SISSA ISAS

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October 2008 – Entrance Examination
PhD in 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.

Problem n. 1 – Write an essay

Write an essay on **two** of the following topics.

1. Discuss the role of protein modifications in regulating protein/protein interactions.
2. Discuss the role of protein modifications in regulating chromatin assembly and protein/DNA interactions.
3. Discuss RNA as a target for therapeutic intervention
4. Discuss strategies in drug screening for neurodegenerative diseases
5. Discuss the validation of a drug target for neurodegenerative diseases
6. Discuss the implications of the mapping of the human genome sequence for drug design.
7. The candidate must design a screening to identify new inhibitors of apoptosis.
8. From the biophysicist's workbench to the pharmacy bench: describe what the ideal path of a successful drug is.
9. Molecular simulation and experiment in biophysics: describe what information they provide and how they are related.
10. Summarise the biological role of small non coding RNAs in the cell.
11. Discuss the physical principles governing the interaction between proteins and nucleic acid.
12. Describe a possible synthetic approach, mechanism of action, and structure-activity relationships (SAR) for a class of drugs belonging to the steroid hormone families.
13. Describe the basic principles of combinatorial chemistry in the drug discovery process.

Problem n. 2 – Stationary probability distributions and detailed balance

Consider a random walk on a lattice with four sites. The master equation for the probability $p_i(t)$ to observe the system in site i at time t is

$$\frac{dp_i(t)}{dt} = \sum_{j=1}^{4} k_{j\to i}\, p_j(t)$$

where $k_{j\to i}$ is the rate for a transition between site j and i. The off-diagonal rates are

$$\begin{aligned} k_{1\to 2} = k_{4\to 3} &= 1 \\ k_{2\to 3} = k_{3\to 4} &= \tfrac{3}{4} \\ k_{2\to 1} = k_{3\to 2} &= \tfrac{1}{4} \\ k_{1\to 3} = k_{1\to 4} = k_{2\to 4} = k_{3\to 1} = k_{4\to 1} = k_{4\to 2} &= 0 \end{aligned}$$

1. Estimate the values of the diagonal rates $k_{i\to i}$, $i = 1, 2, 3$ and 4.
2. Find the stationary probability distribution of the system and characterize its relaxation towards equilibrium. Does the system obey detailed balance?
3. Now take

   $$\begin{aligned} k_{1\to 2} = k_{2\to 3} = k_{3\to 4} = k_{4\to 1} &= \tfrac{3}{4} \\ k_{2\to 1} = k_{3\to 2} = k_{4\to 3} = k_{1\to 4} &= \tfrac{1}{4} \\ k_{1\to 3} = k_{2\to 4} = k_{3\to 1} = k_{4\to 2} &= 0 \end{aligned}$$

   Repeat points 1 and 2.
4. If the system is in its stationary state, what is the probability current between site 3 and 2 if the rates are the ones defined in point 3? Describe a physical system that could be described by a master equation with similiar properties.

Problem n. 3 – Fluid Mechanics

This problem deals, in fact, with hydrostatics. Assume throughout that spatial variations of the acceleration of gravity $\mathbf{g}$ are negligible, so that we can write $\mathbf{g} = g(0, 0, -1)$, where $(0, 0, -1)$ is a vertical unit vector pointing downwards and g is the modulus of $\mathbf{g}$.

Question 1

Prove Archimede's law stating that a body immersed in a fluid at rest is subject to a force equal and opposite to the weight of the fluid it displaces.

Question 2

Assume that a fluid at rest occupies half of the volume of a cubic container of edge length L, which is open on the top and exposed to the atmosphere.

a) Compute the force exerted by the fluid on each of the four lateral sides of the container and the one on the bottom surface (the base).

b) Prove that the top free surface of the fluid must be horizontal.

c) Explain why the system under consideration is different from one where water is substituted by an equal mass of sand (notice e.g. that the top free surface of sand can assume a conical shape while, according to b) this is impossible for water). Is the vertical component (the one along $(0, 0, -1)$) of the force exerted by sand on the bottom surface larger or smaller than the one exerted by an equal mass of water?