

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Molecular, Cellular and Tissue Biomechanics  
BEH.410 / 2.978J / 6.524J / 10.537J

---

**Problem Set #2**

**Issued: 2/21/03**

**Due: 3/5/03 (in class)**

---

Please staple each problem separately as we will have different graders grading each problem. Also please put your name on each problem!

---

**Problem #1 Microtubule Structure**

Problem 2.5 in Boal

**Problem #2 Entropic Elasticity of a 1-D Polymer Chain Model**

In class we discussed the freely jointed chain in 3-dimensions as a model for flexible polymers. Here we will consider a more simple model of a 1-D polymer chain.

The chain is composed of  $N$  links of length  $b$ . Each link has a two state variable  $\sigma_i$  which equals  $+1$  if the link points forward and  $-1$  if it points backward. The total chain

extension is then 
$$z = b \sum_{i=1}^N \sigma_i.$$

a) What is the probability  $P(\sigma_1, \sigma_2, \dots, \sigma_N)$  of a given conformation (set of  $\{\sigma_1, \sigma_2, \dots, \sigma_N\}$ ) when a constant force  $f$  is applied at the chain ends ?

b) Prove that  $\langle z \rangle / Nb = \tanh(fb/kT)$ . Note:  $\tanh(x) = (e^x - e^{-x}) / (e^x + e^{-x})$ .

c) Compare the spring constant for the 1-D chain and 3-D chain in the linear regime (small forces).

d) What do you anticipate the spring constant for a freely-jointed chain in 2-dimensions will be ?

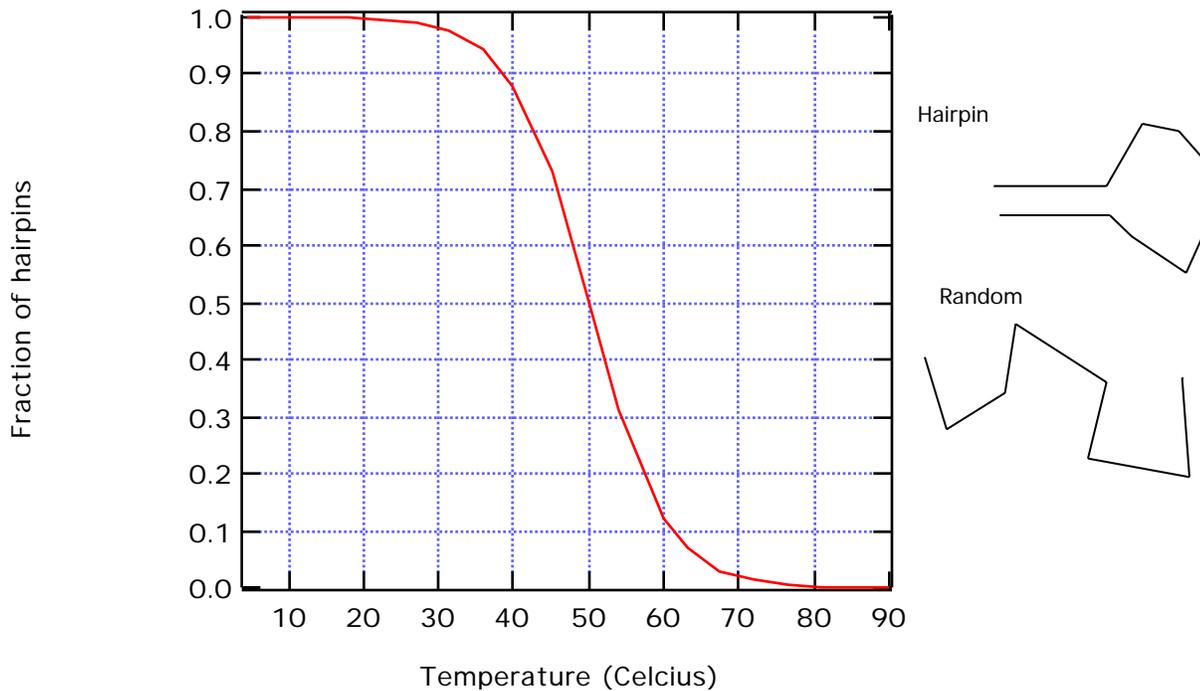
**Problem #3 Properties of Ideal Chains**

