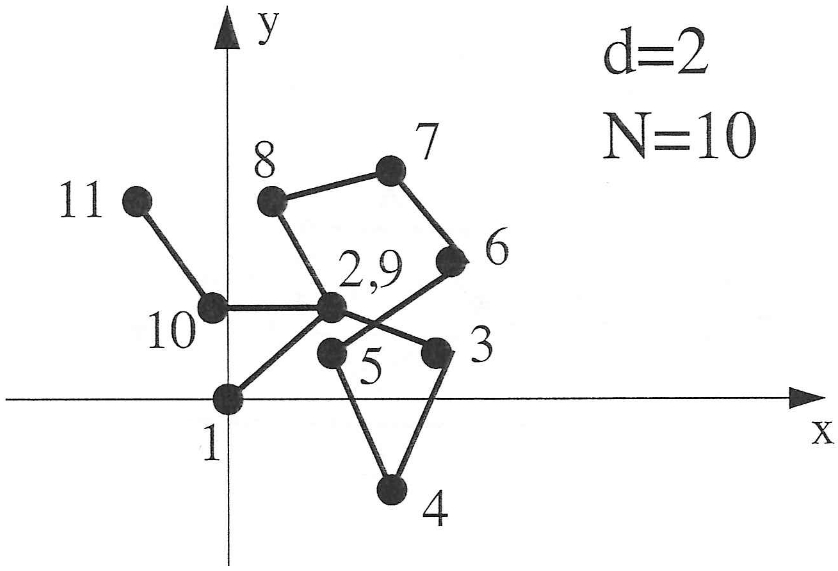
October 5, 2009

PhD in Physics and Chemistry of Biological Systems
Entrance examination

- Solve one of the following problems/essays (no extra credit is given for attempts to solve more than one problem).
- Write out solutions/essays clearly. 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.

Spatial confinement of a phantom polymer

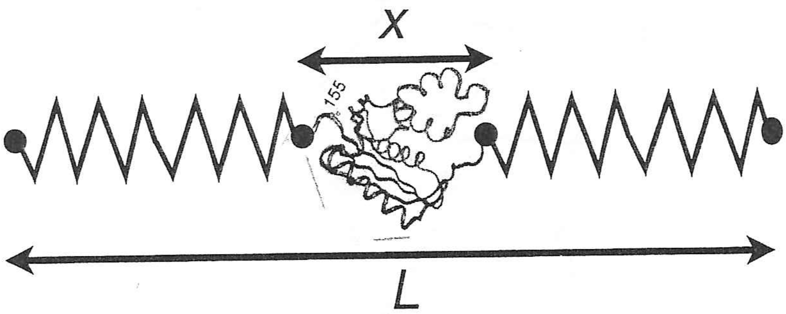
Consider a model polymer made of N rigid bonds of length l embedded in a d-dimensional space . The first polymer site is rooted at the origin, $\vec{x} = 0$. The polymer bonds can overlap without energy penalty and the directionality of any pair of distinct bonds is uncorrelated (see figure).



1. Compute the mean square end-to-end distance for arbitrary d.
2. For $d = 1$ write down an explicit expression for the probability of the last polymer site to occupy the origin.
3. For $d = 1$ write down the probability distribution of the end-to-end distance in the limit $N \gg 1$.
4. Consider again $d = 1$ and assume that impenetrable walls are placed in such a way that the system is constrained to occupy lattice sites in the range $0 \leq x \leq L$. Compute the entropy of the system for $L = N\,l$, $L = (N-1)\,l$ and $L = (N-2)\,l$.

Single-molecule stretching

Consider a protein attached to two molecular handles. The two end points of the handles are kept at a distance L. The protein termini, at which the handles are attached, are constrained to remain on the same axis, so that the system is effectively one-dimensional (see figure). Each handle is approximated by a spring with force constant k. The biomolecule has two possible available states, named U and F, with different energy and different stiffness, so that the energy of the molecule as a function of its end-to-end distance x is $\epsilon_F + \frac{k_F x^2}{2}$ in the F state and $\epsilon_U + \frac{k_U x^2}{2}$ in the U state. The system is in equilibrium at temperature T.

