BE 25 Winter 2025
Homework #7
Due at 9 AM PST, March 4, 2025

Problem 7.1 (Stretching a single molecule, 35 pts)**.**
This problem is based on problem 9.14 from Dill and Bromberg. In single molecule experiments, researchers can grab on to the ends of single polymer molecules and pull on them. They typically apply a constant force f on the ends of the polymer (that is *total* force, not force on each end), and then measure the distance L between the ends of the polymer. This is commonly done for biopolymers, including proteins and DNA.

a) Write an expression $\mathrm{d}E$ for the total differential of the energy $E(S, V, L)$.

b) Write down the total differential for a thermodynamic potential $\Phi(T, p, L)$.

c) Use this potential to derive a Maxwell relation involving $(\partial S/\partial L)_{T,p}$.

d) By doing an experiment at various temperatures, we can use the Maxwell relation you derived to learn about the entropic effects of the polymer. For small displacements, we can write the force as a function of displacements to linear order in L (like a Hookean spring); $f = k(T, p)\, L$, where the spring constant is in general dependent on temperature and pressure. Operating at constant pressure, an experimenter finds a linear dependence on temperature, $k = a_0 + a_1 T$. With this empirically determined relation, derive an expression for the entropy $S(L)$ of the polymer at fixed temperature and pressure.

e) Derive an expression for the enthalpy $H(L)$ of the polymer.

f) Show that if $a_0 = 0$, the resistance to stretching is entirely entropic.

Problem 7.2 (Convex Gibbs free energy, 15 pts)**.**
Prove that the Gibbs free energy of a dilute solution is a convex function of all of the n_i's, where n_i is the number of particles of solute i in the solution. This means that there exists a unique equilibrium concentration of solute species and thermodynamic stability is always maintained. (This is true in for *dilute* solutions, but is not generally true.)

Problem 7.3 (Turgor pressure and hypoosmotic shock, 10 pts)**.**
When a cell is suddenly moved from an environment with a given concentration of solute one with a lower concentration, it is said to experience hypoosmotic shock. The osmotic pressure in the cell jumps and the cell may rupture. Cells have mechanisms for dealing with such shocks, including mechanosensitive ion channels, which open to allow the outflow of solute to help bring the osmotic pressure down. In a study of cellular responses to osmotic shock, Chure and coworkers (Chure, et al., *J.*

Bacteriol., **200**, e00460-18, 2018) used a microfluidic device to transfer cells at 37°C from an LB solution with 500 mM NaCl to an LB solution without any NaCl. Unperturbed, *E. coli* cells have an NaCl concentration of a few hundred mM (Szatmári, et al., *Sci. Reports*, **10**, 12002, 2020). What is the approximate osmotic pressure (which is called turgor pressure in the context of bacterial cells) when the cells are suddenly put in the salt-free solution? How does this pressure compare to the typical turgor pressure of unperturbed cells of about 30 kPa as measured by Deng, et al., *Phys. Rev. Lett.*, **107**, 158101, 2011? (Note that the Deng, et al. measurement is smaller than other measurements, which put the turgor pressure around 1–3 atm.) *Suggestion:* Do not use a calculator or computer for this. Estimates are much more fun without them!

Problem 7.4 (Living actin polymerization, 40 pts)**.**
Living polymers are polymers where each added monomer binds reversibly. Actin is a very important living polymer in cells. The chemical reaction scheme for a living polymer is shown below.

$$\circ + \circ \rightleftharpoons \circ\circ + \circ \rightleftharpoons \circ\circ\circ + \circ \rightleftharpoons \circ\circ\circ\circ + \circ \rightleftharpoons \cdots \tag{7.1}$$

The dissociation constant losing a monomer from the end of a polymer of length $n > 2$ is K_d. The dissociation constant for a dimer falling apart is $K_\mathrm{d,nuc}$. That is, the dissociation constant associated with starting, or **nucleating** a polymer, is different than that for continuing polymer growth. Let c_n be the concentration of polymer of length n, and c_1 be the concentration of monomer. We will consider the length of polymers in solution at equilibrium.

a) Show that for $n \geq 2$,

$$c_n = K_\mathrm{d}\, \kappa\, x^n, \tag{7.2}$$

where $\kappa = K_\mathrm{d}/K_\mathrm{d,nuc}$ and $x = c_1/K_\mathrm{d}$.

b) Show that the probability that a given polymer in solution has length n for $n > 2$ is

$$P_n = \frac{\kappa}{1 + \kappa\, \frac{x}{1-x}}\, x^{n-1}. \tag{7.3}$$

Also show that

$$P_1 = \frac{1}{1 + \kappa\, \frac{x}{1-x}}. \tag{7.4}$$

Hint: Recall the result for a geometric series with $0 < x < 1$,

$$\sum_{n=0}^{\infty} x^n = \frac{1}{1-x}. \tag{7.5}$$

c) Compute the average polymer length $\langle n \rangle$ in terms of κ and x. *Hint:* You may need to compute a sum that can be expressed as the derivative of a geometric series or of a sum you already calculated in part (b).

d) Let c_1^0 be the total amount of monomers (incorporated into polymers and free) in the solution. Show that x may be found by solving the following cubic equation and choosing the real root that lies between 0 and 1.

$$(1-\kappa)x^3 - (2 + x_0 - 2\kappa)x^2 + (1 + 2x_0)x - x_0 = 0, \tag{7.6}$$

where $x_0 = c_1^0/K_\mathrm{d}$.

e) In typical conditions (both in the cell and in the lab) when studying actin, $c_1^0 \gg K_\mathrm{d}$ such that $x_0 \gg 1$. As rough estimates for actin in a cell, take $K_\mathrm{d} \approx 100\,\mathrm{nM}$ (Pollard, 1986) and $c_1^0 \approx 200\,\mu\mathrm{M}$ (Bray, 1992), such that $x_0 \approx 2000$. Make a plot of $\langle n \rangle$ versus κ for this value of x_0. *Hint*: You can find the roots of a polynomial using Numpy.

What does your plot and the fact that for actin $K_\mathrm{d,nuc} \approx 100\,\mathrm{mM}$ (Sept, 2001) tell you about the importance of nucleation in setting polymer length?