

MOLECULAR, CELLULAR, & TISSUE BIOMECHANICS

Spring 2015

Problem Set 1

Distributed: Tuesday, February 3, 2015

Due: Wednesday, February 11, 2015

Problem 1 – Work done by kinesin motors

We each expend about 2 kcal of energy per day. Suppose a quarter of it is used to power kinesin motors for intracellular transport. Estimate how many intracellular cargoes are delivered by kinesin motors from the center of a cell to the cell surface per minute based on the following assumptions:

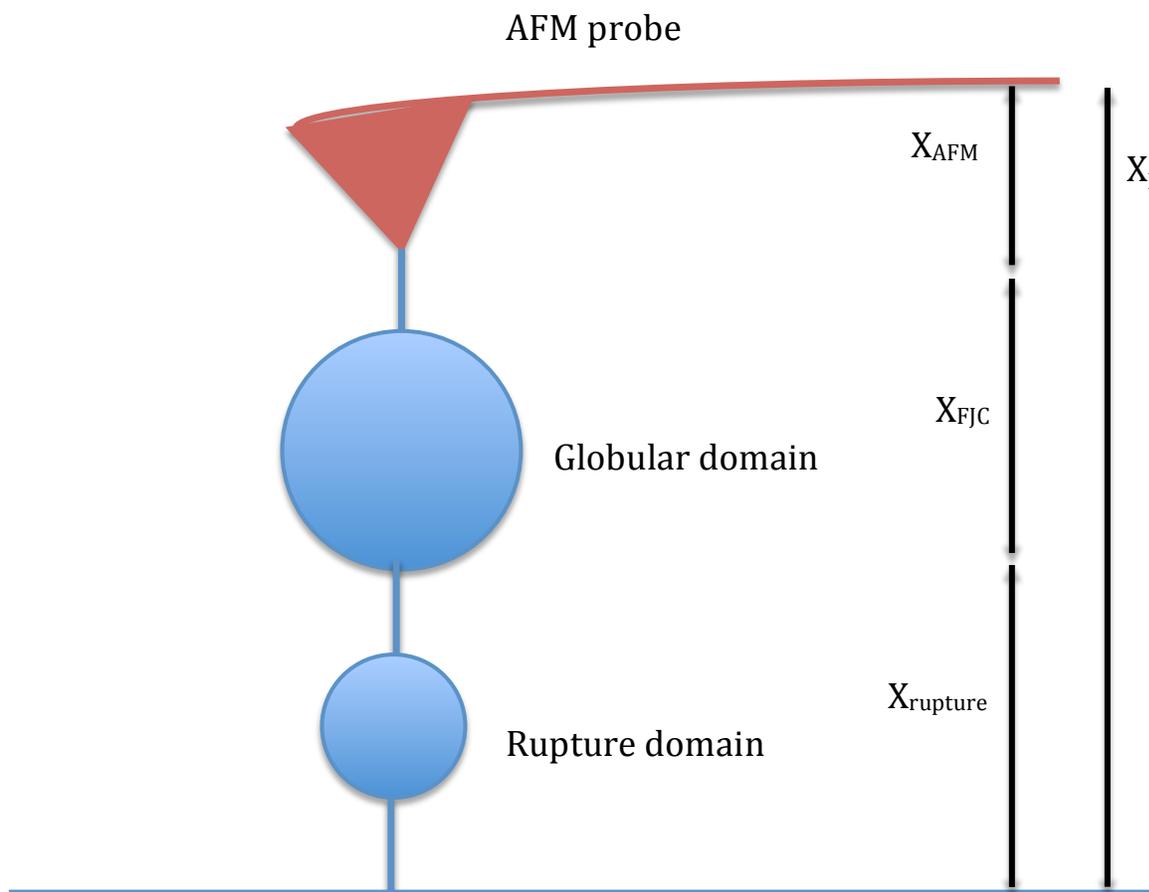
- There are 4×10^{13} cells in our body (excluding other microorganisms) (Bianconi, et al., Ann. Human Physiol. 40 463 (2013)).
- A cell is 5 μm in radius.
- Each cargo is carried by a kinesin, with a speed of 1 $\mu\text{m}/\text{min}$.
- A kinesin uses one ATP per 8-nm step, consuming 100×10^{-21} J.

