Physical Principles in Biology
Biology 3550
Spring 2024

Lecture 22:

Bacterial Chemotaxis

Friday, 1 March 2024

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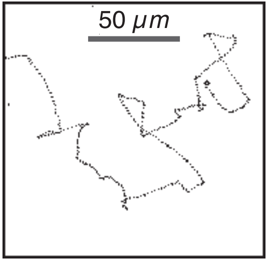
Announcements

- Spring Break next week!:
- Midterm Exam:
  - Friday, 15 March
  - 50 min
- Review Session
  - 5:15 PM, Thursday, 14 March
  - HEB 2002
  - Come with questions!

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 step sizes expected for diffusion.

Berg, H. & Brown, D. (1972). *Nature*, 239, 500–504.
http://dx.doi.org/10.1038/239500a0

Random Walk Parameters, in 3-dimensions

From careful analysis of 3-dimensional data:

- Average step length: $l = 60\,\mu\text{m}$
- Average velocity: $v = 20\,\mu\text{m/s}$
- Average duration of each step ("run"):

$$\tau = l/v = 60\,\mu\text{m} \div 20\,\mu\text{m/s}$$
$$= 3\,\text{s}$$

- Number of steps: $n = t/(3\,\text{s})$

Time for a Bacterium to Travel 1 mm (RMS) Distance From the Starting Point

- Avg. step length: $l = 60\,\mu\text{m}$
- Avg. velocity: $v = 20\,\mu\text{m/s}$
- Avg. time per step: $\tau = l/v = 3\,\text{s}$
- Number of steps in time t: $n = t/3\,\text{s}$

$$\text{RMS}(r) = l\sqrt{n} = 1\,\text{mm} = 10^3\,\mu\text{m}$$

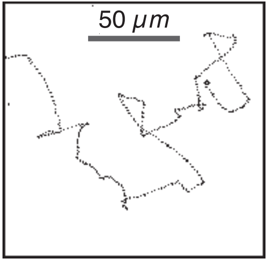
$$\langle r^2 \rangle = nl^2 = (10^3\,\mu\text{m})^2 = 10^6\,\mu\text{m}^2$$

$$(t/3\,\text{s}) \times (60\,\mu\text{m})^2 = 10^6\,\mu\text{m}^2$$

$$t = 3\,\text{s} \times \frac{10^6\,\mu\text{m}^2}{3600\,\mu\text{m}^2} = 833\,\text{s} \approx 14\,\text{min}$$

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

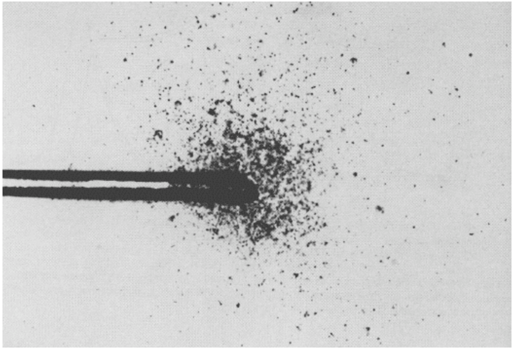
Why Not Take Even Bigger Steps?



30 seconds

- The path starts to curve after about 50 μm.
- There is a limit on how far the bacterium can travel without changing direction.
- Why change direction abruptly?
- They're doing something smarter!

