss the techniques used to simulate different statistical ensemble (microcanonical, canonical and isobaric). Finally, discuss the MD strengths and weaknesses to study the functions of biomolecules.

Exercise 4 - Bioinformatics
Discuss the general principles of the methods used for protein sequence alignment and structural alignment. Provide a description, as detailed as possible, of their algorithmic strategies. Discuss, with the aid of concrete examples, how the current understanding of the relationship between protein sequence and structure has benefitted from these bioinformatics tool.

Exercise 5 - Molecular biology
Discuss one of the following topics:

1. Strategies to target protein aggregation for therapeutic treatments of neurodegenerative diseases.
2. How gene expression profiling can impact drug discoveries.
3. Methods to study gene expression.
4. Gene therapy.
5. Animal models of neurodegenerative diseases.
6. Molecular pathways target for therapeutic treatments of neurodegenerative disease.
7. High-throughput screening for phenotype modifiers of small molecules and gene products.