Problem 2 – Protein stiffness

Consider the measurement of a force-extension (F vs. x) curve of a protein with two distinct domains, a globular one which behaves as a freely-jointed chain (FJC) and another (the 'rupture domain') that also behaves as a FJC but contains one critical internal bond. This protein is represented schematically in the figure by the two spheres connected by a short linker region. Assume that this protein has been functionalized by the addition of short tether sequences (assumed infinitely stiff here) that allow it to be attached to a rigid substrate at the N-terminus and an AFM tip at the C-terminus.

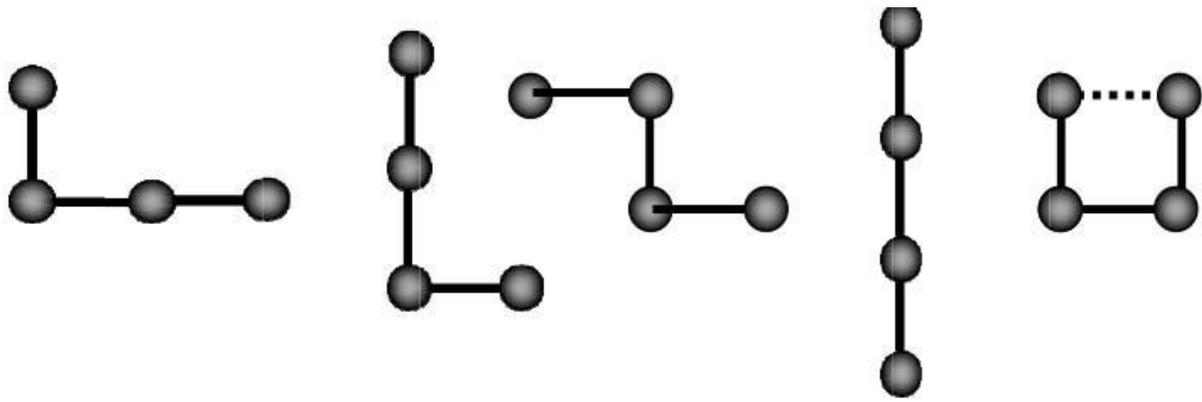
- a) Assume that the two domains (of 15 kDa and 24 kDa for the globular and rupture domains, respectively) can each be treated as a freely-jointed chain, and that the Kuhn length for both domains is 0.6 nm. What is the approximate size $\sqrt{\langle R^2 \rangle}$ of each domain before pulling? [Note that the average molecular weight of an amino acid is 105 Da, and its contour length is 0.4 nm.]
- b) Based on the information provided above, sketch (quantitatively) the force-extension curves of the following components of the system:

- The AFM probe (assume it behaves as a linear spring of stiffness, $k = 0.1 \text{ N/m}$).
 - The globular domain.
 - The rupture domain with a single, critical internal bond. Assume that before internal bond rupture, it behaves as a protein with MW 12 kDa, and that the bond ruptures at a force of 10 pN; after rupture, it behaves as a protein with MW 24 kDa.
- c) Sketch (quantitatively) the complete force extension curve $F(x_p)$.
- d) It has been proposed to use this system as a single molecule detector, but designing the globular domain to have a binding site for the molecule (e.g., a neurotoxin) to be detected. Assume that the target molecule binds irreversibly to two distinct regions in the globular domain. Draw (qualitatively) the overall force–extension curve (as in part (c)) as it would appear before and after binding to the target. Be sure to explain your reasoning.



Problem 3 – Statistical thermo refresher

The two-dimensional four amino acid peptide shown below and discussed in Dill & Bromberg has one folded microstate with energy $E_{folded} = 0$, and four unfolded microstates each have energy levels of $E_{unfolded} = \epsilon_0$. The distance between the chain ends is 1 lattice unit for the folded state, 3 lattice units in the fully extended state, and $5^{0.5}$ lattice units in each of the other three chain conformations (.e., the microstates on the left).



Assume that one lattice unit represents approximately 0.2nm, the typical length of a hydrogen bond.

Plot the average end-to-end distance as a function of temperature, if the bond energy is

- (a) $\epsilon_0 = 1.0$ kcal/mol
- (b) $\epsilon_0 = 3.0$ kcal/mol

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20.310J / 3.053J / 6.024J / 2.797J Molecular, Cellular, and Tissue Biomechanics
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