umdberg: Open 131 Course Materials:The DNA Spring

DNA: A Biological Spring?

Motivation. Over the past 20 years, the development of sensitive physical techniques like atomic force microscopy and optical tweezers has allowed us to characterize the mechanical properties of DNA molecules in great detail. This characterization is important because DNA is subjected to a range of mechanical manipulations within the cell: it must be coiled, zipped, twisted, and deformed in a variety of ways during the replication or transcription process. An understanding of the elastic properties of DNA can give scientists insight into how DNA and proteins interact in order to carry out essential cellular processes. In this problem, you will explore how one of these modern physical techniques – optical tweezers – has allowed us to model the spring-like properties of DNA.

Experimental Set-up. If someone asked you to measure the spring constant *k* for a DNA molecule, how might you do so? Well, as with any spring, you'd probably like to be able to pick it up and tug on it, to see how much force you must apply in order to stretch it a certain distance. This would give you a sense of how taut or tense the spring is, and therefore a sense of its spring constant. Unfortunately, a single DNA molecule is tiny, so we can't just go to the bathroom cabinet and get a pair of everyday tweezers to pick it up. We must devise a more clever tweezer!

The diagram below presents the key features of one such clever device, the "optical tweezer." The important thing to know right now is that one end of the DNA molecule is chemically attached to a small polystyrene bead (the bead's radius is about 10^{-6}m), which is "trapped" in space by one or more laser beams. (If the bead were not trapped, it would just float haphazardly around the fluid in which the experiment takes place... as you just saw in lab!) The other end of the DNA molecule is fixed in place, such as by attaching it to a surface, as shown in the figure.

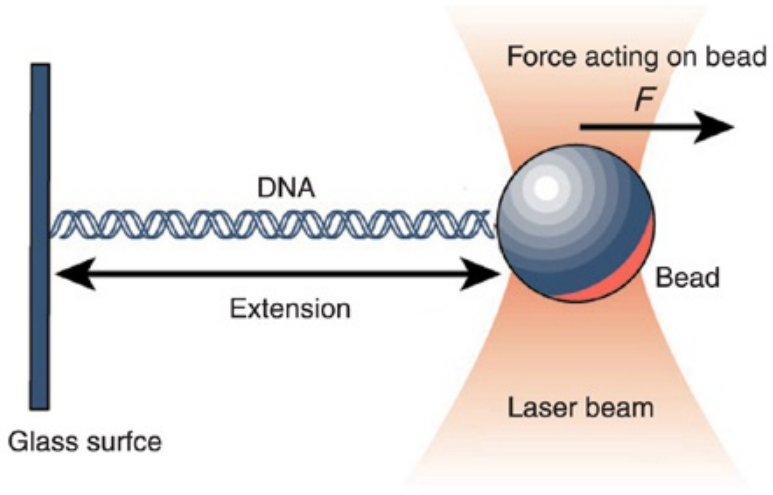

Figure 1. DNA Manipulation Experiment Using Optical Tweezers.

Since the bead is trapped in the center of the laser beam (called the beam's "focus"), it moves as the focus moves. *Why* the bead moves with the focus of the beam is not at all obvious... stay tuned for a discussion later in the course! If you move the laser focus to the right, the bead goes with it. By moving the focus of the beam ever so slightly, we can begin to stretch the DNA. Moving the focus of the beam just a few nanometers to the right causes the DNA to be stretched by a measurable force, and we can begin to construct a plot of the bead's position as a function of the applied force.

Estimating the dsDNA spring constant. When optical tweezer experiments are performed on double-stranded DNA (dsDNA), data of the following form are obtained (the horizontal axis is labeled in micrometers, 10^{-6} m, and the vertical axis in picoNewtons, 10^{-12} N). "Extension" refers to the length beyond the length DNA would have if it were relaxed, i.e., if it were not being stretched by the optical tweezer.

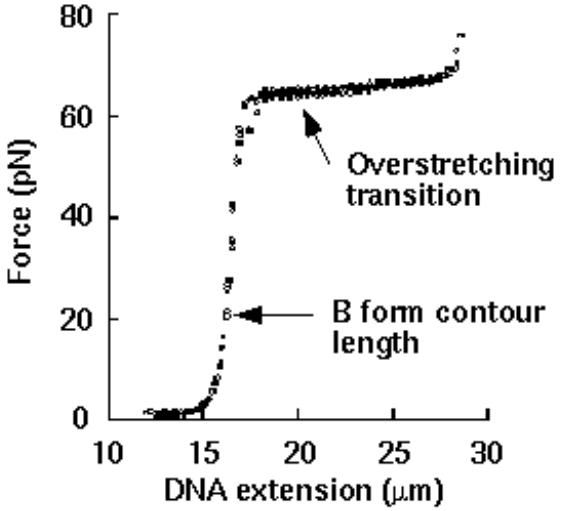

Figure 2. Stretching dsDNA. The "B-form" dsDNA is the type that most often exists under normal physiological conditions in the cell.

As you can see from the data, the DNA behaves somewhat differently depending on how much force is applied. Let's try to examine that behavior more closely. We are going to *model* what happens to DNA as it is stretched, trying to account for the data we observe in Figure 2.

Question 1: Let's try to model the observed behavior in the various regions of data in Figure 2 separately. For each of the following regions, DRAW a picture of the DNA that would explain the force-vs-extension data in that region, DESCRIBE in words how the DNA is deformed in that region, and calculate the spring constant of the DNA in that region.

(a) The region where the applied force is less than a few pN

(b) The region where the applied force is between a few and 65 pN ("B-form region")

(c) The region where the applied force is between 65 and 70 pN ("over-stretched region")

(d) The region where the applied force is greater than 70 pN

Question 2: Let's now consider all the data in Figure 2 at once, rather than breaking it down into regions. What features of the data would be missed if we modeled the entire region of Figure 2 with Hooke's Law all at once?

Question 3: The Hooke's Law spring constant is a measure of a spring's stiffness, as represented by the steepness of the force-vs-extension curve. Name one or two other properties of DNA that we might be able to capture if we did not simplify the situation to a Hooke's Law ideal spring. For example, what property of DNA might determine the force at which the overstretching transition occurs?

Not surprisingly, a model that more accurately describes the behavior of dsDNA as a whole must itself be much more complicated than Hooke's Law, because it must capture more information than just the spring constant (stiffness) of the molecule. For example, the "Worm-Like Chain" (WLC) model is often used to describe semi-flexible polymers in physics, and actually does a remarkably good job of matching the data presented in Figure 2. If you're interested, you can read about such a model on Wikipedia: http://en.wikipedia.org/wiki/Worm-like_chain.

Question 4: The data in Figure 2 show that DNA can be stretched to adopt different structures and different end-to-end lengths. When is it biologically important that the DNA not be under tension? When is it biologically important that it be stretched under tension?

Question 5: Optical tweezers don't exist inside living cells! What then might create the tension on DNA in a real living system?