Problem set 6
(Discussion on July 2)

Problem 1

DNA overstretching transition. Single-molecule stretching experiments in the 1990s revealed that DNA undergoes an overstretching transition if subjected to forces of $\approx$ 65 pN (Cluzel, *et al.*, *Science* 1996; Smith, *et al.*, *Science* 1996), where it lengthens about 1.7-fold compared to its B-DNA structure. A long-standing debate ensued about what exactly happens upon overstretching. The two possibilities usually considered are DNA melting (i.e. conversion of the double-stranded DNA to two single strands) and conversion of DNA to a double-stranded, but extended and underwound configuration called "S-DNA" ("S" for "stretched"). Van Mameren, *et al.*, *PNAS* 2009, investigated this question using a combination of optical tweezers force-spectroscopy and fluorescence imaging (Available online at `http://www.pnas.org/content/106/43/18231.full.pdf`).

a) What do van Mameren, *et al.* conclude about what happens during the overstretching transition, in terms of S-DNA vs. melting?

b) What evidence do they provide for their conclusion?

c) If we assume that overstretching could involve *both* the formation of S-DNA and DNA melting, how conclusive is their evidence? In particular, does their work rule out the formation of S-DNA upon overstretching?

Problem 2

FJC, revisted. Here we will explicitly derive some identities involving the radius of gyration R_g, which is a very useful measure for the size of a polymer in solution. We assume an ideal FJC (without self-avoidance) with N identical segments of length a. The vectors $\vec{r_i}$ point to segment i. One definition of the radius of gyration is

$$R_g^2 = \frac{1}{N}\sum_{i=1}^{N}\langle(\vec{r_i} - \vec{r}_{mean})^2\rangle \tag{1}$$

Where $\langle ... \rangle$ denotes the statistical average and $\vec{r}_{mean}$ the center of mass position:

$$\vec{r}_{mean} = \frac{1}{N}\sum_{i=1}^{N}\vec{r_i} \tag{2}$$

a) Show that the R_g can also be expressed as

$$R_g^2 = \frac{1}{2N^2} \sum_{i,j=1}^{N} \langle (\vec{r_i} - \vec{r_j})^2 \rangle \tag{3}$$

b) Use the fact that for a FJC

$$\langle (\vec{r_i} - \vec{r_j})^2 \rangle = |i - j| a^2 \tag{4}$$

($|...|$ denotes the absolute value; note that this identity gives the end-to-end distance result for $i = 0$ and $j = N$) to show that for the FJC

$$R_g^2 = \frac{1}{6} N a^2 \tag{5}$$

Hints: Turn the two summations into two integrals, starting from zero. Adjust the integral limits of the inner integral such that the absolute value is taken into account.

Problem 3

3D Gaussian chain. The end-to-end vectors of an ideal chain with N segments of length a in 3D are Gaussian distributed:

$$P(N, \vec{R}) = \left(\frac{3}{2\pi \cdot N a^2} \right)^{3/2} \exp\left(-\frac{3R^2}{2 \cdot N a^2} \right) \tag{6}$$

The mean is $\langle \vec{R} \rangle = 0$ and the variance is $\langle \vec{R}^2 \rangle = N a^2$ The square root of the mean squared radius is interpreted as the "unperturbed end-to-end distance".

a) Use the Boltzmann relation (i.e. the connection between probability and entropy) to calculate the free energy change if an ideal chain is perturbed from an unperturbed end-to-end distance to an arbitrary end-to-end distance R.

b) Calculate the force associated with the conformational change in b). *Hint:* You can use that $F = -\partial \Delta G / \partial R$.

c) What is the effective "spring constant" of an ideal chain? Compare your result to the result obtained in class by expanding the Langevin function for low forces.