

**Random walk, diffusion, and dimensionality**

**Reading:** Berg, *Random Walks in Biology*, Chapters posted on WebCT.

**Problems**, due Nov 10.

1. A molecule of the enzyme ribonuclease has a diffusion coefficient of  $10^{-6} \text{ cm}^2 \text{ s}^{-1}$ . How long will it take a single ribonuclease molecule to diffuse in an infinite medium a root-mean-square distance of:

the width of an *E. coli* ( $\sim 1 \mu\text{m}$ )?

the width of a "typical" animal cell ( $\sim 10 \mu\text{m}$ )?

the length of an internodal cell in the alga *Nitella* ( $\sim 1 \text{ cm}$ )?

the length of a spinal motor neuron that innervates a foot muscle in an adult human ( $\sim 1 \text{ m}$ )?

the width of the Atlantic Ocean ( $\sim 6 \times 10^6 \text{ m}$ )?

In the *Nitella* and motor neuron cases, is diffusion adequate to transport macromolecules synthesized at one end of the cell to destinations at the opposite end?

2. Brilliant undergrad honors student Sol O'Sephadex, in trying to comprehend the RNA world of 2 billion years ago, discovers in the Kosow basement floor-drain a primitive eukaryotic organism (he names it *Megachromatinus humongo*) that has a  $100 \mu\text{m}$ -size nucleus. What would be a single transcription factor's "searching time" in this big nucleus.

3. *E. coli* RNA polymerase can transcribe a 2000 nucleotide long piece of linear DNA in about 20 s. It does this by taking unidirectional one-nucleotide-long steps along the DNA. Suppose the steps were not unidirectional but instead were an unbiased one-dimensional random walk. On average, how long would it take to transcribe this DNA if the polymerase starts random walking at one end of the DNA and stops immediately the first time it comes to the opposite end? Assume that the polymerase does not dissociate from the DNA.

4. If you like to play with computers, write a little random walk program to mimic a drunken cockroach stumbling around a tabletop. (2-D random walk) Then, expand your program for a drunken jellyfish swimming around in 3 dimensions, but plot the downward-looking 2-D projection of this 3-D walk. Does it look the same or different than the cockroach's walk? Why? Don't do this if you hate to play with computers. It's for fun (and profit).

5. Brilliant grad student Lao-tsu Goldberg is working in Jeff Gelles' lab on the random motion of individual *E. coli* swimming around on a glass slide under a "tracking microscope." This machine focuses on a single bacterium and follows its random movement around, recording its position (x,y,z coordinates) every millisecond. Think of a way to quantify the track of an individual bacterium, i.e., some way to characterize the "average distance" the bug moves as a function of time.

6. The nuclear envelope (the membrane that surrounds the nucleus in a eukaryotic cell) contains pores which allow the **free diffusion** of small proteins between the nucleus and the cytoplasm. This means that there is zero net movement of such a protein through the pore if its nuclear and cytoplasmic concentrations are equal. One such protein, GFP (diffusion coefficient =  $10^{-7} \text{ cm}^2 \text{ s}^{-1}$ ), is so highly fluorescent that the diffusion of single molecules of GFP can be followed using fluorescence microscopy.

A cell biologist, Dr. Coulter Counter, focuses his microscope on a single pore in a cell in which the free GFP concentrations in the nucleus and the cytoplasm are maintained at  $[\text{GFP}]_{\text{nuc}} = 1 \text{ nM}$  and  $[\text{GFP}]_{\text{cyto}} = 10 \text{ nM}$ , respectively. These concentrations are sufficiently low to ensure that no more than one GFP molecule will be in the pore at a time.

Dr. Counter finds that during 1 minute of observation, 120 GFP molecules travel completely through the pore from cytoplasm to nucleus, while only 15 go all the way through the pore from the nucleus to the cytoplasm, giving a net rate of transport equal to 105 molecules per minute. Predict how both the two unidirectional rates and the net rate will change if the concentration of GFP in the cytoplasm is doubled while the nuclear concentration is left unchanged. Explain your reasoning.

Dr. Counter also decides to tabulate the fate of each molecule that reaches the middle of the pore. For each molecule that comes to the point halfway across the nuclear envelope, Dr. Counter follows it to see whether it exits the pore by going into the cytoplasm or by going into the nucleus. What is the predicted difference between the number per minute of these molecules exiting into the nucleus and into the cytoplasm? Explain your reasoning.

7. Play with random walk simulations on course website. Comment on what you noticed.