Physical Principles in Biology
Biology 3550
Fall 2016

Lecture 22

Bacterial Chemotaxis

Friday, 21 October

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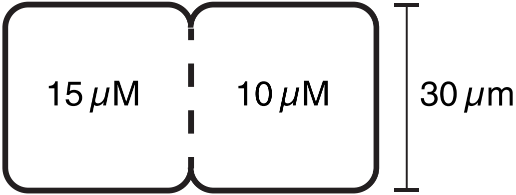
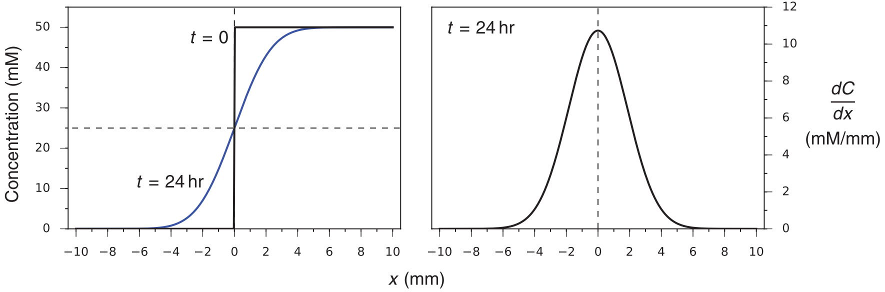
Mid-term Problem 1



- At equilibrium, concentration in both cells will be 12.5 μm
- Concentration in right-hand cell must increase by 2.5 μM
- Number of molecules that need to move:

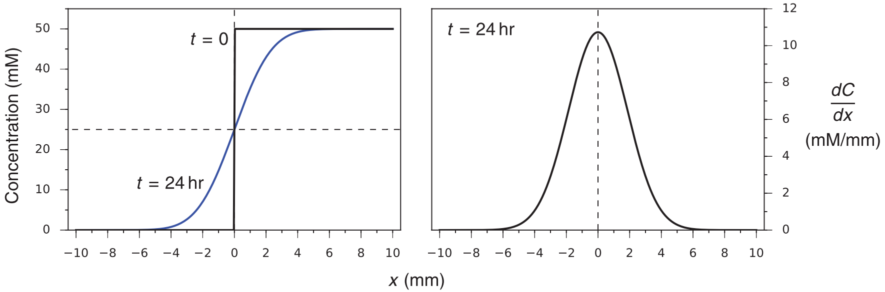
no. of molecules $= 2.5\,\mu\text{M} \times$ cell volume (L) $\times\ 6.02\times10^{23}$ molecules/mol

Mid-term Problem 4a



- Draw curve for $C(x)$ vs. x at $t = 24\,\text{hr}$.
- For a given time, the plot of $C(x)$ vs. t is the integral of dC/dx with respect to x.
- At 24 h, $C(x)$ is still 0 for $x \lesssim -0.6$, and $C(x) = 50\,\text{mM}$ for $x \gtrsim 0.6$.

Mid-term Problem 4b

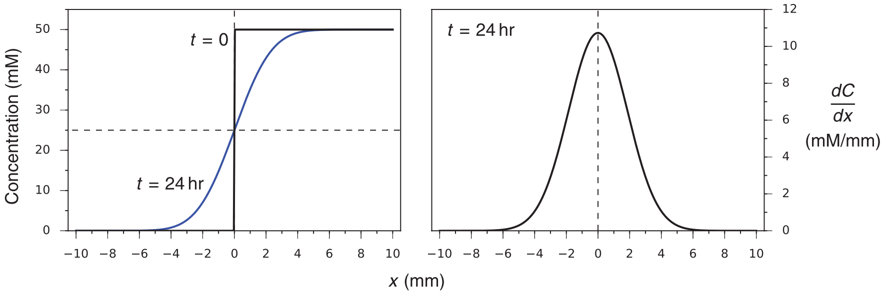


- Calculate flux for $x = 0$ and $t = 24\,\text{hr}$.

