~~Victim~~ Student: Apratim Sahay
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Examiners: Jeff Gore, Mehran Kardar, Jeremy England
Question: Pulling DNA
Length of Exam: 1h 40 mins

My warm-up problem was on polymer models for DNA-specifically a model which takes into account the energy to bend a polymer (problem attached to end of this document). The problem asked me to calculate the polymers persistence length and force-extension curves of pulling DNA by in the limit of a small force. I read Kardar's lecture notes from the stat bio class which described persistence length and setting up a taylor expansion to calculate the partition function in the limit of small external forces. Philips' Physical Biology textbook also had a nice discussion of the differences between the freely-jointed chain and worm-like chain models.

Here are some of the questions I was asked about the warm-up problem (about 40 mins):

Estimate persistence length for a DNA. How would it change with temperatue. What factors go into the bending rigidity?
Estimate the forces an experimentalist would need to stretch or bend the DNA. (answer is on the order of tenth of a piconewton)
If you have a short and a long piece of DNA , how much force would you need to stretch both by the same fraction, say 10%
How does the average length of a polymer scale with its size? What happens to the scaling coefficient in a more realistic self-avoiding polymer? Does it increase or decrease? Do you have any intuition why?

Then started the no holds barred grilling session -

Jeremy- why can equilibrium stat mech ideas be used to describe biological systems that are usually non-eq or open etc. What are the conditions reqd for equilibrium? What is the entropy of a dog in a box- does it increase or decrease with time in a microcanonical ensemble? Is it in equilibrium?Think of an ice cube in water and the evolution of phase space for the ice molecules over time

Jeff- Take a charged plane and put it into water. What happens? Does the screening phenomena depend upon the fact that there are free H ions in water or just the fact that it is a polar compound? Can you describe the length scales over which charge distributions change? Estimate the debye screening length and write down the factors it depends upon. Useful to think of the Bjeuren length. How does it scale with the concentration of ions? Temperature? I tried to intuitively think about the scaling and used dimensional analysis.

Mehran-Can you derive the Poisson-Boltzmann equation and solve it for this distribution to show an explicit exponentially decaying distribution?

Jeff-Suppose you hold a rubber band and attach a small weight to it . Now take a hairdryer and heat the rubber band. What happens to the weight, does it go up or down? Think about the zero T case first and the entropy of the rubber band as you stretch it. This is an example of entropic forces that can do mechanical work.

Style of questioning-
In the spirit of the random walk model, I got stuck and confused a lot of times with the questions asked, and usually ended up doing a random walk towards the correct answer! Luckily, the examiners were very kind and asked me leading questions and used the socratic method when I got stuck.

Preparation-
I studied full time for about 15 days, primarily working through the textbooks Physical Biology of the cell by Rob philips et al. and Biophysics by Philip Nelson. I found the their estimation examples quite helpful in developing intuition about scales of forces and energies and lengths that apply to different biological systems. I found it useful to summarize chapters in a notebook with some key derivations and estimates so that I could revise quickly. Definitely practice explaining things out loud or to friends because it is easy to think that you understand something but don't know how to explain it. Reading the lecture notes from Kardar and Mirny's Stat physics in biology class also helped though that material was on too mathematical a level for an oral exam. I basically followed Jeff's and Hyun's advice to prepare for the exam.

10. *Pulled DNA:* Consider a DNA molecule as a polymer chain with no torsional stress consisting of N segments of length **b** and orientation vector $\vec{t}_i$. The energy of a given chain configuration is the sum of the bending energies of successive segments:

$$E = -\frac{B}{b}\sum_{i=2}^{N} \vec{t}_i \cdot \vec{t}_{i+1}.$$

(a) Show that the persistence length of the DNA molecule is:

$$\xi_T = \frac{B}{k_B T}.$$

(b) Show that the chain end-to-end mean square distance satisfies:

$$R_g^2 = \langle R^2 \rangle = 2Nb\xi_T.$$

where R_g is the typical size of a fluctuating random coil and is called the gyration radiu

(c) Show that in the presence of an external force F, the mean extension L is given by:

$$L = \frac{F}{3k_B T} R_g^2,$$

for small forces ($L \ll Nb$).

(d) Show that in the limit $B = 0$ (Freely Jointed Chain Model):

$$L = Nb\left[\coth\left(\frac{Fb}{k_B T}\right) - \frac{k_B T}{Fb}\right].$$

(e) Design an experiment that could test these predictions.