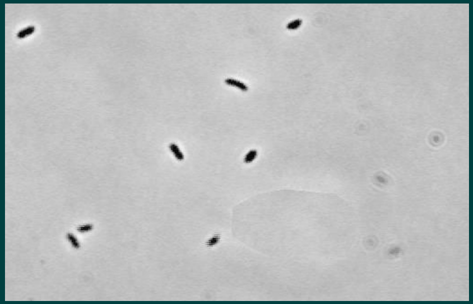
CELL MOTILITY

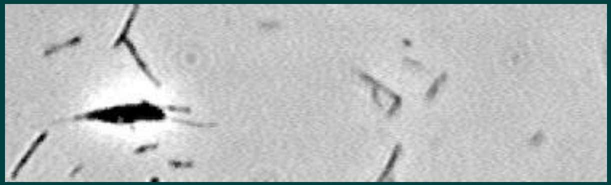
unicellular organisms:

bacteria – flagella driven by electric motor



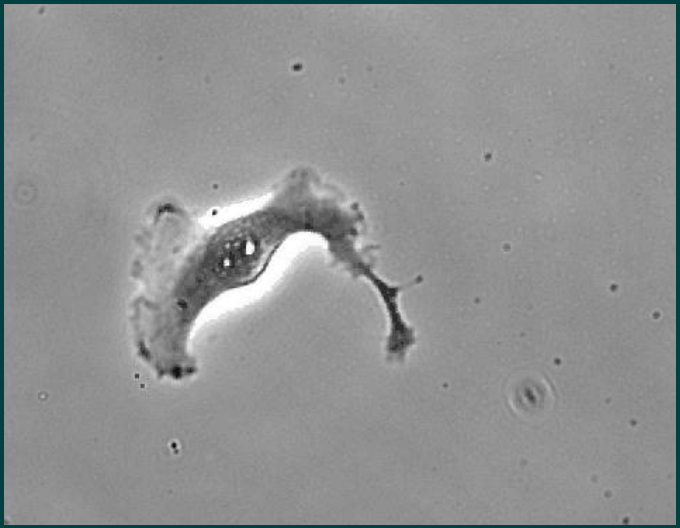
1 min, 40 μm

protozoa - flagella and cilia based on microtubules, crawling motion

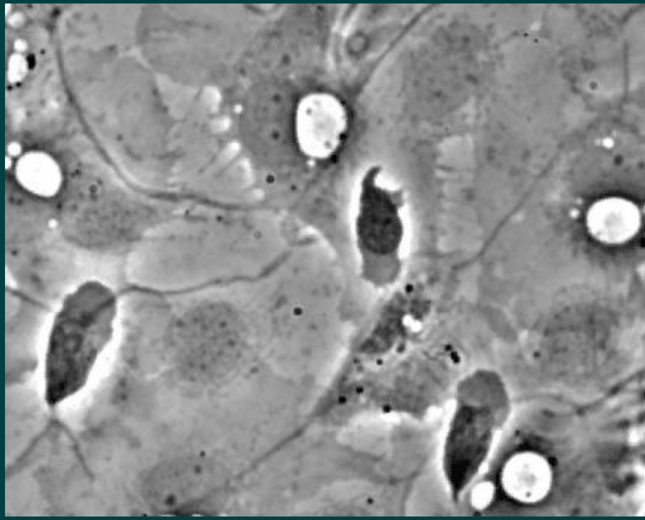


20 s, 35 μm

cells in multicellular organisms –
mostly crawling motion
(development,
wound healing,
immune response,
cancer metastasis, etc.)



melanoma cell,
10 hours, 200 μm



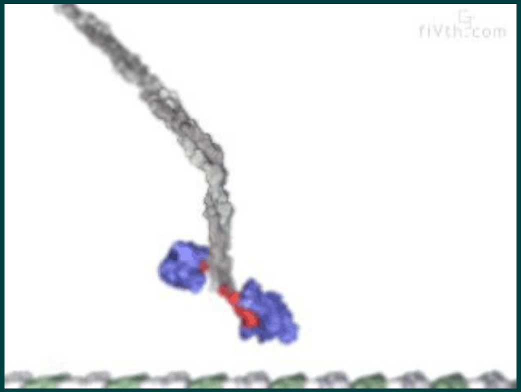
fish skin, 2 min, 85 μm

Different scales: subcellular

rotary molecular motor: F_1 ATPase

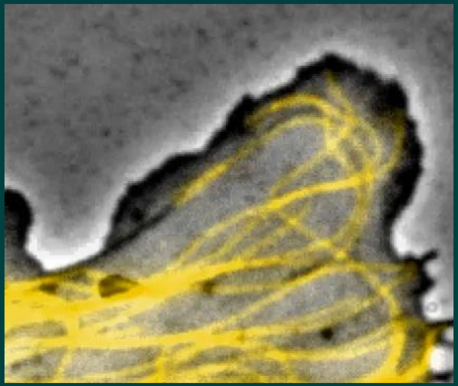
Noji et al., Nature, 1997

cartoon of kinesin

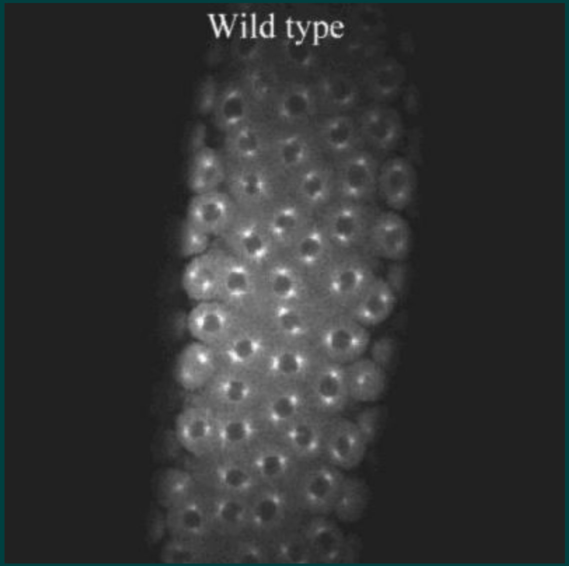


Vale lab site

organelle on microtubule



coordinated nuclear divisions



Sharp et al., 2000

Different scales: cellular

well coordinated cells: isotropic and polarized

model of fish epidermal keratocytes studied in our group

Different scales: subcellular to cellular

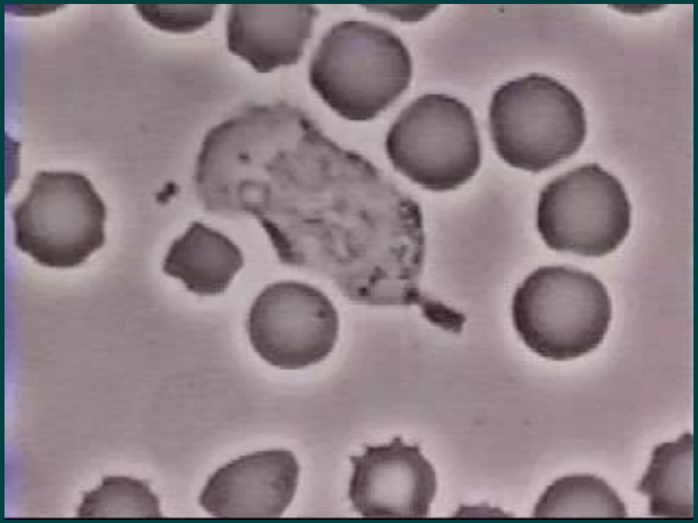
polarity and motion – property of the cytoplasm

Verkhovsky et al, Curr. Biol., 1999

In the context of an organism

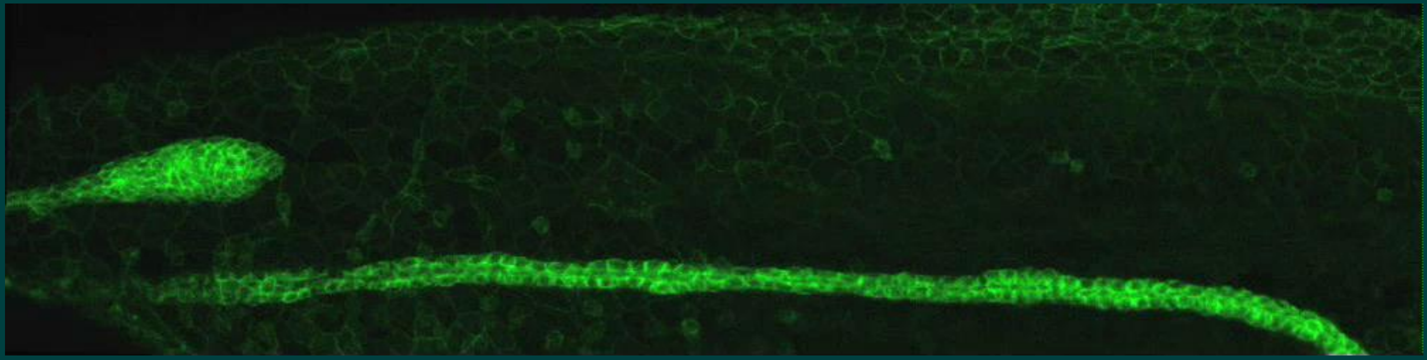
immune response:
neutrophil chasing a bacterium