$$J = -D\frac{dC}{dx} = 2{\times}10^{-11}\,\text{m}^2/\text{s} \times 11\,\text{mM}/\text{mm}$$

$$= -2.2{\times}10^{-7}\,\text{mol}/(\text{m}^2\text{s})$$

Mid-term Problem 4c

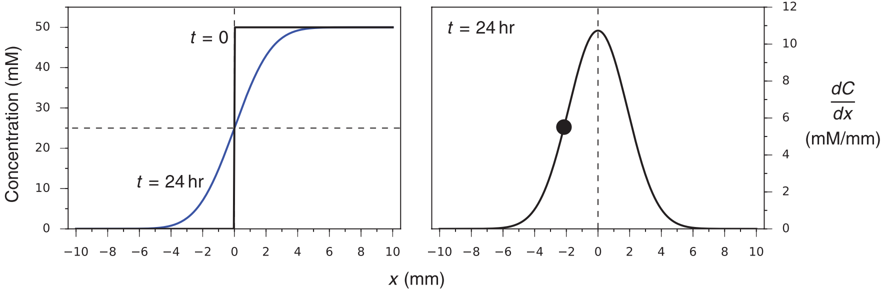


- Calculate the rate of concentration change for $x = 0$ and $t = 24\,\text{hr}$.
- Fick's second law:

$$\frac{dC}{dt} = D\frac{d^2C}{dx^2}$$

- What is the second derivative of $C(x)$ with respect to x at $x = 0$?
- 0, for any $t > 0$!

Mid-term Problem 4d

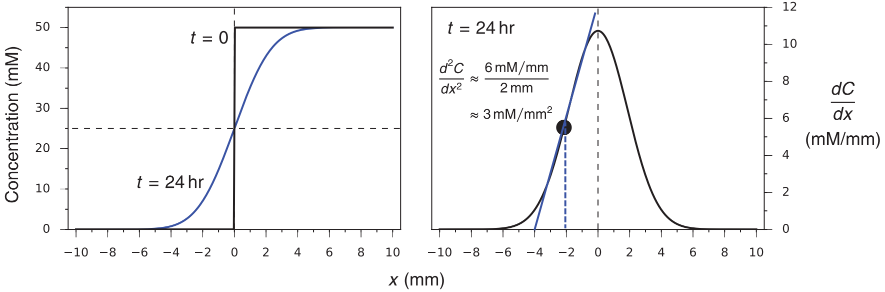


- Identify the point at which the rate of concentration change is greatest at $t = 24$ hr.

$$\frac{dC}{dt} = D\frac{d^2C}{dx^2}$$

- Where is the second derivative of $C(x)$ with respect to x greatest?

Mid-term Problem 4e

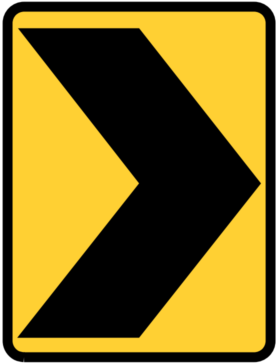


- Calculate the rate of change in concentration at the point where the concentration changes most rapidly at 24 h
- Fick's second law:

$$\frac{dC}{dt} = D\frac{d^2C}{dx^2}$$

- How do we find the second derivative of $C(x)$ with respect to x at $x \approx -2\,\text{mm}$?

Warning!



Direction Change

(In more than one sense)

Diffusion of a Bacterial Cell

- Assume a spherical cell with radius of 1 μm.
  (or an oblong cell with an "effective radius" of 1 μm)
- Use the Stokes–Einstein equation to estimate the diffusion coefficient in water.

$$D = \frac{kT}{6\pi r}$$

$$k = \text{Boltzmann's constant} = 1.38\times10^{-23}\,\mathrm{Kg}\cdot\mathrm{m}^2\mathrm{s}^{-2}\mathrm{K}^{-1}$$

$$T = 300\,\mathrm{K}$$

$$\eta = \text{viscosity} = 1\,\text{centipoise} = 10^{-3}\,\mathrm{Kg}\cdot\mathrm{m}^{-1}\mathrm{s}^{-1}$$

$$D = 2\times10^{-13}\,\mathrm{m}^2\mathrm{s}^{-1}$$

- Compare to $2\times10^{-10}\,\mathrm{m}^2/\mathrm{s}$ for a small molecule (1 nm).
- *D* decreases by 10-fold for each 10-fold increase in radius.

Diffusion via a Random Walk

For diffusion along a single direction:

- Calculate $\langle x^2 \rangle$ (mean-square projection along the x-axis) directly from the diffusion coefficient and total time, t:

$$\langle x^2 \rangle = n\delta_x^2 = 2Dt$$

- The other two dimensions:

$$\langle y^2 \rangle = 2Dt$$

$$\langle z^2 \rangle = 2Dt$$

- Mean-square end-to-end distance in three dimensions:

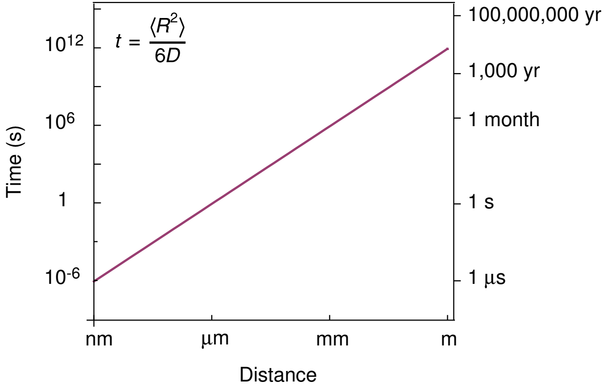
$$\langle r^2 \rangle = \langle x^2 \rangle + \langle y^2 \rangle + \langle z^2 \rangle = 6Dt$$

Time to Diffuse a Given (RMS) Distance From the Starting Point

- $\langle r^2 \rangle = 6Dt$
- Solve for t for $\mathrm{RMS}(r) = R$ (a specified value), and $\langle r^2 \rangle = R^2$:

$$R^2 = 6Dt$$

$$t = R^2/(6D)$$



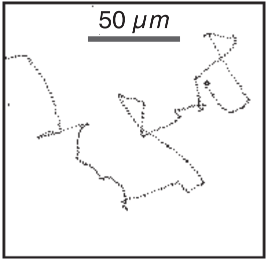
- For 1-μm bacterium, $D = 2{\times}10^{-13}\,\mathrm{m^2 s^{-1}}$.
- How is a bacterium to find food 1 mm ($\approx 1\,\mathrm{week}$) away?

Bacteria Under the Microscope

(Swimming E. coli Movie)

- Movie from: `http://www.rowland.harvard.edu/labs/bacteria`

Tracking the path of a single *E. coli* Cell



30 seconds

- It looks like a random walk! (with variable step size)
- Step sizes are larger than the bacterium ($\approx 1\ \mu m$) and *much* larger than expected for diffusion (≈ 1 nm).

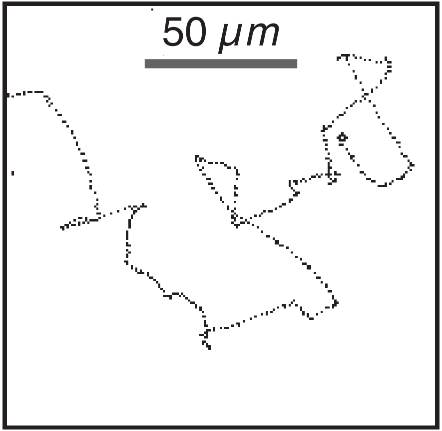
Berg, H. & Brown, D. (1972). *Nature*, 239, 500–504.

`http://dx.doi.org/10.1038/239500a0`

Clicker Question #1

Estimate the average step length in the random walk
(projection onto two dimensions).

- 5 μm
- 10 μm
- 20 μm
- 40 μm
- 60 μm



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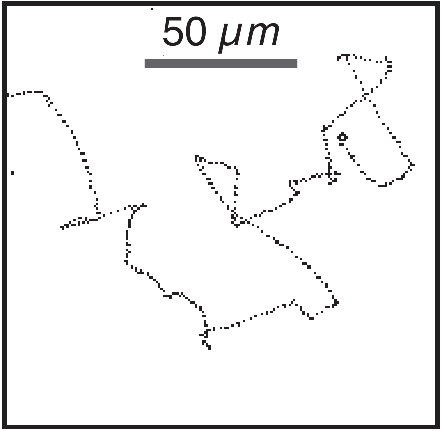
Clicker Question #2

Estimate the velocity of the bacteria
(projection onto two dimensions).

- 10 μm/s
- 20 μm/s
- 40 μm/s
- 80 μm/s
- 200 μm/s



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Random Walk Parameters, in 3-dimensions

From careful analysis of 3-dimensional data:

- Step length: $\delta = 60\,\mu\text{m}$
- Velocity: $v = 20\,\mu\text{m/s}$
- Duration of each step ("run"):

$$\tau = \delta / v = 60\,\mu\text{m} \div 20\,\mu\text{m/s}$$

$$= 3\,\text{s}$$

- Number of steps: $n = t/(3\,\text{s})$
- mean-square end-to-end distance:

$$\langle r^2 \rangle = n\delta^2 = \frac{t}{3\,\text{s}}(60\,\mu\text{m})^2 = t/1\,\text{s} \times 1200\,\mu\text{m}^2$$

