Announcements

Office hours this week:
4-5 pm (right after section) on Tuesday the 11th

7-8:30 PM on Wednesday the 12th, virtual at https://harvard.zoom.us/j/98197473635.

or by appointment.

Section next week:
In-person on October 19th at 3 pm in M217. Next week, section will be combined with office hours and will be an exam review session.

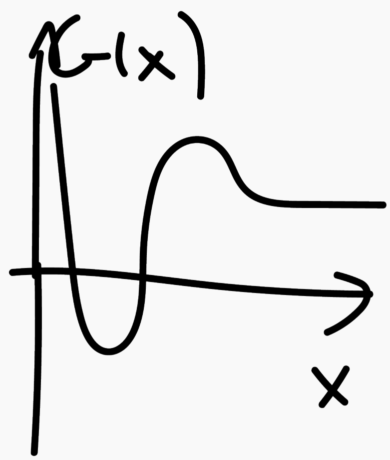
Problem 1: Dynamic Force Spectroscopy

Consider an Arrhenius model of reaction rates:

$$k = f_0 exp(-\Delta E/k_B T). \tag{1}$$

Recall that f_0 is some attempt frequency and ΔE is the barrier height. In this analysis, we'll restrict ourselves to cases in which there is a single high-energy transition state to cross.[1] We want to explore how external forces affect the rate of barrier crossing. While we'll primarily consider mechanical forces in this problem, the results also apply to the generalized forces we considered earlier, e.g. voltage, membrane tension.

a) Consider the following free energy landscape:



Sketch the landscape when you apply a constant force of magnitude F along x. Thermodynamically, what state is now favored?

b) This force modulates the free energy landscape in all sorts of complicated ways, but it turns out that by far the most significant one is to lower the height of the transition state. Using this information, write down a relationship between the original reaction rate k_0, the reaction rate under force k, the applied force, and the coordinate of the transition state x_{ts}.

You may see k_BT/x_{ts} referred to as the thermal force F_β. Do you see why?

c) Let's now consider the case of a linearly increasing *force ramp* (rather than a constant force). The force may now be written as $F(t) = rt$. We first want to derive an expression for the most likely rupture time for a bond with a time-dependent off rate. To do this, maximize the first-order kinetic equation:

$$\frac{dA}{dt} = -k_{off}A. \tag{2}$$

Here, A is the probability that our particle is in the bound state, and we assume that the system is far from equilibrium, i.e. no rebinding takes place.

d) Now combine your results from parts (b) and (c) to derive an expression for the most likely force at which a bond ruptures. You should find that this force is:

$$F^* = F_\beta ln(r/k^0_{off}F_\beta) \tag{3}$$

This is a key result in dynamic force spectroscopy. Notice that we've related the off rate *in the absence of a force* to the most likely rupture force over many measurements. Using this result, we can find the off rate of many interactions that are difficult to measure using ensemble techniques.

[1] You might consider generalizing Kramers theory and the results of this problem to more complicated free energy landscapes for your final project.

Problem 2: Computational test of the previous result

You can test the result you obtained in the part (a) of the previous problem using some code you may have already written in the homework. Problem 5 of the current homework asked you to use your Brownian dynamics simulation to examine a particle in a double well potential:

$$U = ax - \frac{1}{2}kx^2 + \frac{1}{4}mx^4. \tag{4}$$

Recall that you can compute the rate of barrier crossing by fitting an exponential distribution to a histogram of the dwell times in either state. Use this method to compute the rate constant for different values of a. You can choose any reasonable plotting method you like to verify that your result agrees with theory.