David Rogers, Biochemweb.org



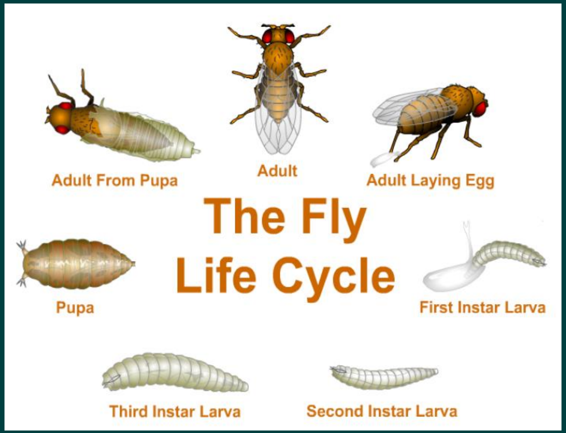
collective cell motion: Zebra fish lateral line:

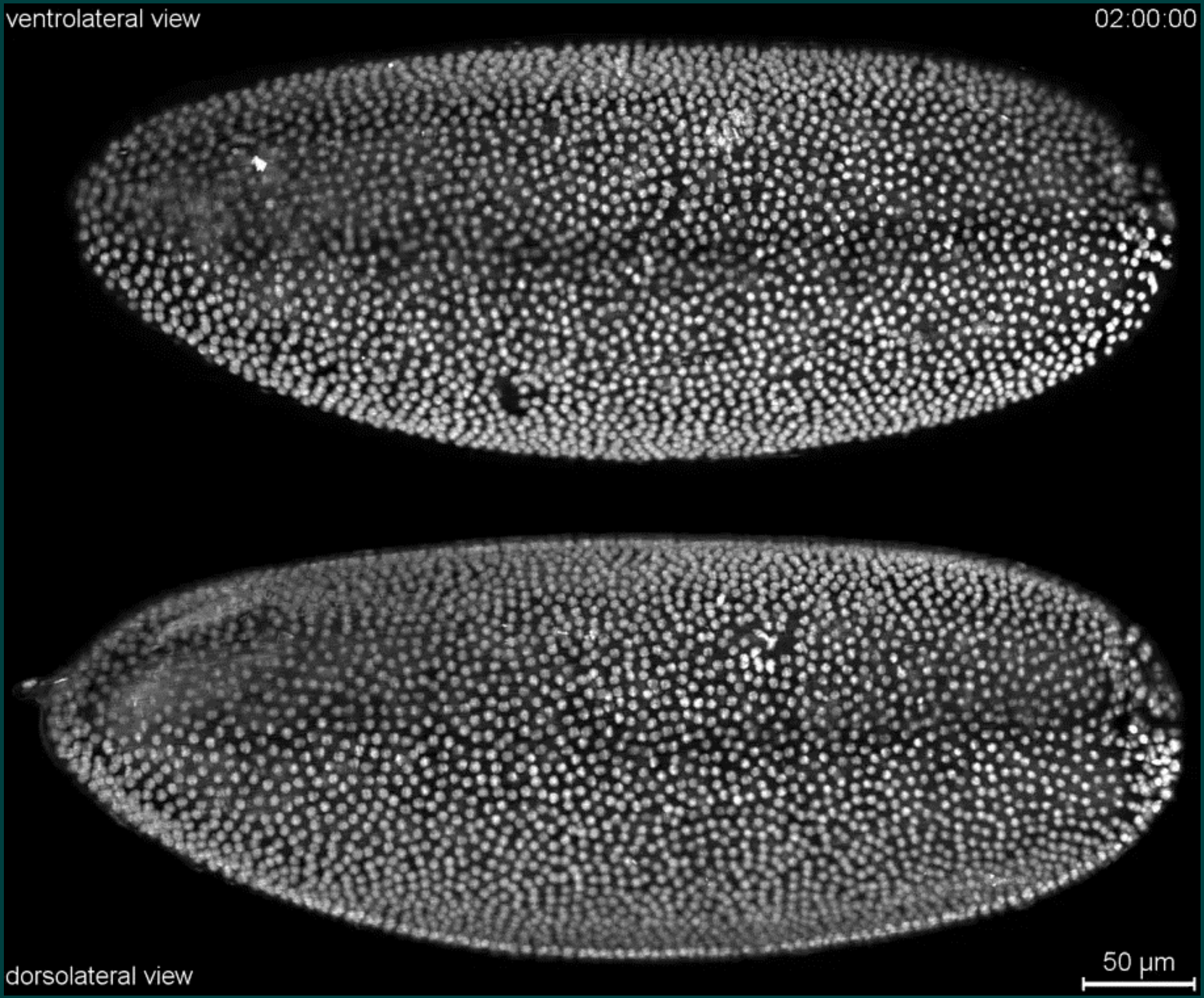
Haas and Gilmour, Dev. Cell, 2006



In the context of an organism

embryonic development (fruit fly Drosophila)





Tomer et al., Nat. Methods, 2012

Questions at different levels:

Molecular components and chemical reactions producing mechanical forces

Physics of motion at microscopic scale

Coordination in space and time within the cell, symmetry breaking

How external signals are detected and interpreted

How the cells behave collectively

Approximate plan

1. Different types of cell motility. Bacterial motility, eucaryotic cilia and flagella, crawling motility

2. Motile machinery: cytoskeleton, components, mechanisms of assembly.

3. Methods to study cytoskeletal dynamics in the cell.

4. Mechanisms of actin assembly at the cell leading edge.

5. Biophysics of actin assembly, forces and modeling.

6. Motor proteins, active cycle, steps and forces.

7. Microtubule-dependent motors, role in intracellular transport and mitosis.

8. Myosin superfamily of motor proteins, non-conventional myosins.

9. Cell-substrate adhesion.

10. Myosin II, coordination of protrusion, attachment and contraction.

11. Cytoplasmic flows, membrane tension, blebbing motility

12. Interaction between actin/myosin system and microtubules

13. Cell polarity, pattern formation, detection of external signals

14. Collective cell motion, motility in development.

15. Oral exam

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Sources:

Molecular Biology of the Cell
Bruce Alberts et al.
Garland Science, 2014 (6th edition)

Physical Biology of the Cell
Rob Phillips et al.
Garland Science, 2012 (2nd edition)
(chapters posted on Moodle)

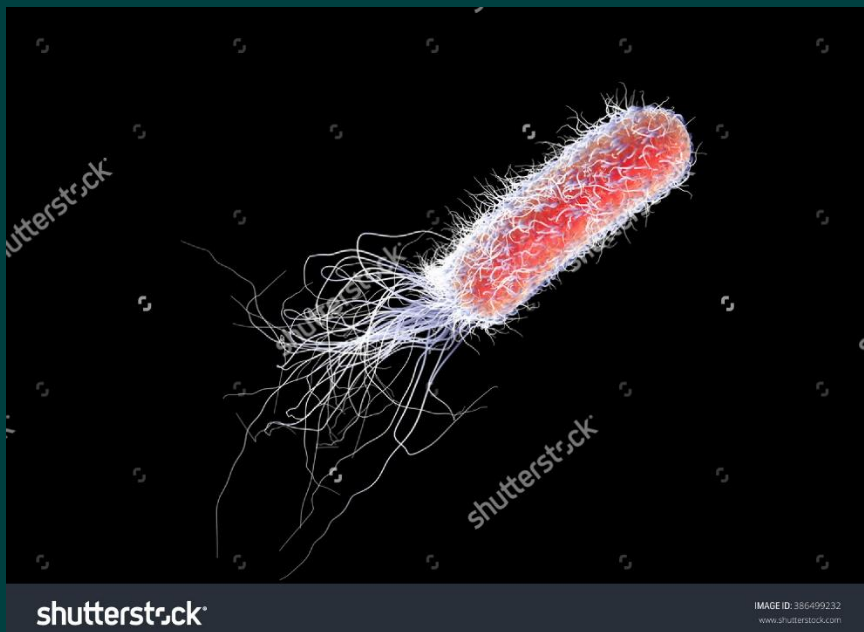
Internet, e.g. https://www.mechanobio.info/

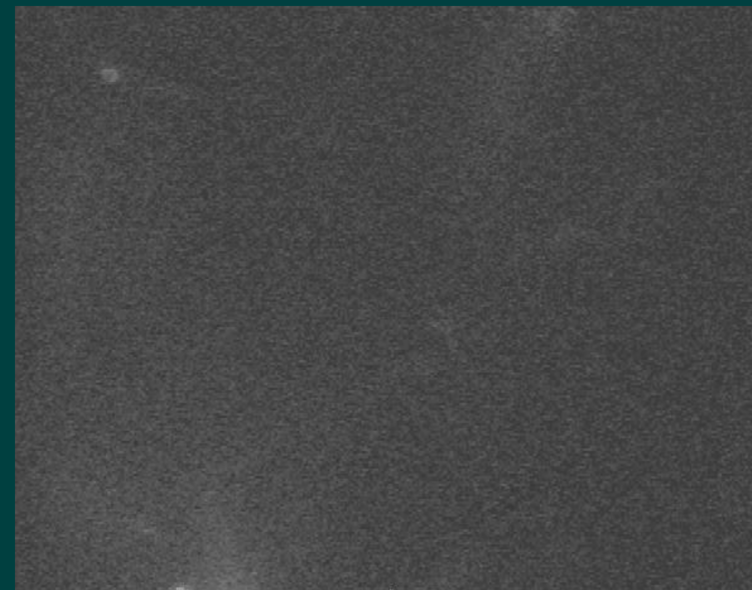
Original research papers

Moodle

Bacteria swim with flagella at ~ 10 – 20 μm/s

(i.e. many body sizes per second)

