

Biology 3550: Physical Principles in Biology

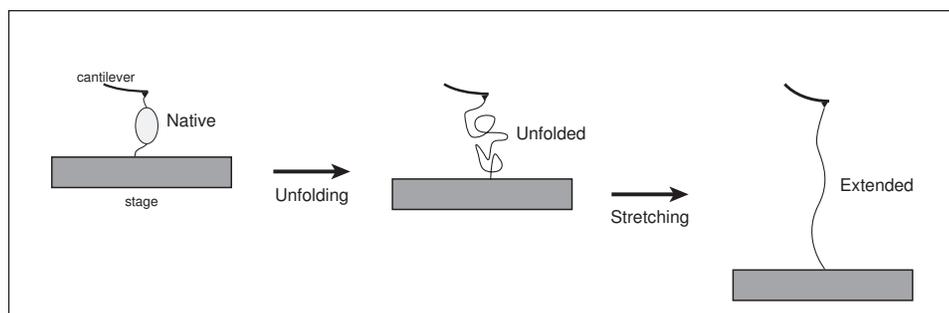
Fall Semester - 2016

Problem Set 6

Due: Wednesday, 7 December, at 11:59 PM.

Note: Be sure to show your work, and use the proper units. You are encouraged to consult one another, or other resources, but the work that you hand in must be your own (except for problem 3). References should be given for any information obtained from outside of the course materials. Your solutions should be submitted as a single pdf file via Canvas.

1. In class, we briefly discussed the use of an atomic force microscope (AFM) to measure the entropy change for stretching a polypeptide chain into an (almost) unique conformation. In practice, these experiments usually begin with a native protein, as illustrated schematically below:

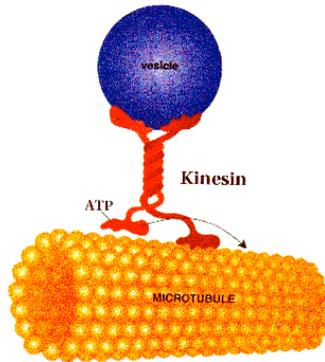


In this type of experiment, the two termini of the polypeptide chain are chemically attached to the AFM tip and stage, sometimes with short linker polypeptides to facilitate the connection. For single domain proteins that undergo a two-state unfolding transition, force exerted over a relatively short distance, a few nanometers, is sufficient to completely unfold the protein.

For this exercise, assume that a protein of 100 amino acid residues is subjected to this procedure at 25°C and that the unfolding free energy change for this protein is 30 kJ/mol.

- (a) What is the minimum amount of mechanical work that would be required to unfold the protein? Assuming that the unfolding process occurs a distance of 2 nm, calculate the average force applied by the AFM
- (b) Calculate the minimum amount of work required to stretch the unfolded polypeptide chain into a single conformation.
- (c) Explain, in structural and thermodynamic terms why the work required for the two steps is so different. (The work that you calculate for one of the steps should be about 20-times larger than for the other.)

- (d) Calculate the distance between the ends of the fully extended polypeptide chain. (This corresponds to the structure in a single β strand.)
- (e) Calculate the average force for the step of stretching the unfolded polypeptide into a single conformation.
2. Kinesin is a motor protein that uses the energy of ATP hydrolysis to move along microtubules. One of its many functions is to translocate vesicles, as illustrated schematically below:¹



The kinesin “walks” along the microtubule, with each step consuming 1 molecule of ATP and moving 8 nm. Assume for the following that the free energy change for ATP hydrolysis is 30 kJ/mol and that the motor has an efficiency of 75%, so that the maximum mechanical energy is about 22 kJ/mol per step.

- (a) What is the maximum average force generated by kinesin during one step of 8 nm?
- (b) The maximum theoretical speed of a kinesin molecule carrying a vesicle would be determined by the viscous drag of the vesicle, which is given by:

$$F_d = -bv$$

where v is the velocity and b is the viscous drag coefficient. The negative sign indicates that the force acts in the direction opposite to the motion. For a spherical object in the absence of turbulence, the drag coefficient is given by the Stokes equation (the Stokes part of the Stokes-Einstein equation discussed in Lecture 20):

$$b = 6\pi r\eta$$

where r is the radius and η is the solution viscosity. Assume that the vesicle has a radius of 100 nm and the viscosity is about that of water, 10^{-3} Pas. Calculate the maximum, drag-limited velocity of the kinesin-vesicle, *i.e.*, the speed at which the force generated by the motor is just balanced by the viscous drag.

¹I believe that this figure originally came from a report published by the US National Academy of Science, but I can no longer find the reference!

(c) The actual velocity measured for kinesin is about $[640]\text{nm/s}$, which should be much smaller than the number you calculated above. Suggest a reason for this discrepancy.

3. Propose a question for the final exam for this course!

This problem can be completed by working in groups of up to 3 students. But, be sure to identify your collaborators when you turn in your work.

A good exam question should have the following features:

- The question should be based on an important principle from the course.
- The answer should require careful thought, not just repetition of facts.
- The problem can be quantitative, but doesn't have to be.
- It should be possible for a well-prepared student to solve the problem correctly in about 10–15 minutes.
- The problem should not require reference materials.
- Additional information can be included in the question.

In addition to the problem, provide a complete solution.

One or more student-submitted problems *may* be used on the actual exam, but will probably be modified somewhat so that they aren't too easy for the students who proposed them.