

Problem Set 2

Problem 1: In class we considered a system that can be in two states, corresponding to ‘correct’ and ‘incorrect’ outcomes of a reaction. Let the energy difference between two states be ΔE , and let the fraction of molecules in the ‘incorrect’ state be f . Then the average energy is

$$\langle E \rangle = f\Delta E, \tag{1}$$

and the entropy of the distribution of states is

$$S = -f \ln f - (1 - f) \ln(1 - f). \tag{2}$$

The free energy is defined by $F = \langle E \rangle - k_B T S$.

- a. Make plots of the free energy vs. the fraction of incorrect reactions. It is convenient to plot $F/k_B T$, and then you can make different choices for the parameter $\delta = \Delta E/k_B T$. Make enough plots to show convincingly that the minimum free energy occurs at smaller values of f when δ is larger.
- b. Try to solve the problem of minimizing F analytically. Recall that when you are at a minimum, the derivative of the function must be zero, so the equation you have to solve is

$$\frac{d}{df} F = 0. \tag{3}$$

Can you show that, at the minimum, $p_{\text{incorrect}}/p_{\text{correct}} = f/(1 - f) = e^{-\delta}$?

Problem 2: To help you make the connection between macroscopic chemical kinetics and probabilities in single molecules, consider the following simulation. Take one molecule that can have two states (e.g., and enzyme with substrate bound or not). Let’s call the states 1 and 2, and assume that there is a rate constant k_+ for the transition $1 \rightarrow 2$ and a rate constant k_- for the back reaction $2 \rightarrow 1$. What this means at the level of single molecules is that if we are in state 1, then in a small time dt there is a probability $k_+ dt$ that there will be a transition to the state 2, and similarly for the back reaction. Recall from the first problem set that we can make transitions with these probabilities by comparing a random number to a threshold. So, let’s try the following `MATLAB` program, in which `sigma` will keep track of the state of the molecule at each moment in time:

```
kplus = 1;
kminus = 0.5;
dt = 0.01;
sigma = zeros(10^5,1);
```

```

for n=1:10^5-1;
    if sigma(n)==1;
        if rand(1)>1-kplus*dt;
            sigma(n+1) = 2;
        else
            sigma(n+1) = 1;
        end
    end;
    if sigma(n)==2;
        if rand(1)>1-kminus*dt;
            sigma(n+1) = 1;
        else
            sigma(n+1) = 2;
        end
    end;
end;
end;

```

where we have chosen units of time in which $k_+ = 1$ and $k_- = 0.5$.

- Convince yourself that this program really does what it should, making transitions between the two states with the correct probabilities. Is the choice of Δt sensible? Note that I have written the program to be very explicit, not necessarily very efficient!
- Based on the macroscopic kinetics, what fraction of molecules that we observe should be in state 2? From your simulation, what fraction of time is this one molecule in state 2? Do these results agree? Is it plausible that disagreements result from “experimental error,” that is from making only a small number of observations in the simulation? What happens if you make the simulation run ten times as long?
- Suppose you think of your simulation as coming in ten pieces, and you make separate measurements of the fraction of molecules in state 2 in each piece. Can you then use these ten measurements put an error bar on your estimate of this fraction? Does this sharpen up your discussion of agreement or disagreement in [b]?
- Pick out all the moments in time when the molecule is in state 2 (that is, `find(sigma==2)`), and compute the probability that the molecule still is in state 2 a time τ later. Plot your results, being careful to use a real time axis (not the number of steps). Again, you might try to put error bars on this plot.
- If we have a macroscopic number of molecules, then the fraction which are in state 2 should obey the equation

$$\frac{df}{dt} = k_+(1-f) - k_-f. \quad (4)$$

Be sure that you understand why this is true, and then solve the equation assuming that at $t = 0$ all the molecules are in state 2, i.e. $f(0) = 1$. Hint: look for solutions of the form $f(t) = Ae^{\lambda t} + B$, and find the correct values of the parameters. How does this macroscopic result compare with what you found in [d] for the probabilities in a single molecule?