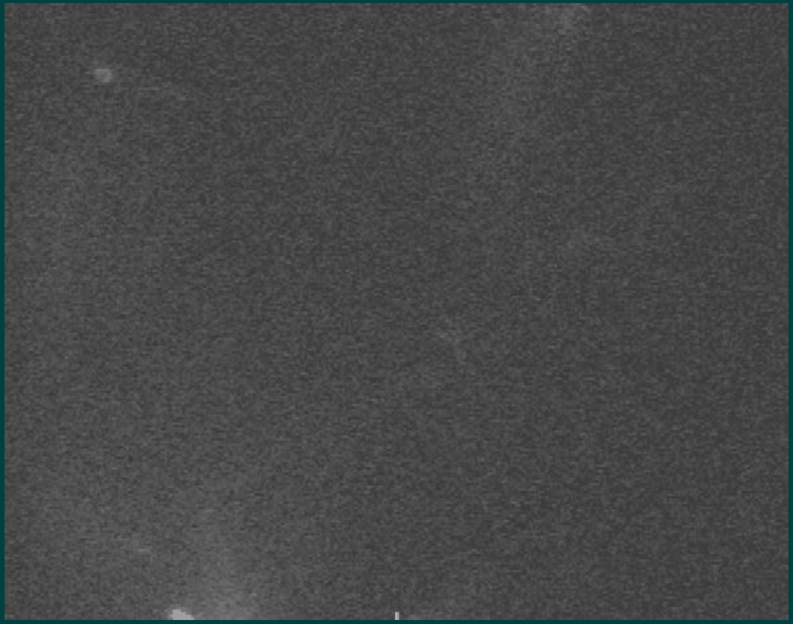




can detect gradients with decay distances of 20 mm
at concentrations of 10^{-6} M (difference of concentration
over bacterial body of ~ 0.1 nM)

Strategies to move directionally

prokaryotic cells



Fluorescently labeled bacteria

Berg lab http://www.rowland.org/labs/bacteria/index_movies.html

eukaryotic cells

Dictyostelium: chemotaxis to cAMP In the pipette

Firtel lab web page

Can bacteria measure attractant gradient across their bodies?

How do they move towards the attractant?

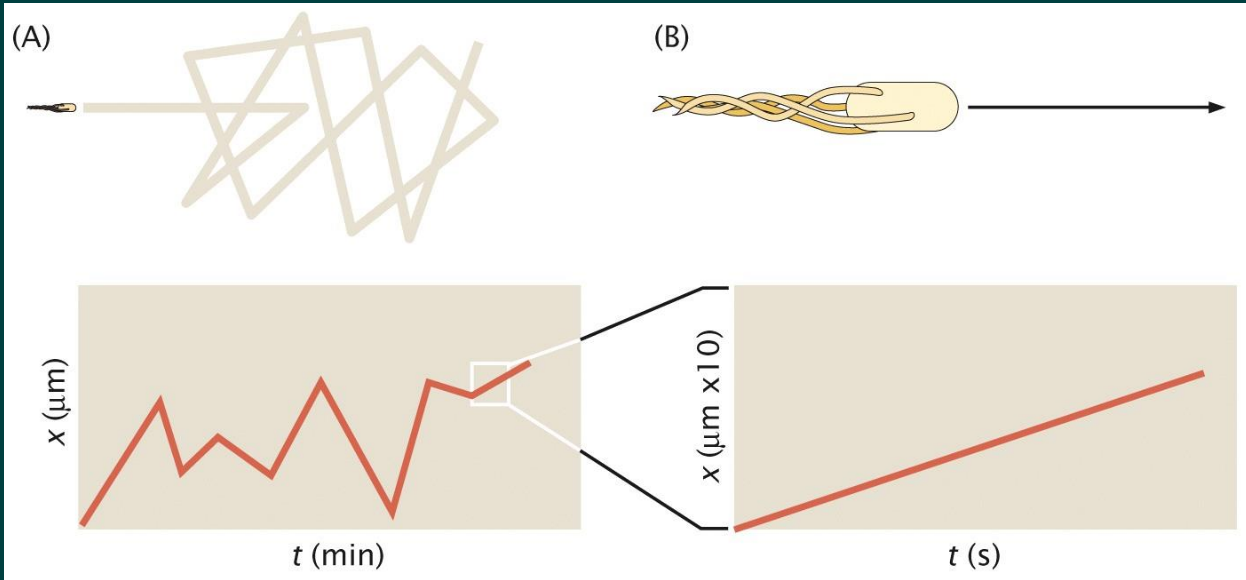
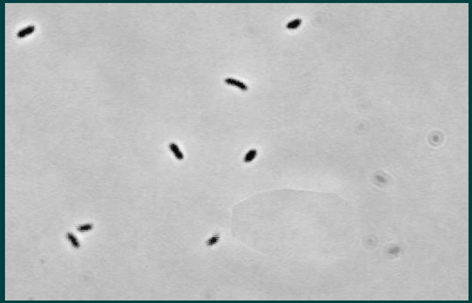


Figure 13.3 Physical Biology of the Cell, 2ed. (© Garland Science 2013)



swimming trajectories consist of straight segments of different directions with the directions of the sequential segments not correlated

at a large scale looks like random walk (biased)

How many molecules of attractant (repellent) arrive at a steady state at bacterial surface?

Diffusion equation

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}$$

$$\frac{\partial c}{\partial t} = D\nabla^2 c$$

3D case

steady state

$$D\nabla^2 c = 0$$

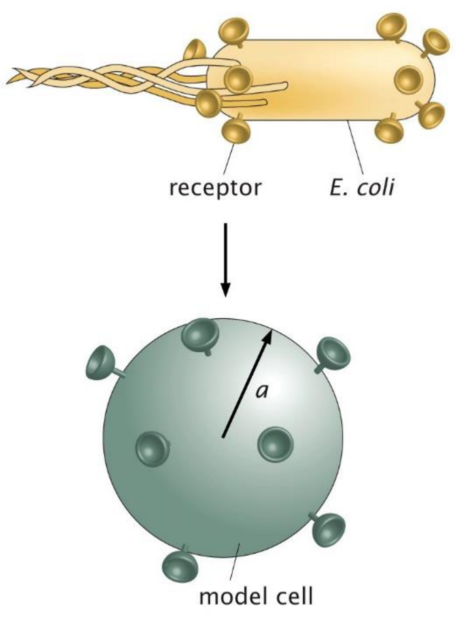


Figure 13.21 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

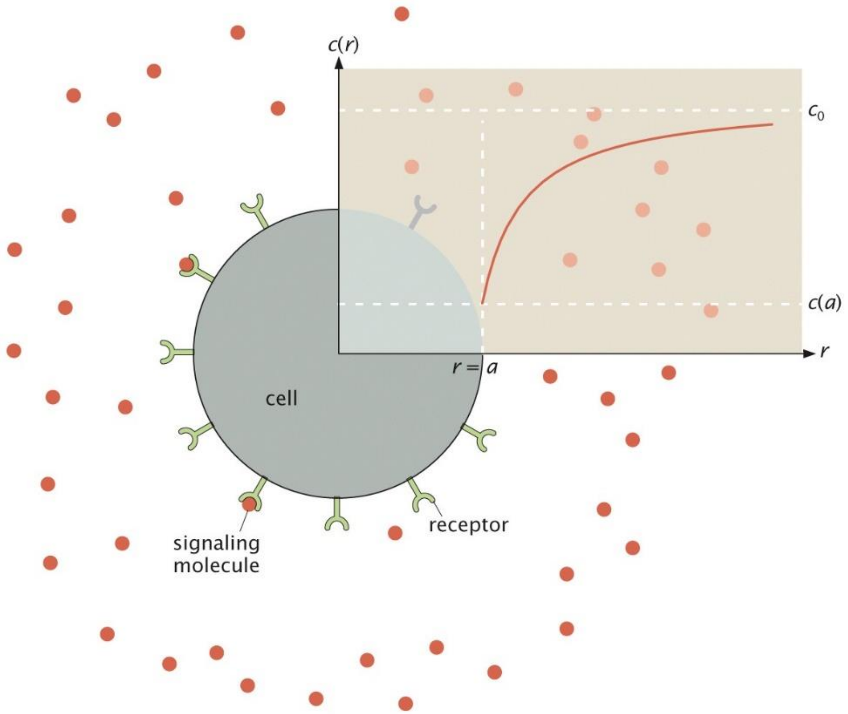


Figure 13.22 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

$$\frac{dn}{dt} = -j(a)4\pi a^2 = 4\pi D a c_0.$$

for a = 10^{-4} cm, D = 10^{-5} cm^2/s, c = 10^{-6} M

$dn/dt = 4\pi Dac = 10^6$

Poisson distribution

(standard deviation)/mean = mean $^{-1/2}$ = 10 $^{-3}$

for gradient scale of 1 cm relative concentration difference over bacterial body is 10^{-4}

to measure such difference bacteria would need to integrate the signal for ~ 100 s

too long!! bacteria must use a different mechanism to sense the gradient

Berg, H. C. & Purcell, E. M. (1977) Biophys. J. 20 , 193-219

Strategies to choose a good direction:

Big cell (eukaryotic)

measure concentration in several spots simultaneously

make decision

small cell (prokaryotic)

can only measure in one spot at a time

make decision..???