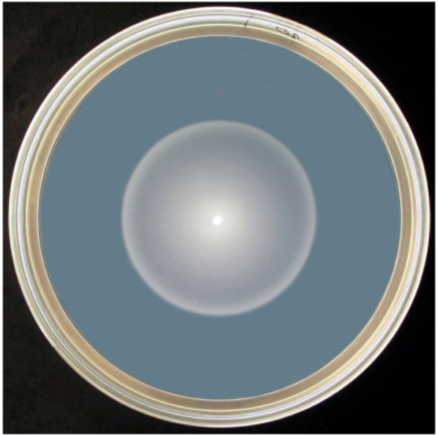
Bacteria Can Swim Towards Food



- 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

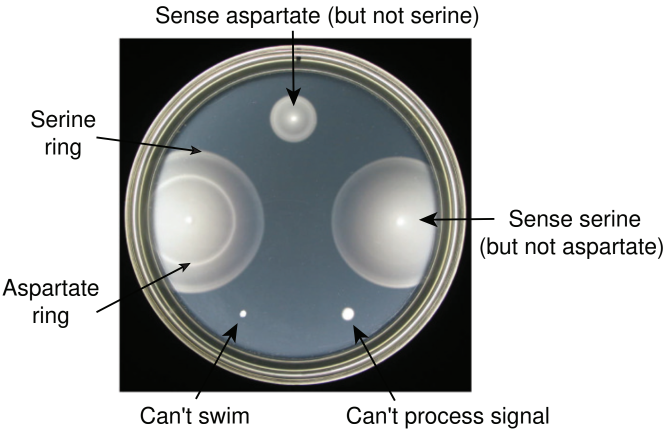
Another Way to Observe Chemotaxis



- 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.
- Form a ring at boundary of high nutrient concentration
- How do they know which way to go?

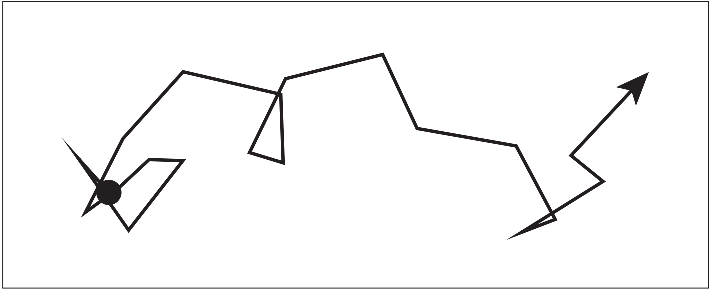
Picture from J.S. Parkinson, University of Utah

Genetic Mutants Identify Multiple Functions Required for Chemotaxis



Picture from J.S. Parkinson, University of Utah

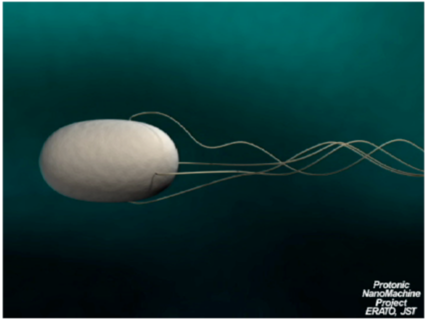
The Trick: A Biased Random Walk



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.

Bacteria Swim Using Flagella and a Rotary Motor

(Tethered E. coli Movie)



- Movie shows bacteria “tethered” by their flagella to a microscope slide.
- Movie from: http://www.rowland.harvard.edu/labs/bacteria
- Computer image of *E. coli* by group of Nobuhiko Nomura

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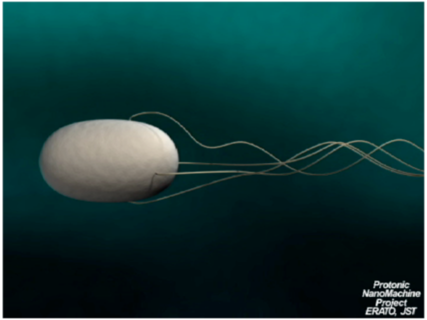

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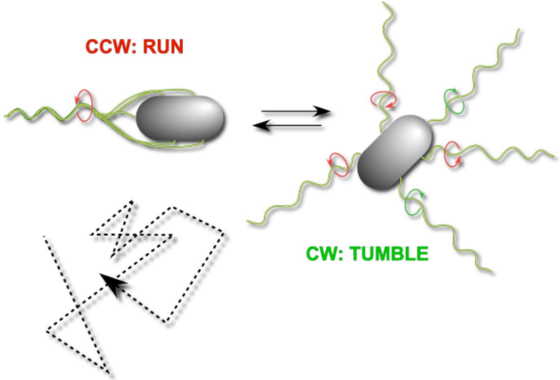
Rapid Turns Are Controlled by Motor Direction



- Random walk is controlled by timing of motor reversals.

Picture from J.S. Parkinson, University of Utah

Fluorescence Microscopy of Live Cells

(Swimming Bacteria Movie)

- From the Rowland Institute of Science (Cambridge, MA)
  http://www.rowland.harvard.edu/labs/bacteria/index_movies.html

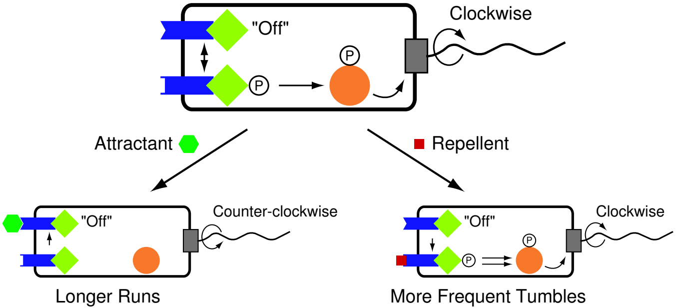
Another Mechanism for Turning

(flick and turn movie)

- *Vibrio alginolticus* (and other species) has only a single motor and flagellum.
- Reversal of a single flagellum does not cause tumbling.
- *Vibrio* somehow “flicks” its flagellum to cause a sudden change in direction.

