CH163: HW4

Due 10/13/22

Howard problems 5.2, 5.4

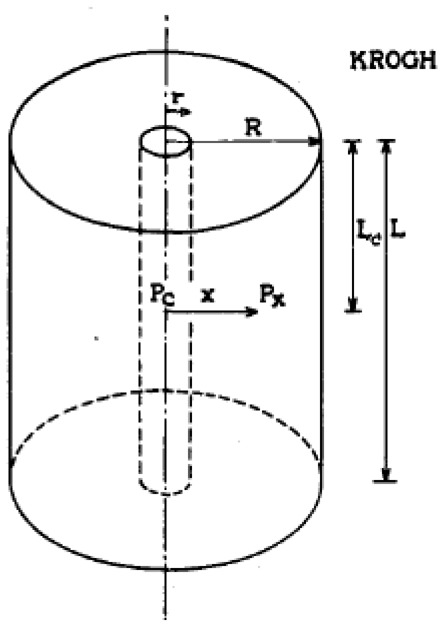
Problem 3) Variance of a binomial distribution

Consider a two-state system where the probability of being in state A is P_A and the probability of being in state B is P_B (so $P_A + P_B = 1$). The total number of particles is n and the number in state A is n_A. In class we said that the variance in n_A is $\sigma_A^2 = nP_AP_B$. Let's prove this.

a) First consider a single particle. What values can n_A take on? Draw a probability distribution for n_A in this case. Calculate the mean, $\langle n_A \rangle$.
b) Now calculate the variance, $\langle (n_A - \langle n_A \rangle)^2 \rangle$. Evaluate the quantity inside the $\langle \quad \rangle$ for each value of n_A, and then weight that outcome by the probability of that value of n_A. Simplify your result as much as possible.
c) Use the central limit theorem to calculate the mean and variance of n_A when the number of particles, n, is large.

Problem 4) Krogh Analysis

In 1919 August Krogh developed a model for the spacing of capillaries in tissue. The essential idea is that capillary spacing is set by the diffusion of oxygen from the capillaries to the surrounding tissue: if the capillaries are too far apart, the tissue doesn't get enough oxygen. In this problem we will work through Krogh's model. Krogh's original paper is included in the assignment too.



Assume that the concentration of oxygen in the capillaries is constant (oxygen is continually replenished by blood flow). Oxygen diffuses outward and is consumed at a constant rate within tissue. Thus the concentration of oxygen satisfies:

$$\frac{\partial C}{\partial t} = D\nabla^2 C - M$$

D is the diffusion coefficient of oxygen in tissue, M is the rate of consumption of oxygen (assumed to be independent of local oxygen concentration).

a) Verify that this equation is solved by the steady-state concentration profile:

$$\Delta C = C_c - C(x) = \frac{M}{D}\left(\frac{R^2}{2}\operatorname{Ln}\left[\frac{x}{r}\right] - \frac{(x^2 - r^2)}{4}\right)$$

where C_c is the concentration in the capillary, r is the radius of the capillary and R is the radius of the piece of tissue served by that capillary (hint: remember to use cylindrical coordinates!).

b) Try plugging in some reasonable numbers: Exercise physiologists tell us that a person running consumes about 60 ml/min of oxygen gas, per kg body weight. The diffusion coefficient of oxygen in normal tissue is about 4×10^{-5} cm^2/s. The concentration of free oxygen in blood plasma (which is different from the oxygen bound to hemoglobin) is about 0.05 mM. Assume that tissue has a density of 1g/mL and that a capillary has a radius of 5 μm. Make a plot of the oxygen concentration at $x = R$ as a function of R.

c) How closely should capillaries be spaced so that no tissue becomes anoxic (i.e. deprived of oxygen)?

In tumors, one cell type starts to proliferate wildly. Once the tumor exceeds a critical size, it would die unless it recruited more blood vessels to supply the inside of the tumor with oxygen (a process called angiogenesis). One approach to cancer therapy is to try to block angiogenesis.

Problem 5) Simulation of a double-well potential

This problem uses the `Langevin` function you wrote last week. Here you will use it to simulate motion in a double-well potential

Write a script to simulate motion in a double-well potential:

a) Run a simulation with the conditions:

***D* = 10^{-10} m^2/s**: This corresponds to a ~4 nm diameter particle in water.
dt = 10^{-3} s
nsteps = 100000: This corresponds to 100 s of data.
T = 298 K: Room temperature.
x0 = 0
X = (-1000:1000)*1e-8: This corresponds to a field of view from -10 μm to 10 μm.

$U = a\,x - \frac{1}{2}\,k\,x^2 + \frac{1}{4}\,m\,x^4$,

Try a = 6 x 10^{-16} N, k = 1.8 x 10^{-9} N/m, and m = 70 N/m^3.

b) Plot a trajectory of the particle with the axes appropriately labeled in units of seconds and microns.

c) Submit a plot of $U(x)$ in units of k_BT, and on the same axis a histogram of the probability distribution for x. You can scale the amplitude of the probability distribution to give it approximately the same scale as U(x).

d) You should find that the potential has two minima, and the probability distribution has two maxima. Calculate the ratio of the populations in the two wells, and compare to the expected Boltzmann factors for the two wells.

e) Make a histogram of the dwell times in each of the wells (you may need to run the simulation multiple times to accumulate enough statistics). Fit the histogram to a single exponential decay, and compare the time constant to what you would expect from Kramers' theory. Do the two agree?

Problem 6) Motion in a washerboard potential

Consider a single particle subject to a sinusoidally varying potential,

$$U(x) = A \sin kx \,,$$

and let the particle have a diffusion coefficient D and a free space drag coefficient γ. This is a decent model for a DNA-binding protein (e.g. Human oxoguanine DNA glycosylase 1 (hOgg1) enzyme diffusing along DNA). To learn more about proteins migrating along DNA, see:

P. C. Blainey, A. M. van Oijen, A. Banerjee, G. L. Verdine, and X. S. Xie
"A base-excision DNA-repair protein finds intrahelical lesion bases by fast sliding in contact with DNA," PNAS **103** 5752-5757 (2006).

The particle will occasionally hop from one local minimum to the next. Over a time long compared to the hopping time, the particle will appear to perform a 1-D random walk.

a) Calculate an effective diffusion coefficient, D_{eff} for the long-time random walk. (Hint: calculate the mean time between steps using Kramers' Theory, and then apply the central limit theorem).
b) Now imagine that a uniform weak force is applied to the particle pulling it to the right, so

$$U(x) = A \sin kx - Fx$$

The particle then experiences a "washerboard" potential. The particle will now undergo a biased random walk, hopping to the right more often than to the left. Calculate an effective drag coefficient for the particle at long times, so the velocity $v = F / \gamma_{eff}$

c) Do D_{eff} and γ_{eff} obey the Stokes-Einstein relation?