

APh105c
Homework 5
Due Date: Friday, May 5, 2006

“As sight is good in the body, so is rationality in the mind.” -Aristotle

Reading: Read chaps. 14, 15, 16, 29 and 30 of Dill and Bromberg.

1. Excluded Volume Interactions

(a) In class I worked out a general statement of the free energy between two objects which was based upon the osmotic pressure and the excluded volume. Repeat that derivation and show that the general expression for the free energy as a function of the distance between the two large particles is

$$F(D) = -\Pi_o V_{excl}(D), \quad (1)$$

where $\Pi_o = Nk_B T/V$ is the osmotic pressure. Then, make an estimate of what this osmotic pressure is by using the density of proteins inside of a cell like *E. coli*. To figure that out, use the fact that such a cell has a volume of about $1 \mu m^3$ and roughly 2×10^6 proteins in its cytoplasm. Using this value for Π_o and the excluded volume between two spheres of radius $1 \mu m$, work out the force as a function of distance and make a plot using pN as your unit of force and nm as your unit of distance. Assume that the small particles have a radius of 3 nm.

(b) Treat the case of two cylinders and work out the free energy of interaction when they are parallel and when they are end to end. Then, compute the excluded volume force between them.

2. Continuous Distributions, Missing Information and Functional Minimization.

All of our discussion of entropy maximization thus far in the course has centered on probability distributions that are discrete. That is, we asked for the probability distribution on a finite set of possible outcomes. But what

happens in the case where the outcomes are continuously distributed? Finding out the answer to that question is the goal of this problem. Your task is to learn how to write the Shannon entropy and associated constraints for the case in which we have a probability distribution that is continuous. Then, you are going to find the *best* (in the Shannon sense) continuous distribution that has first moment $\mu_1 = \langle x \rangle$ and second moment $\mu_2 = \langle x^2 \rangle$. That is, all the information you are given is that the average value of x over the entire distribution is μ_1 and that the expectation $\int_{-\infty}^{\infty} p(x)x^2 dx = \mu_2 = \langle x^2 \rangle$. The wonderful outcome of this analysis is that the best guess you can make is a Gaussian distribution.

The tool needed to perform such minimization and maximization is the functional calculus. Finding the extrema of functionals is more subtle than minimizing a function as in ordinary calculus. A functional is a mapping between functions and numbers. A clean (and conventional) notation to distinguish functions $f(x)$ from functionals $F[g(x)]$ is the use of the brackets $[]$. The basic idea of a functional is that we are given a function $g(x)$ and the functional spits out a number $F[g(x)]$. For example,

$$F[g(x)] = \frac{1}{2\pi} \int_0^{2\pi} g(x) dx, \quad (2)$$

is a functional since for each function $g(x)$ that you can dream up (and for which the integral exists) we obtain a number $F[g(x)]$. One of the key questions posed in the calculus of variations is: find that $g(x)$ that minimizes $F[g(x)]$. We will come to this later. For our problem involving entropy maximization, the idea is to construct a functional $S[p(x)]$ of the unknown probability function $p(x)$.

(a) Show (and explain) that the entropy *functional* that requires minimization is

$$\begin{aligned} S[p(x)] = & - \int_{-\infty}^{\infty} p(x) \ln p(x) dx - \gamma_0 \left(\int_{-\infty}^{\infty} p(x) dx - 1 \right) \\ & - \gamma_1 \left(\int_{-\infty}^{\infty} p(x)x dx - \langle x \rangle \right) - \gamma_2 \left(\int_{-\infty}^{\infty} p(x)x^2 dx - \langle x^2 \rangle \right). \end{aligned} \quad (3)$$

In particular, explain why there are three Lagrange multipliers, why we have to write this problem in terms of integrals, etc.

(b) Next, we take the functional derivative of this expression and set it equal to zero. This amounts to finding that *function* $p(x)$ that maximizes the entropy subject to our various constraints. To do this, we need to define what we mean by the functional derivative which we will define as

$$\frac{\delta S[p(x)]}{\delta p(x)} = \lim_{\epsilon \rightarrow 0} \frac{S[p(x) + \epsilon \eta(x)] - S[p(x)]}{\epsilon}. \quad (4)$$

The first quantity on the left with the δ is the notation for the functional derivative. The stuff on the right side is how you actually implement it. Note that we have introduced a function $\eta(x)$ which is an excursion of the function $p(x)$. That is, we perturb $p(x)$ by adding some other function $\eta(x)$ to it. However, that perturbation is “small” because it is controlled by the small parameter ϵ which we send to zero in the end. Take the functional derivative of your result from part (a) and show that the probability distribution is of the form

$$p(x) = e^{-1-\gamma_0-\gamma_1 x-\gamma_2 x^2}. \quad (5)$$

I will walk you through the hardest of the terms and you do the rest. Let’s work out the functional derivative of the log term.

Show that if the only term we have in our functional is the log term then the definition of the functional derivative leads us to

$$\frac{\delta S[p(x)]}{\delta p(x)} = \lim_{\epsilon \rightarrow 0} \frac{-1}{\epsilon} \left(\int_{-\infty}^{\infty} (p(x) + \epsilon \eta(x)) \ln(p(x) + \epsilon \eta(x)) dx + \int_{-\infty}^{\infty} p(x) \ln p(x) dx \right). \quad (6)$$

Now, by rewriting $\ln(p(x) + \epsilon \eta(x)) = \ln p(x) + \ln(1 + \epsilon \frac{\eta(x)}{p(x)})$, make a Taylor expansion to linear order in ϵ and show that we are left with

$$\frac{\delta S[p(x)]}{\delta p(x)} = \int_{-\infty}^{\infty} (-1 - \ln p(x)) \eta(x) dx = 0. \quad (7)$$

Now, the way this goes is that we say that because $\eta(x)$ itself is an *arbitrary* excursion, this result must be true for *any* $\eta(x)$ and hence the part of the integrand in parentheses must be zero. Now that you have seen how to do this using the log term, repeat this exercise for the full functional of part (a) and prove that the probability distribution has the form shown in eqn. 5.