Strategies to choose a good direction:

Big cell (eukaryotic)

measure concentration in several spots simultaneously

make decision to go in the direction of “the best measurement”

small cell (prokaryotic)

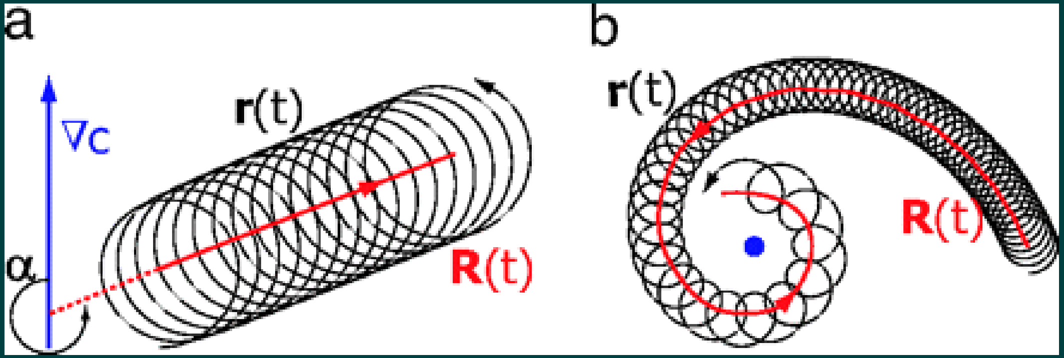
can only measure in one spot at a time

move, measure in another spot

make decision to continue to move, or to change direction other possible strategies when direction is not known:

- grid search as with analog avalanche beacons (requires memory)

- helical trajectory with signal-dependent curvature



chemotaxis in sea urchin sperm (Friedrich and Jülicher, PNAS, 2007)

What are the forces that bacteria need to overcome? (nm to μm, s to min)

Inertia ?

Gravity ?

Resistance from the fluid?

What are the forces that bacteria must overcome to swim?

naively: should displace liquid with velocity *v* in a cross-section *A*

work $mv^2t/2 = Av\rho v^2t/2 = Fvt \quad F = A\rho v^2/2$

$$F_d = 0.5\,\rho\,V^2\,C_d\,A$$

drag coefficient accounts for the shape $C_d = 2F/A\rho v^2$

What are the forces that bacteria must overcome to swim?

naively: should displace liquid with velocity v in a cross-section A

work $mv^2t/2 = Av\rho v^2t/2 = Fvt \quad F = A\rho v^2/2$

drag coefficient accounts for the shape $C_d = 2F/A\rho v^2$

c_d	Item
0.26	BMW i8
0.26	Nissan GT-R (2011-2014)
0.27	Nissan GT-R (2007-2010)
0.28	1969 Dodge Charger Daytona and 1970 Plymouth Superbird
0.28	1986 Opel Omega saloon.[18]
0.28	Mercedes-Benz CLA-Class Type C 117.[19]
0.29	Mazda3 (2007) [20]
0.295	bullet (not ogive, at subsonic velocity)
0.3	Saab 92 (1949), Audi 100 C3 (1982)
0.31	Maserati Ghibli Sedan (2014) [21]
0.324	Ford Focus Mk2/2.5 (2004-2011, Europe)
0.33	BMW E30 3 Series (1984-1993, Germany)
0.35	Maserati Quattroporte V (M139, 2003–2012)
0.36	Citroen CX (1974-1991, France)
0.37	Ford Transit Custom Mk8 (2013, Turkey)
0.48	rough sphere ($Re = 10^6$), Volkswagen Beetle[22][23]
0.58	Jeep Wrangler TJ (1997-2005)[24]
0.75	a typical model rocket[25]
1.0	coffee filter, face-up[unreliable source?][26]
1.0	road bicycle plus cyclist, touring position[27]

What are the forces that bacteria must overcome to swim?

naively: should displace liquid with velocity v in a cross-section A

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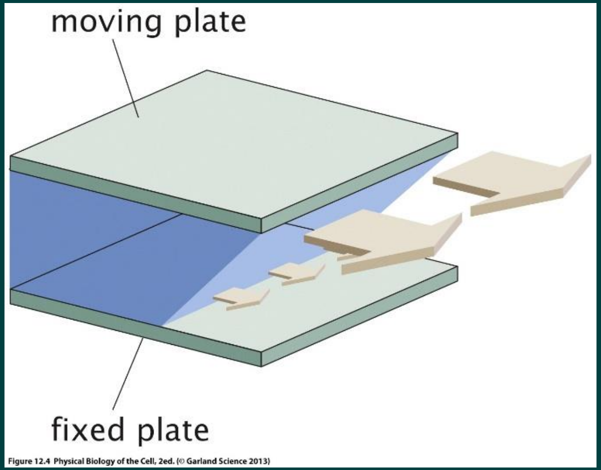
What's wrong with this?

viscosity



$$\frac{F}{A} = \eta \frac{v}{d}$$

$$\Delta m\mathbf{a} = \delta\mathbf{F}_p + \delta\mathbf{F}_\nu$$

$$\frac{\partial\mathbf{v}}{\partial t} + (\mathbf{v}\cdot\nabla)\mathbf{v} = -\frac{1}{\rho}\nabla p + \nu\nabla^2\mathbf{v}$$

$$\nu = \eta/\rho$$

Navier-Stokes equation

Reynolds number $Re = \rho LU/\eta = LU/\nu$ (rigid body of size *L* moves in the fluid with velocity *U*)

~ ratio of kinetic energy $\mathrm{KE} \sim \rho a^3 u^2$

to viscous dissipation $W \sim \underbrace{\eta\frac{u}{a}}_{\text{viscous stress}} \times \underbrace{a^2}_{\text{area}} \times \underbrace{a}_{\text{distance traveled}}$

for Re « 1 Navier-Stokes equation simplifies into Stokes equation:

$$\nabla p = \eta\nabla^2\mathbf{v}$$

for a spherical object moving at a constant velocity v

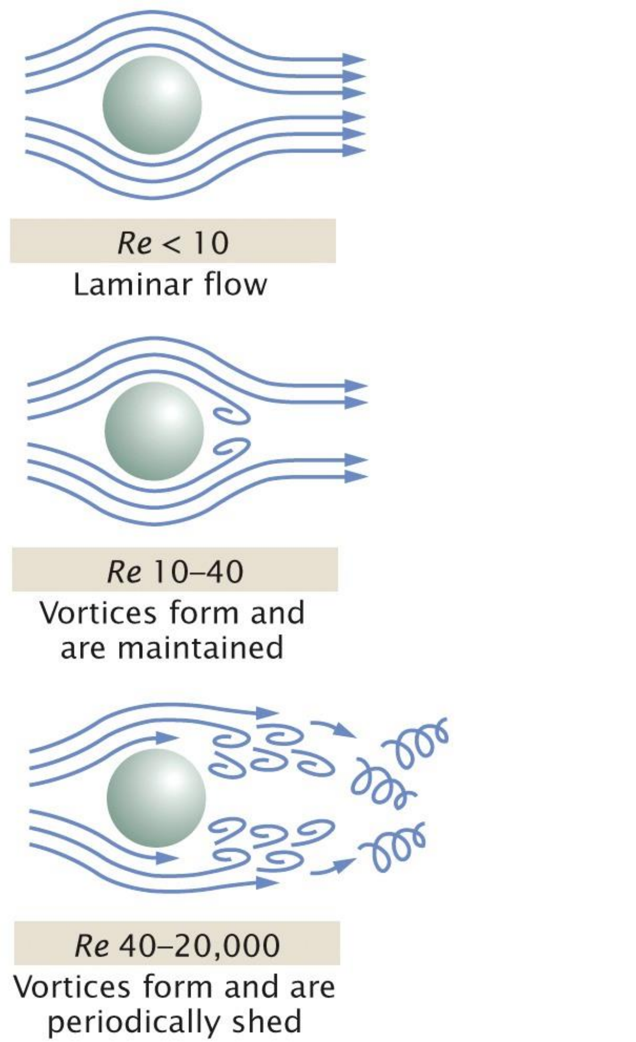


Figure 12.12 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

$$F_S = 6\pi\eta R v$$

Stokes drag force

for water at room temperature $\eta/\rho = 10^{-6}\ m^2/s$

for 10 cm fish swimming at 1 m/s $Re = 10^5$

for 1 mm bacterium swimming at 10 μm/s $Re = 10^{-5}$

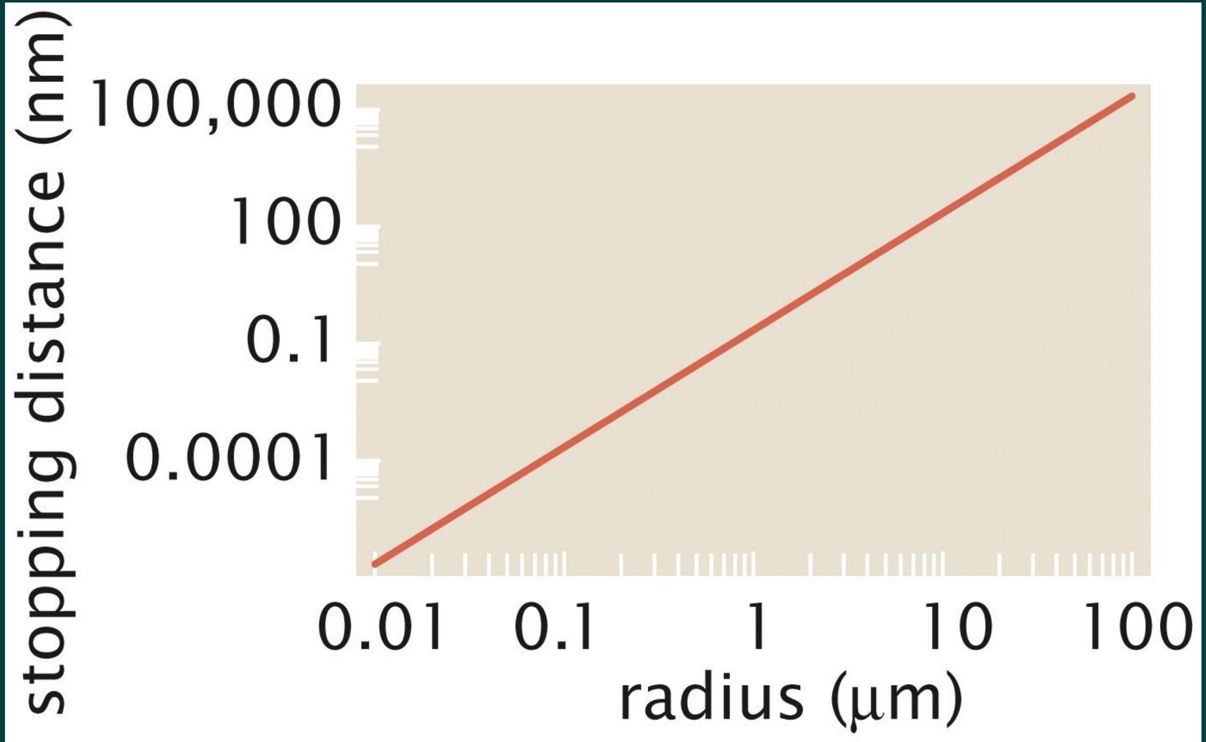
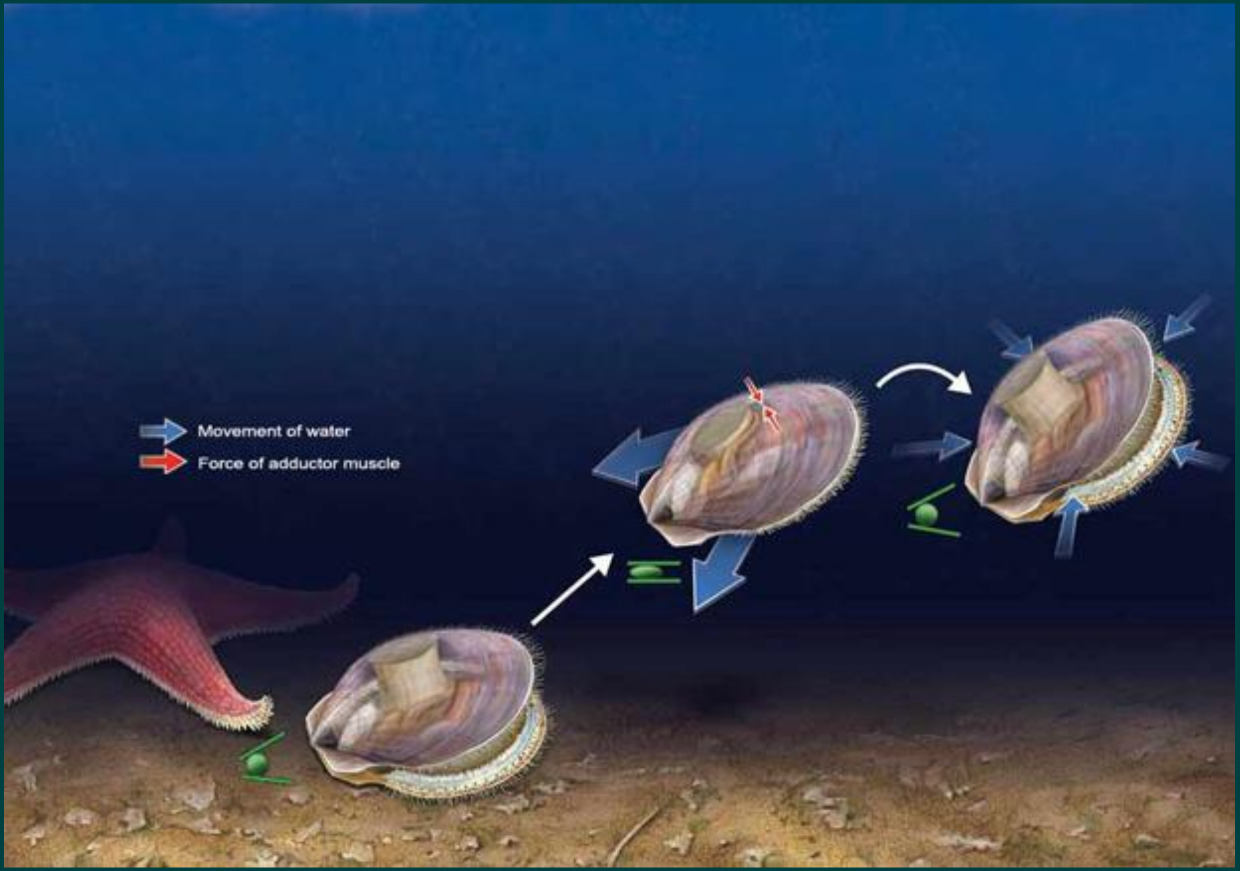


Figure 12.15 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

for initial velocity equal one diameter/s

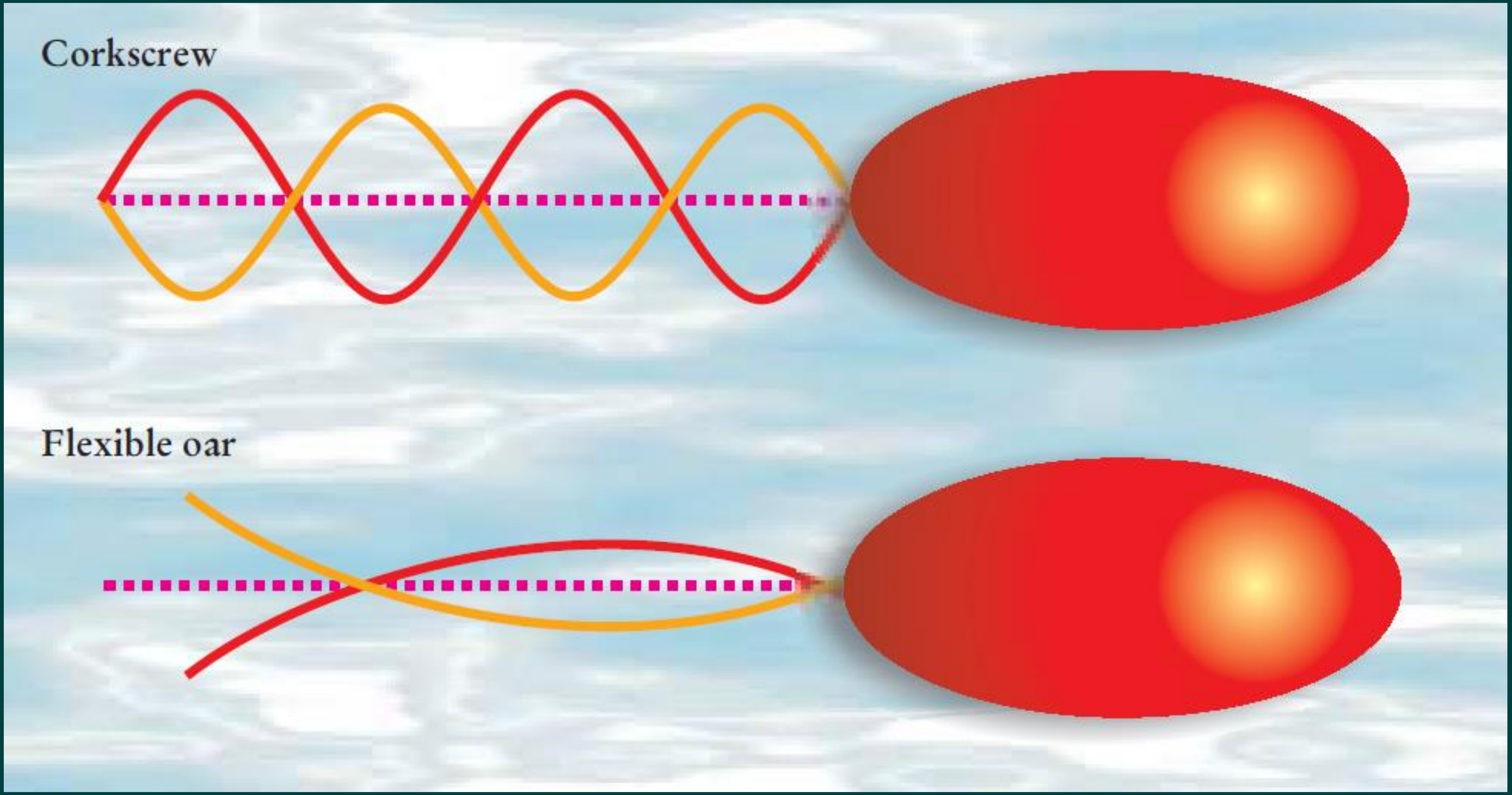
Reciprocal deformation, like in scallops, cannot produce swimming at low Reynolds numbers



http://www.naturalhistorymag.com/biomechanics/201394/cold-squirts

How to swim at low Reynolds numbers?

