BE 25 Winter 2026
Homework #5
Due at 9 AM PST, February 17, 2026

Problem 5.1 (A concave entropy, 10 pts)**.**
Prove that the entropy

$$S = -k_B \sum_i p_i \ln p_i \tag{5.1}$$

is a concave function of the probabilities $\mathbf{p} = \{p_1, p_2, \ldots\}$. What implications does this concavity have on the probability distribution(s) that maximize(s) entropy?

Problem 5.2 (Boltzmann's grave, 10 pts)**.**
Consider a system where each microstate has the same energy. Show that the partition function Ω of such a system is equal to the number of microstates. Show further, starting with the Gibbs entropy, that $S = k_B \ln \Omega$. This equation is on Boltzmann's grave, except written as $S = k \log W$.

Problem 5.3 (Disulfide linkages in ribonucleases, 30 pts)**.**
This problem is heavily based on a problem written by Doug Rees.

Christian Anfinsen won the Nobel Prize in Chemistry in 1972 for his work on ribonuclease. He learned that disulfide bonds in the enzyme were crucial for its function. His clever insight for his experiment was that the native state of ribonuclease could be recovered after unfolding the protein by reducing the disulfides, and then re-folding the protein under oxidizing conditions to yield nearly 100% active protein with the proper disulfide bonds.

In his 1972 Nobel Prize address, he said (emphasis added):

> "Many others, including Anson and Mirsky in the '30s and Lumry and Eyring in the '50s, had observed and discussed the reversibility of denaturation of proteins. However, the true elegance of this consequence of natural selection was dramatized by the ribonuclease work, since the refolding of this molecule, after full denaturation by reductive cleavage of its four disulfide bonds, required that *only one* of the 105 possible pairings of eight sulfhydryl groups to form four disulfide linkages take place."

Stanford Moore and William Stein (who shared the Nobel Prize with Anfinsen), figured out specifically which disulfide bonds formed. Labeling cysteines residues as A: 26, B: 40, C: 58, D: 65, E: 72, F: 84, G: 96, and H: 110, they found that the

disulfide bonds were A-F, B-G, C-H, and D-E. As Anfinsen said, to get refolding, *only* this configuration works.

a) If each of the 105 configurations of disulfide bonds has the same energy, what is the probability that a given refolded protein has the Moore-Stein configuration of disulfide bonds?

b) Assuming all 104 configurations that are *not* the Moore-Stein configuration have the same energy, what must the energy difference be between the Moore-Stein configuration and each of the other 104 configurations in order to have 99% of the folded ribonucleases in the Moore-Stein configuration? What do you think about the magnitude of this energy difference?

c) How many possible disulfide configurations are there for an even number n cysteines and $n/2$ disulfide bonds? Repeat part (b), say, for $n = 16$, which is twice as many disulfide bonds as in ribonuclease.

Problem 5.4 (From discrete to continuous, Boltzmann to Gaussian, 25 pts)**.**
This problem was inspired by problem 10.14 of Dill and Bromberg.

In this problem we will explore how a Gaussian distribution arises from a Boltzmann distribution when the energy is a quadratic function of an observed variable. We will do this through a simple example problem.

Imagine a protein that binds a ligand. When the ligand is a distance x_0 from the center of the protein, the energy of the ligand-protein interaction is minimal. We can write down the energy as a function of the distance x of the ligand from the center of the protein, $E = E(x)$. We do not know what $E(x)$ is, so we can write it as a Taylor expansion about x_0,

$$E(x) = E_0 + \left.\frac{\mathrm{d}E}{\mathrm{d}x}\right|_{x=x_0} (x - x_0) + \frac{1}{2} \left.\frac{\mathrm{d}^2E}{\mathrm{d}x^2}\right|_{x=x_0} (x - x_0)^2 + \cdots . \tag{5.2}$$

The first derivative vanishes at x_0 because that position has minimal energy. Truncating the Taylor series to second order, we have

$$E(x) = E_0 + \frac{k}{2}(x - x_0)^2, \tag{5.3}$$

where we have defined the spring constant

$$k \equiv \left.\frac{\mathrm{d}^2E}{\mathrm{d}x^2}\right|_{x=x_0} . \tag{5.4}$$