(c) Determine all of the Lagrange multipliers explicitly in terms of μ_1 and μ_2 by imposing the constraints. This means you are going to have to do

various integrals. Obtain a clean and simple expression for the probability distribution and make sure you explain the sense in which this is the classic Gaussian distribution that you know and love.

3. Biofunctionalized Cantilevers

Read the article from Nature Biotechnology by Wu *et al.* (Wu G., Datar R.H., Hansen K.M., Thundat T., Cote R.J. and Majumdar A., *Bioassay of prostate-specific antigen (PSA) using microcantilevers*, Nature Biotech., **19**, 856 (2001)). You can obtain this article online from the Caltech library. The goal of this problem is to compute the deflection from the perspective of variational calculus and then to use the numbers associated with the actual experiments discussed in that paper.

As has already been mentioned in class several times, one way to view thermodynamic questions is through the prism of the competition between energetic and entropic contributions to the free energy. In this problem we will examine the thermodynamics of biofunctionalized cantilevers in which as a result of the attachment of specific biological molecules to the surface of the cantilever, the cantilever undergoes spontaneous bending, an effect that can be exploited to make sensors. Indeed, such devices have already been used to detect prostate specific antigen in screening for prostate cancer. In this problem, we will begin our preliminary preparations for investigating that problem by considering the kinematics of beam bending.

(a) Consider a beam of thickness h bent into a circular arc like I did in class. There is a line running the length of the beam which has the same length in the deformed configuration as it did before being bent - this line is called the neutral surface. Little elements of material below this line are compressed, while those above are stretched. The net result is that this little beam is strained. If the undeformed length of the beam is L , find the length of the beam as a function of the distance z from the neutral surface. This is straightforward geometry. Now, if we define the elongational strain as $\epsilon(z) = (L(z) - L_0)/L_0$, compute the elongational strain as a function of z .

(b) We will repeatedly wish to write down elastic contributions to free energies as the course proceeds. As a first exercise in doing so, we find the

total strain energy that is present in the beam by virtue of its bending. Recall from class that I said that elasticity is a way of writing a continuum description of the energetics of bond stretching and bending. For a *uniformly* strained material of volume V , the strain energy is $E_{strain} = \frac{1}{2}E\epsilon^2V$, where E is known as the Young's modulus of the material. In our case, the beam is *not* uniformly strained, but we can obtain the total strain energy by adding up all of the different pieces of material, treating each as a little uniformly strained region. So, write an expression for the energy of the beam as an integral over the beam and then work out the integrals for the particular case of a beam bent in the way envisioned in part (a). This is an incredibly fundamental result and is useful for thinking about everything from the Golden Gate bridge, to the atomic force microscope, to the packing of DNA in viruses.

(c) In this part of the problem, your goal is to write down an energy functional for the biofunctionalized cantilever that appropriately reflects the competition between bulk energies (in this case the bending energy) which oppose bending of the beam and surface terms which favor the spontaneous bending of the beam. The mathematical goal of this problem is to find the vertical displacement function $u(x)$ which tells how much the beam is deflected at a distance x along the beam. In particular, you will write an energy *functional* $E_{tot}[u(x)]$ for the unknown displacement of the form

$$E_{tot}[u(x)] = E_{elastic}[u(x)] + E_{surface}[u(x)]. \quad (8)$$

Your result will involve the sum of two integrals, one of which captures the bending energy and is basically of the form

$$E_{elastic} = \frac{k}{2} \int_0^L (u''(x))^2 dx. \quad (9)$$

Use the result from earlier in the problem and make sure that the constant k has the right units and includes both the Young modulus and a geometric factor. The trick will be to write the curvature in terms of derivatives of $u(x)$. On that note, feel free to invoke the approximation that $|u'(x)| \ll 1$ in writing the final form for the curvature. For the surface energy terms, you will need to write the surface energy in the form

$$E_{surface} = \gamma_{top}A_{top} + \gamma_{bottom}A_{bottom}, \quad (10)$$

where we have defined γ_{top} as the surface energy of the top face and A_{top} as the area of the top face. Note that the area of the surfaces will depend upon the displacement profile of the beam. So, the bottom line is that you need to write an energy functional which depends upon $u(x)$ and its derivatives.

(d) To minimize this functional there is a clever trick. In particular, the integrand is of the form $au''(x)^2 + bu''(x)$. As a result, you can complete the square and end up with an integrand that is ≥ 0 . Hence, the least value of the functional occurs if you set this integrand to zero. This now gives you a differential equation for $u(x)$. Solve it and obtain the displacements.

(e) Using the numbers given in the paper of Wu *et al.* for the dimensions of the cantilever as well as the numbers they report for the Young modulus, compute the deflections you predict for the beam. In particular, use their fig. 5 in order to characterize the difference in the surface energy between the top and bottom surfaces. Note that they report different values depending upon the concentration of the PSA molecules. Use several different values. Then compare the deflections you get to those they observe and report in fig. 4.

Note from Rob: This problem is open ended and kind of hard. a) If you don't succeed with the variational calculation, do the numbers in part (d) anyway. b) If you can come up with a better way of making contact with the data given in the Wu paper, by all means, let me hear it.