(cannot move like a scallop, cycle must be asymmetric)



from Astumian and Hanggi, 2002

bacteria swim by rotating helical flagellum

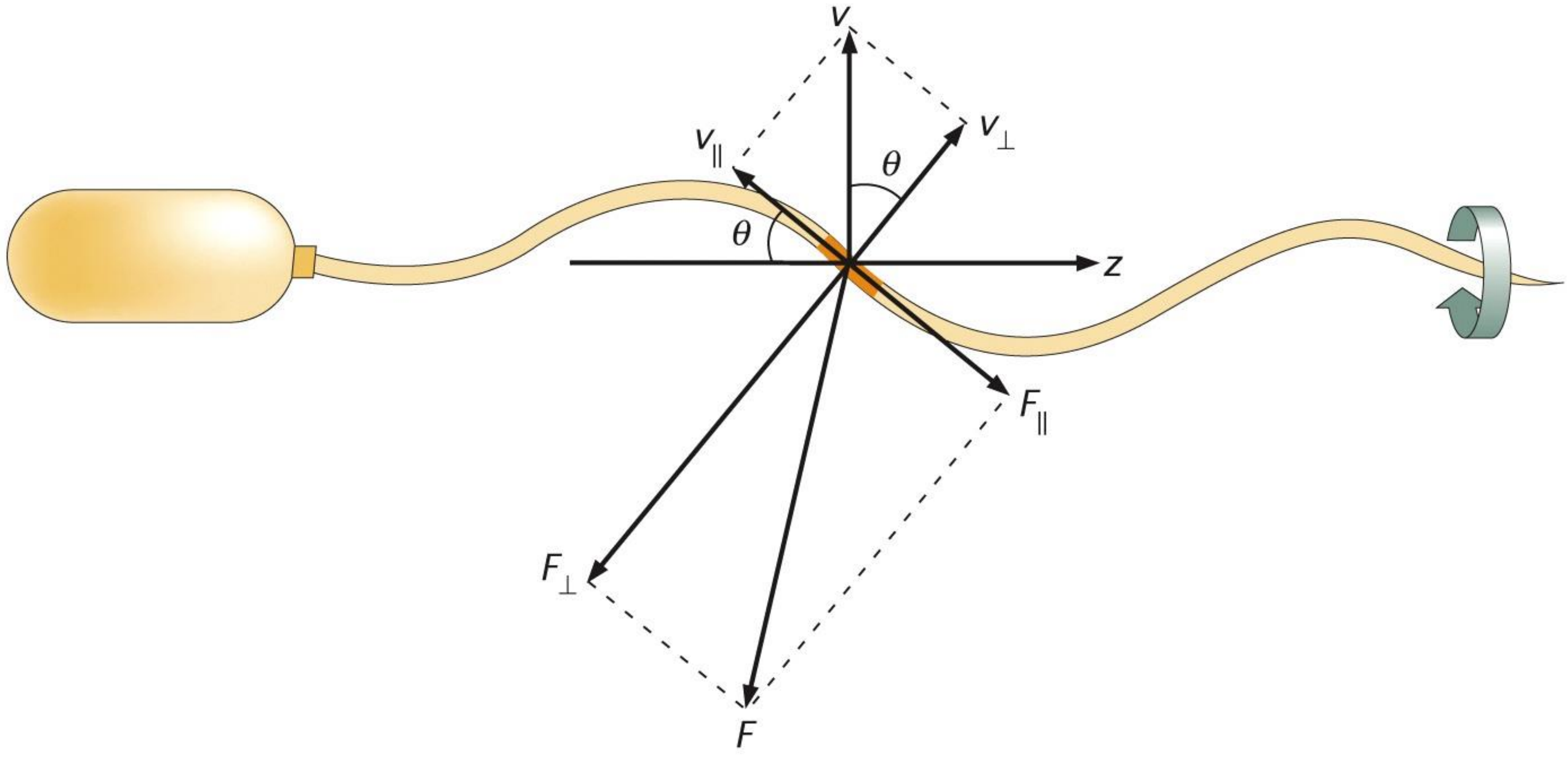
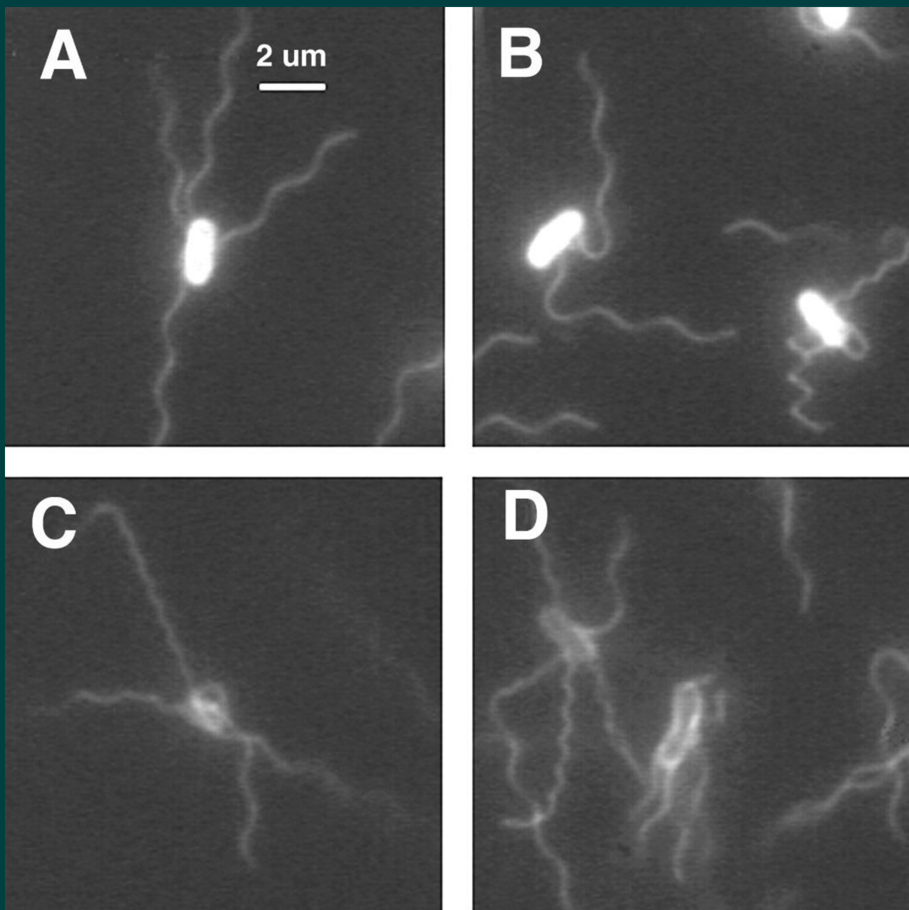
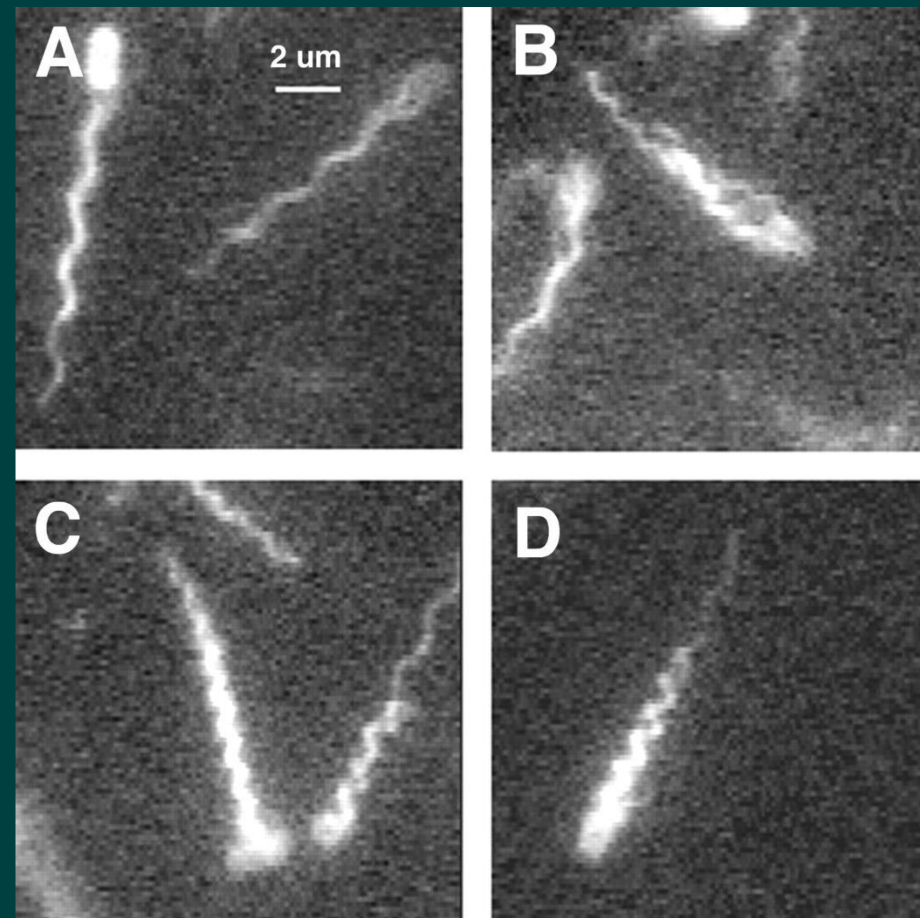


