Prof. Raghuveer Parthasarathy
University of Oregon; Spring 2015

Physics 610: Homework 5

Due date: Friday, May 1, 5pm in or outside WIL 372.

1 Loops in random walks (3 pts.)**.** You've seen, in the *Physical Biology of the Cell* excerpt, the probability distribution $p(\mathbf{R}; N)$ for the end-to-end distance ($\mathbf{R}$) of a three-dimensional random walk polymer of N segments (Eq. 8.23).

(a, 2 pts.**)** Evaluate the probability that two points N links apart are separated by a distance δ or smaller. Consider $\delta \ll N^{1/2}a$, so that the exponential in the integrand of your probability expression is approximately 1.

(b, 1 pt.**)** As noted in class, clever experiments probing $p(\delta;N)$ for human chromosomes find $p \sim N^{-1}$. (See E. Lieberman-Aiden et al., *Science.* **326**, 289-293 (2009); http://www.sciencemag.org/content/326/5950/289.full). There's a nice schematic of the experiment in Figure 1. Note the discussion related to Figure 4. Is this finding consistent with a random-walk model? What do the authors speculate is advantageous about the observed conformation?

2 Lipid bilayer viscosity (5 pts.). [Rewritten] Tristan images and tracks the motions of "domains" of different compositions in lipid membranes, from which he can infer the membrane's viscosity. (Please see https://vimeo.com/124040405 for one of his movies.) The zipped file "DomainDiffusionData.zip" (In \Canvas\Random walks and diffusion) contains six files, each of which lists the positions of a domain. For each file, Row 1 is x, Row 2 is y, both in units of microns. The time between measurements is 0.0681 seconds. The domain radius, a, is given in the filename in microns, e.g. "Domain3_dt0.068_a0.83.txt" is a domain with a = 0.83 microns.

(a, 2 pts.**)** Using your favorite programs from Homework #4, determine the diffusion coefficients (D) of each of these domains. Make a graph of D vs. a. (Hint: You should find D somewhere between 0.01 and 10 μm^2/s.)

(b, 2 pts.**)** For the diffusion of an object of radius a in a two-dimensional liquid embedded in a three-dimensional liquid (such as a lipid membrane in water), D, the membrane viscosity η_m, and the external fluid viscosity η_w are related by[1]

$$D = \frac{k_B T}{4\pi\eta_m}\left[\ln\left(\frac{\eta_m}{\eta_w a}\right) - \gamma\right]$$, where γ=0.5772... is Euler's constant.

[1] This expression holds for large η_m (or more precisely η_m / $a\,\eta_w$ >> 1), and was first figured out by P. Saffman and M. Delbrück. Yes, that Delbrück! The classic paper: P. G. Saffman, M. Delbrück, Brownian motion in biological membranes. *Proc Natl Acad Sci USA.* **72**, 3111–3113 (1975).

Superimpose on your graph the theoretical $D(a)$ curves, using the above equation, for ηm = {1, 3, 10, 30} x 10^{-9} Pa s m (the SI units). Just by eye, estimate the "best-fit" membrane viscosity. (Note that you can't simply invert the D equation above to solve for ηm. Also, the equation will behave badly for small ηm – see the footnote. There's a more general expression for arbitrary ηm, but it can only be expressed as a messy infinite series, not as a short equation.)

(c, 1 pt.**)** You can divide a two-dimensional viscosity by a thickness to get something dimensionally equivalent to a three-dimensional viscosity. Do this with your answer to (b), using the typical thickness of al lipid bilayer. Find some three-dimensional liquid with a similar viscosity, to get an intuitive feeling for what a lipid bilayer is "like."

3 Runs, tumbles, and diffusion. (5 pts.) As we've seen, *E. coli* (and other bacteria) "run" with constant velocity v; the runs are punctuated by tumbles that randomize the direction. In the absence of a chemoattractant, the distribution of run times is a Poisson distribution with mean τ.

(a, 1 pt.**)** Make a rough argument that the diffusion coefficient of this random walk of runs and tumbles has to be something like $D \approx v^2\tau$.

(b, 1 pt.**)** We've discussed the Poisson distribution $P(\ell;\mu) = \frac{\mu^\ell}{\ell!}e^{-\mu}$, the probability of getting l counts for a Poisson process of mean μ. Explain why we can turn this into a probability distribution of tumble times (i.e. times between tumble events), given a mean time τ:

$$P(t;\tau) = \tau^{-1}\exp\left(-\frac{t}{\tau}\right)dt$$

Hint: Note that we're looking for the probability of getting l=1 tumbles in some amount of time.

(c, 3 pts.**)** Show that the diffusion coefficient of our random walk of runs and tumbles, in three dimensions, is:

$$D = \frac{1}{3}v^2\tau$$

Also state what the answer would be in 2D.