Problem 2.11 in Boal

## Problem # 4 DNA Folding

Self-complementary sequences of RNA or single-stranded DNA can form hairpins that are in equilibrium with a open, random coil conformation, with equilibrium constant  $K$  dependent on temperature.

The figure below plots the fraction of molecules that are in the hairpin conformation as a function of temperature for a DNA strand with 14 base-pairs in the stem and 8 bases in the loop.



(a) Calculate the free energy difference at 40 C, 50 C, and 60 C.

(b) From the temperature-dependence of  $A$  estimate:

(i) the change in internal energy in  $kT$  (from base-pairing) when a hairpin is formed

(ii) the ratio  $W_{\text{hairpin}}/W_{\text{random}}$  where  $W_{\text{hairpin}}$  and  $W_{\text{random}}$  are the number of different configurations accessible to the molecule in the hairpin and random states respectively.

## Problem #5: Dynamics of actin polymerization

Consider the polymerization of an actin filament using the rate laws shown in class. Actin is a polar filament and so we would expect that rate constants  $k_{on}^+$   $k_{on}^-$  where the plus and minus refer addition to end of the chain considered. Furthermore, polymerization is more rapid when the actin monomers have ATP bound. Sample data for actin containing ATP *in vitro* are:

$$k_{on}^+ = 11.6 \text{ } (\mu\text{M s})^{-1}$$

$$k_{on}^- = 1.3 \text{ } (\mu\text{M s})^{-1}$$

$$k_{off}^+ = 1.4 \text{ s}^{-1}$$

$$k_{off}^- = 0.8 \text{ s}^{-1}$$

a) Plot  $dn/dt$  for the +end and –end as a function of concentration of monomers. Identify the 3 regimes of growth for the filament.

b) At what concentration of monomers will the *total* filament length be constant in time ? Draw a sketch of a simple filament of length  $n=6$  as a function of time and position in this regime to explain why this is called “treadmilling”.

c) How fast is the leading edge (positive end) of the filament moving forward in time when the filament is treadmilling ?

Compare this to the typical velocity of a keratocyte cell ( $\sim 0.1 \mu\text{m/s}$ ) where treadmilling has been observed.

d) The slow velocity found in c) is due to the fact that we have neglected to account for proteins which change the polymerization process:

- some bind monomeric actin and modify its polymerization properties.
- capping proteins can bind to the ends of filaments and prevent monomers from being added to them.
- severing proteins.

Severing proteins may increase  $k_{off}^-$  by two orders of magnitude or more (Pollard et al. 2000)! How would this change your answer for part c) ?

e) The concept of equilibrium force  $F_{eq} = \frac{kT}{\delta} \ln \frac{[M]}{K_c}$  was introduced in class (and in Howard chapter 10) where  $\delta$  is the length change in the filament (5.5/2 nm for actin) when a monomer is added,  $[M]$  is the concentration of monomers and  $K_c$  is the critical dissociation constant in the absence of an external force. We also considered rate processes for the dynamics and said that for the diffusion limited model the velocity of an end of the filament ( $v = \frac{dn}{dt} \delta$ ) was equal to  $\frac{2D}{\delta^2} \delta$  in the limit that there is no external force. We then said that drag force on the particle is  $-\xi v$  so the filament must be exerting a force of  $\frac{2kT}{\delta}$ . Why is this value different than  $F_{eq}$ ? What speed does this give for actin pushing a 10  $\mu\text{m}$  particle (bacteria) versus a 100  $\mu\text{m}$  particle?