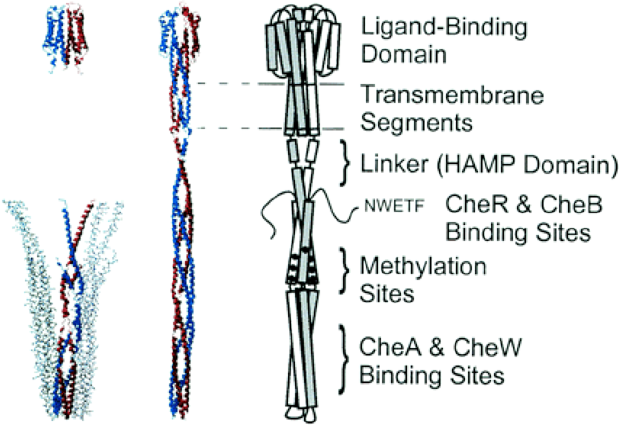
Xie, L., Altindal, T., Chattopadhyay, S. & Wu, X.-L. (2011). *Proc. Natl. Acad. Sci., USA*, 108, 2246–2251. http://dx.doi.org/10.1073/pnas.1011953108

Signaling Pathway for Chemotaxis



- Receptor has two interconverting states.
- Signal from “on” receptor promotes tumbling.
- Attractant suppresses signalling.
- Repellent enhances signalling.
- Receptor adapts: More attractant required to keep it off. “Memory”

Structure of Receptors

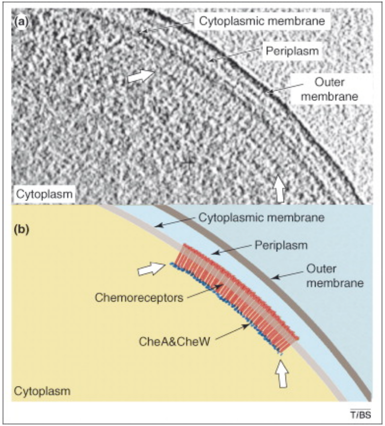


- Receptors can detect 1% change in concentration.
- Sensitive to concentrations from 10^{-10} M to 10^{-3} M

Hazelbauer, G., Falke, J. & Parkinson, J. (2008). *Trends Biochem. Sci.*, 33, 9–19.
http://dx.doi.org/10.1016/j.tibs.2007.09.014

Kim, S.-H., Wang, W. & Kim, K. K. (2002). *Proc. Natl. Acad. Sci., USA*, 99, 11611–11615.

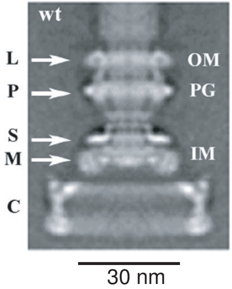
Receptors Form Large Arrays in the Cell Membrane

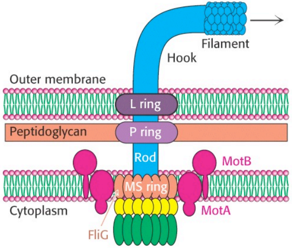


- Physical contact between receptors allows communication.
- Allows high sensitivity over a very wide range of ligand concentrations.

Zhang, P., Khursigara, C., Hartnell, L. & Subramaniam, S. (2007). *Proc. Natl. Acad. Sci., USA*, 104, 3777–3781.
http://dx.doi.org/10.1073/pnas.0610106104

Anatomy of the Flagellar Motor





From Berg, Tymoczko & Stryer, Biochemistry, 5th Ed.

- Driven by flow of H^+ ions across membrane
- Up to ≈ 10,000 RPM
- EM image shows only the rotating parts.

EM reconstruction of motor:

Thomas, D., Morgan, D. & DeRosier, D. (2001). *J. Bacteriol.*, 183, 6404–6412.
http://dx.doi.org/10.1128/JB.183.21.6404-6412.2001