Hints: In 3D, note that if the mean step size is $<L>$, the mean step size in x is given by $<L_x^2> = <L>^2/3$. Figure out from the properties of the Poisson distribution how $<L^2>$ and $<L>^2$ are related.

4 Runs, tumbles, and diffusion – part II. (8 pts.) As we noted in class, bacterial "runs" aren't really straight paths, due to rotational diffusion. How does this influence the effective "D" of Problem 4? You can limit yourself to 2D if you want.

Write a program to simulate bacterial runs and tumbles. Your bacterium should have some direction of motion θ, and some (constant) speed v, so that in time dt its "drift" will be dx = v cosθ dt, dy = v sinθ dt. Also during time dt, the bacterium undergoes translational Brownian motion (drawing dx and dy from Gaussian distributions of variance 2 D dt) and rotational Brownian motion (drawing θ

from a Gaussian distribution of variance 2 D_r dt, as you saw in Homework 4). The tumble probability, for *completely randomizing* θ in the interval *dt*, is dt/τ.

Using bacterial radius a = 1 micron, and v = 30 microns/second, "sample" your swimming trajectory at intervals separated by at least 2 τ for several hundred seconds. Do this for many bacterial trajectories. Use your homework #4 programs to calculate the effective diffusion coefficients for a range of τ values (including τ = 0.1, 1, and 10 seconds). What is the τ that gives the highest *D*?

5 Chemotaxis in one dimension (6 pts.). (From Problem 49 of W. Bialek, *Biophysics: Searching for Principles* (Princeton University Press, Princeton, NJ, 2012), slightly modified.) As discussed in class, *E. coli* (and many other bacteria) navigate towards desirable regions by increasing their run lengths (i.e. decreasing their tumble probabilities) when the perceived rate of change of some attractant is positive. Can we turn this rough picture into a quantitative statement about how the bacterial density and the density of attractants are related?

Let's consider motion in just one dimension. We'd like to figure out the steady-state spatial distribution of bacteria given some concentration of attractant $c(x)$ that is not changing with time. The concentration is not changing with time. Denote the probability that a bacterium is moving to the right as $P_+(x,t)$, and to the left as $P_-(x,t)$. (You can think of these as the concentration as rightward- and leftward-moving bacteria, if you want.) The bacteria move with speed *v*.

$r(\dot{c})$ is the probability of changing direction, which is a function of the perceived rate of change of the concentration:

$\dot{c} = v\dfrac{\partial c}{\partial x}$ (Think about why this has the form it does.)

As we noted in class, we can write a differential equation for the rate of change of $P_{+,-}(x,t)$. Consider just an instant in time, space. All the change in *P* comes from particles "flipping" and so:

$$\frac{dP_+}{dt} = -\frac{1}{2}r(\dot{c})P_+ + \frac{1}{2}r(-\dot{c})P_-$$

(a) Explain why this equation has the form that it does. Write the corresponding equation for $\dfrac{dP_-}{dt}$.

(b) In general[2], we can write $\dfrac{dF(x,t)}{dt} = \dfrac{\partial F}{\partial t} + v\dfrac{\partial F}{\partial x}$. Using this, write expressions for $\dfrac{\partial P_+}{\partial t}$ and $\dfrac{\partial P_-}{\partial t}$. Considering the **steady-state** behavior of the system (i.e. no explicit change of either P_+ or P_- with time), write a differential equation for the total bacterial concentration $P = P_+ + P_-$, and for $\Delta P = P_+ - P_-$.

[2] This is a "convective derivative," also known as a Lagrangian derivative or material derivative. It separates the time derivative of *F* into an explicit time dependence and a contribution from the motion of *x*. (For example, if F is the temperature T of a fluid, there is a contribution to dT/dt from the "pieces" of the fluid moving with velocity v.) If you've never seen this, spend a few minutes looking at, for example, http://www.maths.bris.ac.uk/~majge/week2.pdf, or http://www.chem.mtu.edu/~fmorriso/cm4650/2012SubstantialDerivative.pdf. The latter has some examples.

(c) Writing $r(\dot{c}) = r_0 + \frac{\partial r}{\partial \dot{c}}\dot{c} + \ldots,$ let's assume we can just keep the constant and linear term (i.e. the tumble probability depends only linearly on the rate of change of the attractant). Note that the $\partial r / \partial \dot{c}$ is a constant. Derive a differential equation for **P(x),** and show that it is satisfied by

$$P(x) = \frac{1}{Z}\exp\left[-\frac{\partial r}{\partial \dot{c}}c\right]$$

You may have to make some argument about what ΔP has to be. Note that you've shown that the bacteria a **Boltzmann distribution**, with the attractant concentration playing the role of energy!