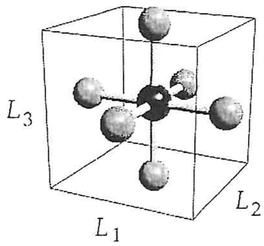


1. Calculate the partition function of the system as a function of L and the average force required to keep the handles at a given distance L.
2. Draw a sketch of the free energy of the system as a function of L. Discuss what happens for different values of ϵ_U and ϵ_F.
3. Assume the system is prepared in an equilibrium condition at $L = L_0$, and subsequently L is increased infinitely slowly until it reaches $L = \bar{L}$. Calculate the total work that is performed on the system.
4. Assume now that the experiment of point 3 is repeated increasing L faster, in such a way that the molecule has no time to undergo a transition. Calculate the average work performed on the system if this experiment is performed a very large number of times.
5. Indicate which of the two works at points 3 and 4 is larger and motivate your answer.

The Jahn-Teller Distortion

In 1937 Hermann Arthur Jahn and Edward Teller demonstrated that non-linear degenerate molecules cannot be stable and undergo structural distortions which remove the degeneracy. The Jahn-Teller theorem is of paramount importance in chemistry, in particular in coordination metals chemistry.

Although Jahn and Teller demonstrated their theorem using group theory only, a quantum particle in a three-dimensional box represents a simple model to describe this effect on an octahedrally coordinated metal ion (see the figure below).



The energy states and wave functions for a particle in a three-dimensional box, whose lengths are L_1, L_2, and L_3, are given by

$$E(n_1, n_2, n_3) = \frac{h^2}{8m}\left[\left(\frac{n_1}{L_1}\right)^2 + \left(\frac{n_2}{L_2}\right)^2 + \left(\frac{n_3}{L_3}\right)^2\right],$$

and

$$\psi(x, y, z;\ n_1, n_2, n_3) = \sqrt{\frac{8}{L_1 L_2 L_3}} \sin\left(\frac{n_1 \pi x}{L_1}\right) \sin\left(\frac{n_2 \pi y}{L_2}\right) \sin\left(\frac{n_3 \pi z}{L_3}\right).$$

Assuming that the *d*-electrons of the metal can be ascribed to non-interacting particles in a box, address the following points:

1. Show that the lowest energy level is non-degenerate and the second energy level is triply degenerate if $L_1 = L_2 = L_3$. What values of the quantum numbers n_1, n_2, and n_3 characterize the states belonging to the triply degenerate level?

2. For a cubic box of volume $V = L_1 L_2 L_3$, show that for three electrons in the box (two in the non-degenerate lowest "orbital", and one in the next) a rectangular distortion (*e.g.*, $L_1 = L_2 \neq L_3$) which preserves the total volume will result in a lower total energy than the undistorted box. Why (in terms of the central metal atom or ion) is it necessary to assume the volume fixed?

3. Show that the degree of distortion (ratio of L_3 to L_1) that maximizes the total energy is $L_3 = \sqrt{2} L_1$.

4. Discuss how this problem relates to Jahn-Teller distortions. Give some examples of coordination compounds in which the Jahn-Teller distortion applies.

Medicinal Chemistry

Address one of the following issues, in essay format.

1. Describe a possible synthetic approach, mechanism of action, and structure-activity relationships (SAR) for anti-mitotic agents.
2. Describe the technique of QSAR (Quantitative Structure-Activity Relationship) and 3D QSAR applied to computational drug design.
3. Discuss parallel syntheses of novel drugs.

Cellular and Molecular Biology

Address one of the following issues, in essay format.

1. Describe the eukaryotic cell cycle and its regulation.
2. DNA damage and its role in cancer development.
3. Give an overview of the role of post-translational modifications in the cell and its relevance to disease.

Structural Biology

Address one of the following issues, in essay format.

1. Characteristics and properties of intrinsically unstructured proteins.
2. Describe an important structure published over the last 5 years and its relevance to health.
3. Compare protein crystallography and NMR, and their role in drug design.

Nanoscale biophysics and biotechnology

Address one of the following issues, in essay format:

1. Biomolecules and the physical principles of their reactions: the candidate should describe an experiment, based on at least two different monitoring techniques, to address a specific biomolecular reaction or interaction of his/her choice. Describe with particular enphasis how the two techniques are both necessary. If at least one of the two measurements/phenomena occurs at the nanoscale it will be best but the presence of nanotechnology is not a must. Avoid in as much as possible vague and qualitative statements using numbers and units or at least orders of magnitude for the quantities involved.

2. Transport mechanism in (bio)molecular systems: the candidate should describe an experiment, based on at least two different physical techniques, where electron or ion transport is involved in a biologically or at least molecularly relevant context. Describe with particular enphasis how the two techniques are both necessary. If at least one of the two measurements/phenomena occurs at the nanoscale it will be best but the presence of nanotechnology is not a must. Avoid in as much as possible vague and qualitative statements using numbers and units or at least orders of magnitude for the quantities involved.