Note that this description of the energy is only valid for x close to x_0. As $|x|$ gets very large, the energy would drop again toward zero.

a) Let $P(x)$ be the probability that the ligand-protein distance is x. Write down the x-dependence of of $P(x)$, ignoring any normalization constants.

b) From your expression in part (b), you can derive a normalization constant. In class, we have been considering discrete states, but here, x is continuous. While there are subtleties to moving from a discrete distribution to a continuous, in many applications you can in practice simply replace

$$\sum_{\text{all values of } x} \longrightarrow \int \mathrm{d}x. \tag{5.5}$$

Perform the necessary integral to get the normalization constant and write a complete expression for $P(x)$.

c) What is the average distance, $\langle x \rangle$?

d) What is the mean square deviation from this distance, $\langle (x - \langle x \rangle)^2 \rangle$, also called the variance? Importantly, comment on how the variance depends on the thermal energy $k_B T$. (It will help you to notice that the distribution you derived is Gaussian, also called normal.) Finally, sketch $P(x)$.

Problem 5.5 (Patch clamp experiments, 25 pts)**.**
In a patch clamp experiment, current flowing through a single ion channel in a cell membrane may be measured. Furthermore, a voltage may be applied across the membrane to provide a driving force for ion current. Traces from patch clamp experiments look like those below, which were take for a sodium channel.

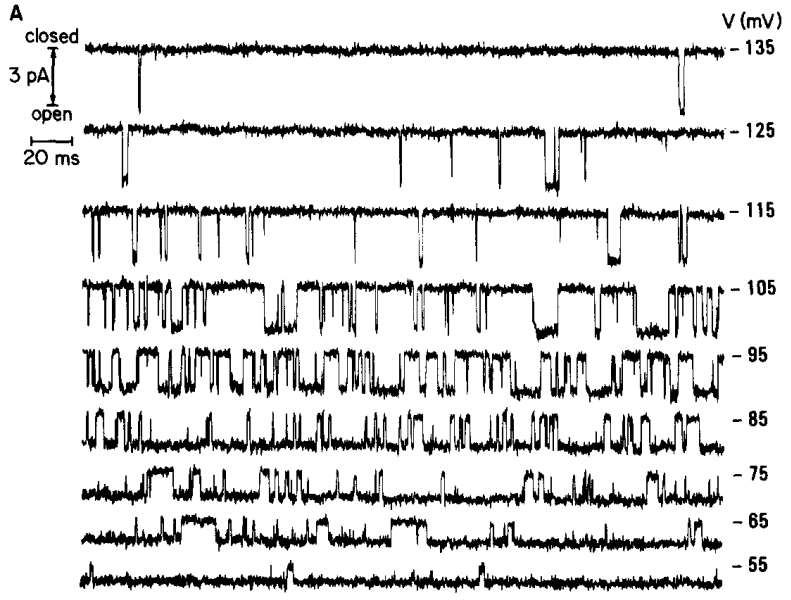

Figure 1: Current (vertical axis) versus time (horizontal axis) for patch clamp experiments for various applied voltages. Taken from Keller, et al., *J. Gen. Physiol.*, **88**, 1–23, 1986.

From the traces, we clearly see two states, an open state where current flows through the channel, and a closed state where it does not. By analyzing the traces, one may calculate the probability that a channel is open as

$$p_{\text{open}} \approx \frac{\text{time open}}{\text{time open} + \text{time closed}}. \tag{5.6}$$

In the above traces, for low-magnitude applied voltage ($V = -55$ mV), the probability of being open is high, and for high-magnitude applied voltage ($V = -135$ mV) the probability of being open is small. Let $\Delta E = E_{\text{open}} - E_{\text{closed}}$ be the energy difference between an open and a closed state. Assume that we can write ΔE as a linear function of applied voltage, V. Derive an expression for p_{open} as a function of voltage and sketch a plot of p_{open} versus V. Eyeballing the traces above, does the function you derived and the sketch jibe with the experimental measurement? (You will not be able to compare quantitatively; just check to see if what you derived is roughly consistent.)