Announcements

Office hours this week:
4-5 pm (right after section) on Tuesday the 27th

7-8:30 PM on Wednesday the 28tt, virtual at https://harvard.zoom.us/j/98197473635. Note the extra hour this time!

or by appointment.

Section next week:
In-person on October 4th at 3 pm in M217.

Cool paper
https://www.biorxiv.org/content/10.1101/2022.08.03.502284v1. Expansion microscopy + fluorescence imaging for sub-nm protein imaging. Could this become a tool for **de novo** protein structure determination?

Problem 1: Power spectrum analysis of a Brownian particle in an optical trap

This problem will guide you through the calculation of the power spectrum for a particle under both a random Langevin force and a confining potential. This procedure is commonly used to calibrate the stiffness of an optical trap.

a) Let's start with the Langevin equation for our Brownian particle:

$$\gamma \frac{dx}{dt} = -kx + \xi(t). \tag{1}$$

We claimed in class and in the notes that for a random white noise force, $\langle \xi(t+\tau)\xi(t) \rangle = 2\gamma k_B T \delta(\tau)$. By applying the Wiener Khinchin formula, compute the power spectrum of $\xi(t)$.

b) By taking the Fourier transform of both sides of the Langevin equation and then computing the squared modulus of your result, show that the power spectrum for the particle is described by a Lorentzian distribution:

$$S_x(f) = \frac{k_B T}{2\gamma\pi^2(f_c^2 + f^2)}, \tag{2}$$

and give the expression for the corner frequency f_c. You may want to use the fact that if we define the Fourier transform of $x(t)$ as:

$$x(t) = \int_{-\infty}^{\infty} \tilde{x}(f)e^{-2\pi f i t}df, \tag{3}$$

then the transform of $\frac{dx}{dt}$ is $-2\pi i f \tilde{x}(f)$.

c) Plug in some values for the constants and make a plot of the resulting power spectrum on a log-log plot. You can use Matlab or another program of your choice. Observe what happens as you vary f_c. Can you see why this is called the corner frequency? Your plot should have two regimes. Can you describe what's happening with the particle in each regime?

d) Calibrating the stiffness of an optical trap is normally done by taking the power spectrum of a trapped particle, fitting to a Lorentzian, and using the corner frequency of this fit to extract the trap stiffness. You may be wondering why we need to go through all this trouble when we can just use equipartition to write down an expression for k in terms of the variance of the particle's position. Write down this expression. Can you think of any reasons why this may not be the best approach experimentally? *Hint:* It may help to look up the power spectrum of a bead in an optical trap and compare to the ideal expression. Where is it noisy?

Problem 2: First passage time for a general potential

This derivation can be found in the appendix of Howard. We'll walk through it here.

a) Recall the one-dimensional Smoluchowski equation:

$$j = -D\frac{d\rho}{dx} - \frac{\rho}{\gamma}\frac{dU}{dx}. \tag{4}$$

Here, we will use this to solve a first-passage problem in which particles are released at a reflecting boundary at $x = 0$ and diffuse to an absorbing boundary at $x = x_0$. This problem will guide you through the steps to derive a general expression for the first passage time.

Multiply both sides by[1] $-\frac{1}{D}\exp\frac{U(x)}{D\gamma}$, and show that you can rewrite the RHS as $\frac{d}{dx}(\rho(x)\exp\frac{U(x)}{D\gamma})$.

Integrate both sides from x to x_0, and use the boundary condition at x_0 to cancel one of the terms.

Then, rearrange so that $\rho(x)$ is on one side of the expression, and integrate again from 0 to x_0. Express the first passage time as the inverse of the flux — there should be two integrals in your expression.

Hurray! This is very powerful, because now you can plug in any potential you want and integrate away.

b) What is the first passage time to an absorbing boundary at x_0 in the absence of a potential, described by $U = 0$? Is this what you expect?

c) What is the first passage time to an absorbing boundary at x_0 for a constant force, described by a potential $U = Fx$?

[1] I guess this is an integrating factor!