Problem set 5
(Hand in by June 20)

Problem 1

Estimates of molecular forces. In this problem, we will carry out some very simple estimates of the forces required to break interactions in biomolecular systems. A simple estimate of the force F required to break a certain interaction can be obtained by considering the characteristic energy E and the typical length scale Δx over which it acts: $E = F \cdot \Delta x$.

a) Estimate the forces required to break covalent bonds. A C-O bond has a binding energy of 84 kcal/mol; a S-S bond has an energy of 51 kcal/mol (data from `https://www.ncbi.nlm.nih.gov/books/NBK21595/`). You can assume that the bonds break over a characteristic distance of ≈ 1 Å.

b) Biological interactions are often mediated by non-covalent bonds. Non-covalent interactions tend to be weaker and longer ranged than covalent bonds. Obtain a rough estimate of the energies and rupture forces of non-covalent interactions, by assuming that they act over distances of ≈ 1 nm and taking into account that they are much weaker than covalent interactions but still stronger than forces due to thermal fluctuations. Hint: the thermal energy at room temperature is $k_B T \approx 4$ pN·nm.

Problem 2

DNA overstretching transition. Single-molecule stretching experiments in the 1990s revealed that DNA undergoes an overstretching transition if subjected to forces of ≈ 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 3

Force-extension relationship for the 1D freely-jointed chain. In class, we derived the extension response of a 3D freely-jointed chain to an external force f. In this problem, you will carry out a similar derivation, for the simpler, one-dimensional case. Consider a chain of N stiff segments of length b that always lie along the z-axis. There is a two-state variable σ that takes on the value $\sigma_i = +1$ for each segment that points "forward" in the z-direction, along the external applied force, or $\sigma_i = -1$ for segments that point "backwards", against the external force. The total extension is then given by

$$z = b \cdot \sum_{i=1}^{N} \sigma_i \tag{1}$$

Derive an expression for the average extension $\langle z \rangle$ as a function of N, b, f, and $k_B T$. Hint: You probably want to first write out the partition function Z. Using the partition function, you can write an expression for the ensemble average $\langle z \rangle$, which you can simplify using the "logarithm trick" used in class and familiar from stat mech courses.