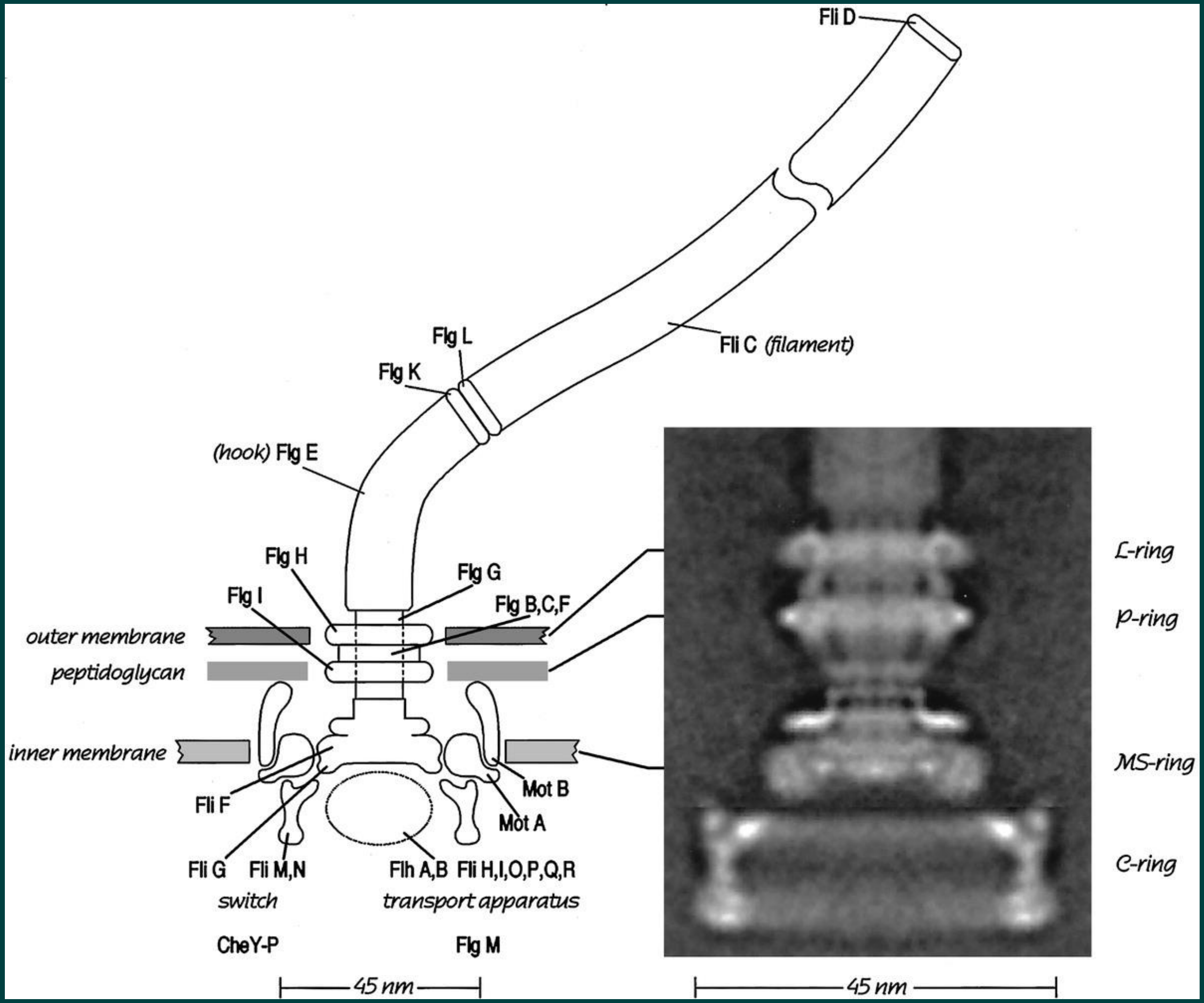
Figure 12.16 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