Time for a Bacterium to Travel a Given (RMS) Distance From the Starting Point

- $\langle r^2 \rangle = t/1\,\mathrm{s} \times 1200\,\mu\mathrm{m}^2$
- Solve for t, for $\mathrm{RMS}(r) = R$ (a specified value), and $\langle r^2 \rangle = R^2$:

$$R^2 = t/1\,\mathrm{s} \times 1200\,\mu\mathrm{m}^2$$

$$t = R^2/(1200\,\mu\mathrm{m}^2) \times 1\,\mathrm{s}$$

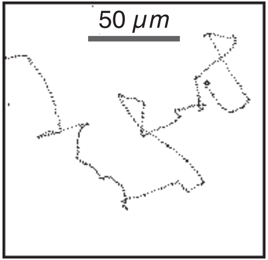
- For 1 mm = 1000 μm:

$$t = 1\,\mathrm{s} \cdot \frac{(1000\,\mu\mathrm{m})^2}{1200\,\mu\mathrm{m}^2} = 1\,\mathrm{s} \cdot \frac{10^6\,\mu\mathrm{m}^2}{1200\,\mu\mathrm{m}^2}$$

$$= 830\,\mathrm{s} = 14\,\mathrm{min}$$

- Compare to $\approx$ 1 week for diffusion!
- A smaller number of longer steps in a given time period always goes further!

Why Not Take Even Bigger Steps



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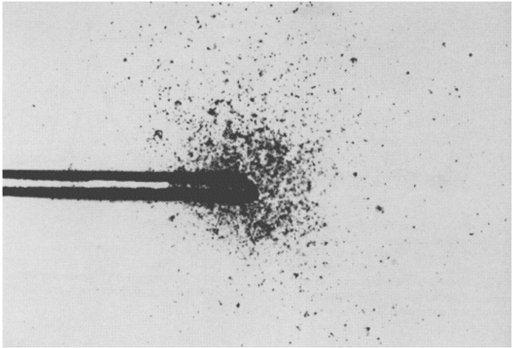
- The path starts to curve after about 50 μm.
- Why change direction abruptly?

Bacteria Can Swim Towards Food

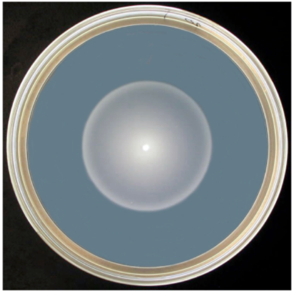


- Bacteria swim towards an amino acid diffusing from a capillary.
- Described by W. Pfeffer in 1884.

Adler, J. (1969). *Science*, 166, 1588–1597.

http://dx.doi.org/10.1126/science.166.3913.1588

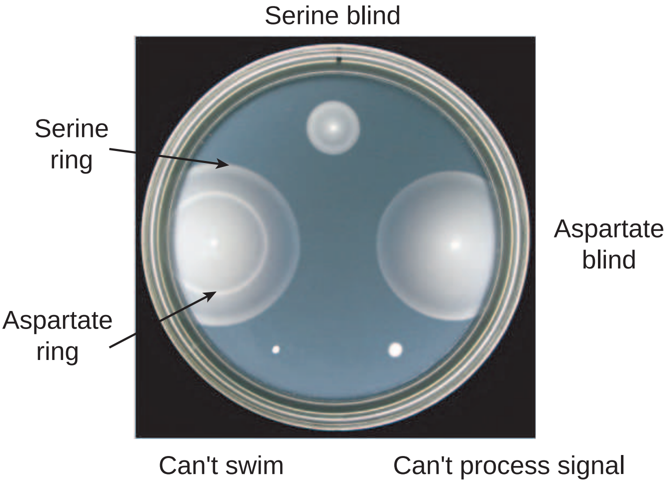
Another Way to Observe Chemotaxis



- Bacteria inoculated at the center of the plate, in very porous agar.
- Consume nutrients as they divide, creating a concentration gradient.
- Swim outward to find more nutrient.
- How do they know which way to go?

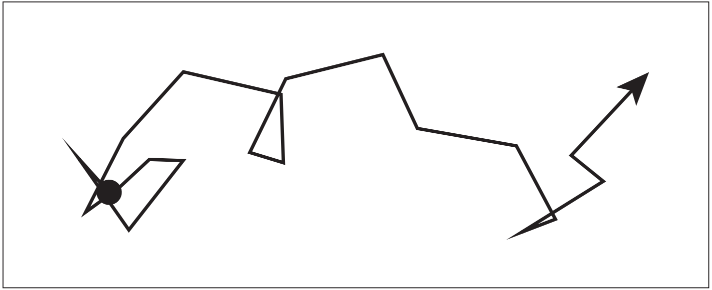
Picture from J.S. Parkinson, University of Utah

Genetic Mutants Identify Multiple Functions Required for Chemotaxis



Picture from J.S. Parkinson, University of Utah

The Trick: A Biased Random Walk



1. Choose a random direction.
2. Swim for a while.
3. Is life getting better? (more food, less poison)
   - Yes: keep going.
   - No: Stop and choose a new *random* direction.
4. Repeat.