bacterial flagella and their bundles

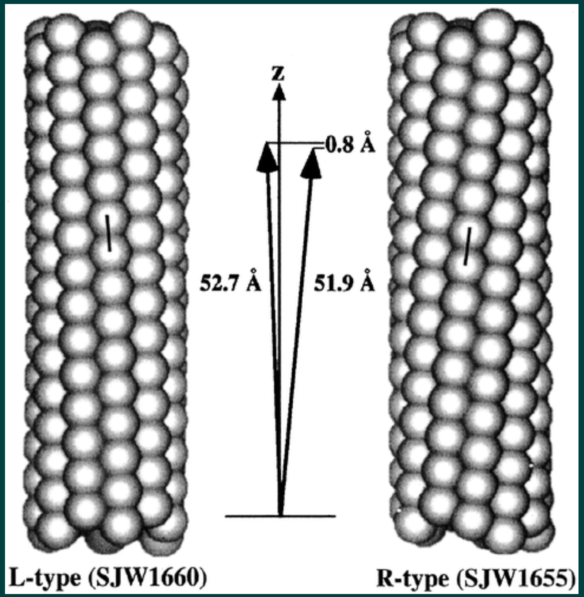




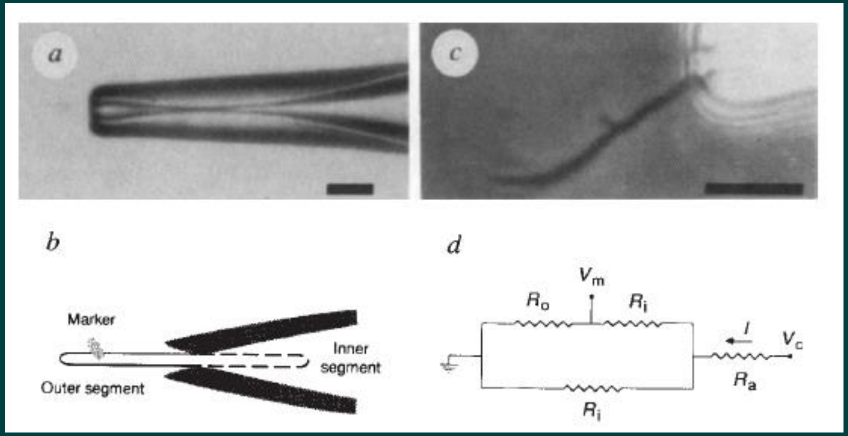
flagellar motor

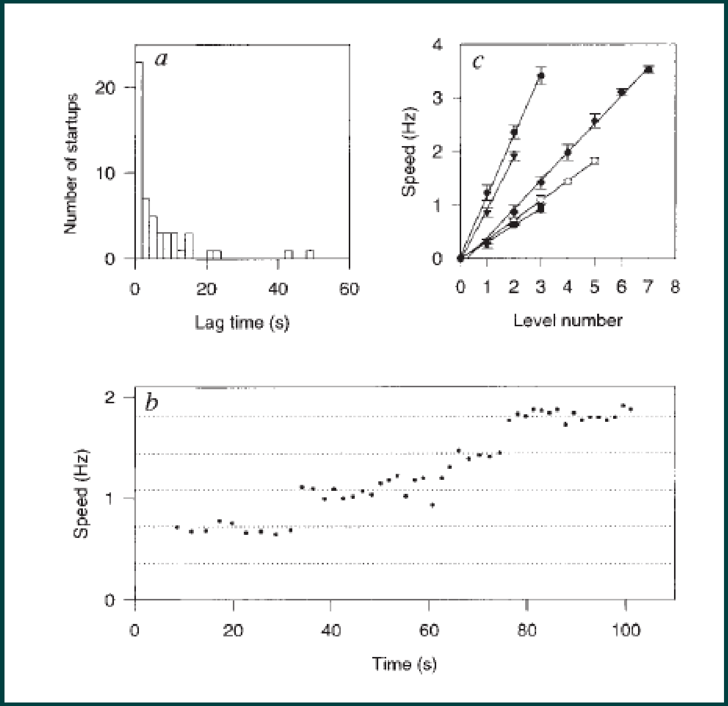


flagellin lattice



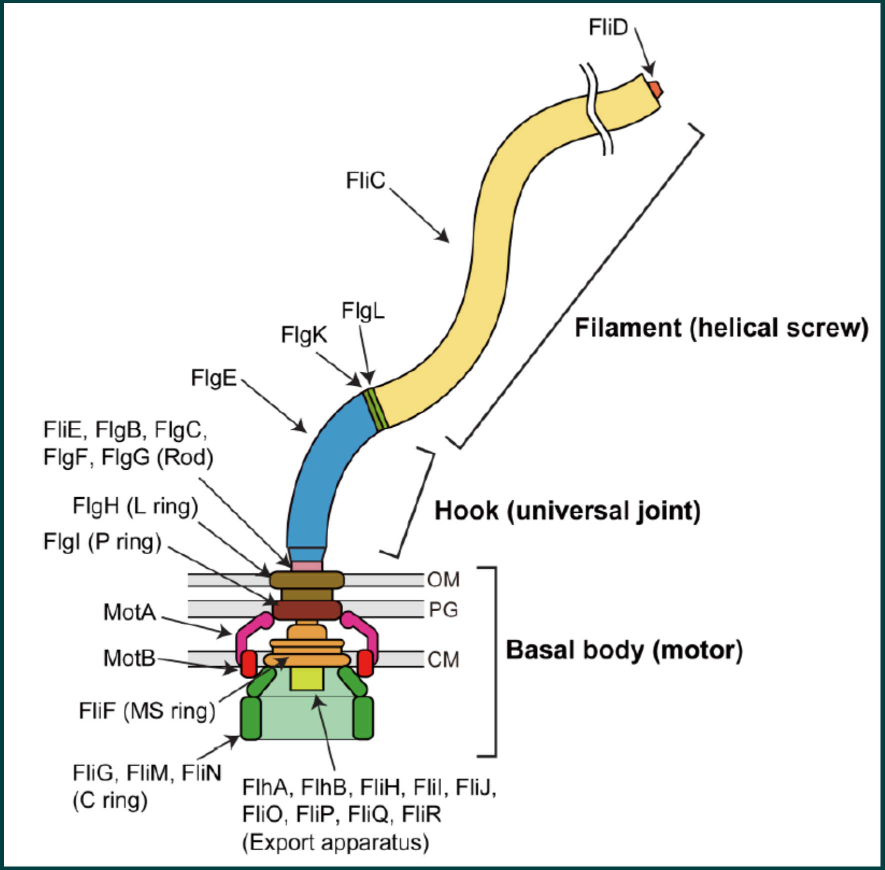
Electric motor could be powered by external voltage

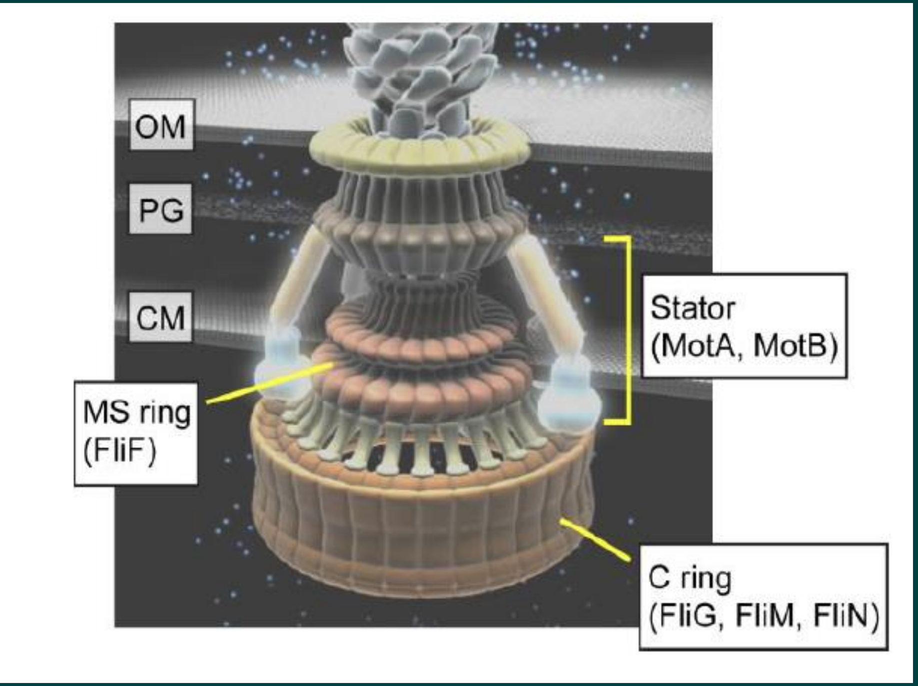




Fung and Berg, Nature, 1995

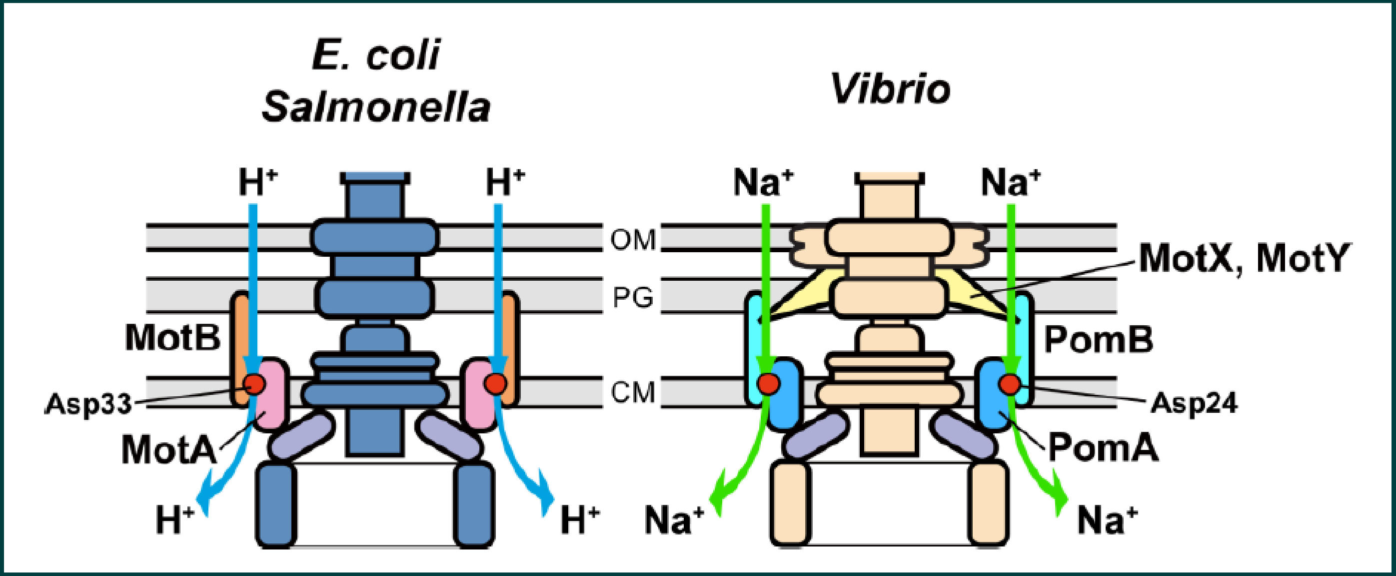
Rotor and stator of bacterial flagellum

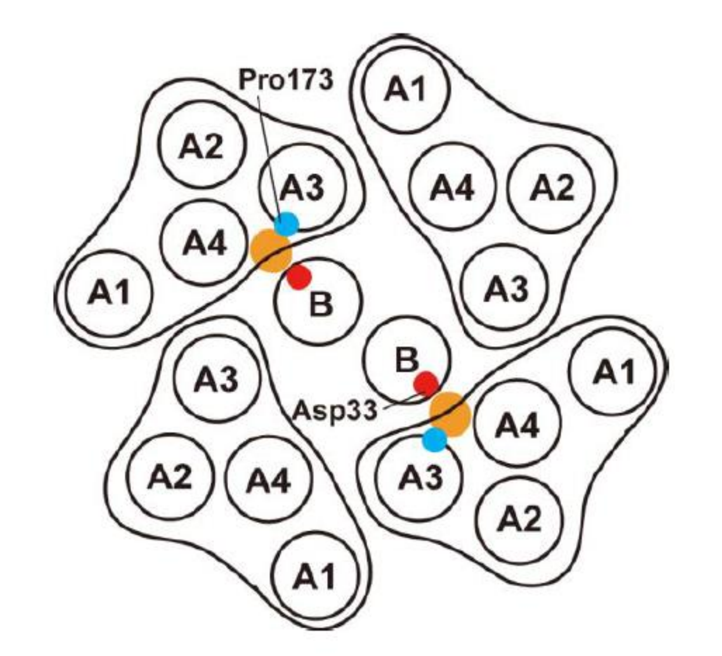


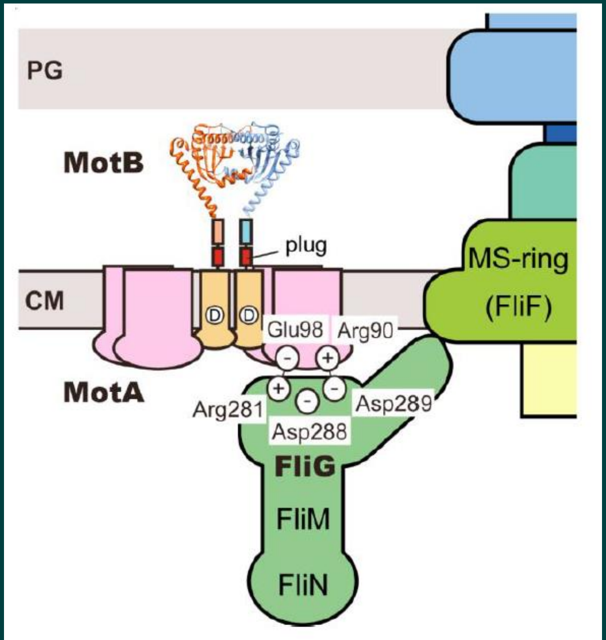


Morimoto and Minamino, Biomolecules, 2014

Stator is a ion channel

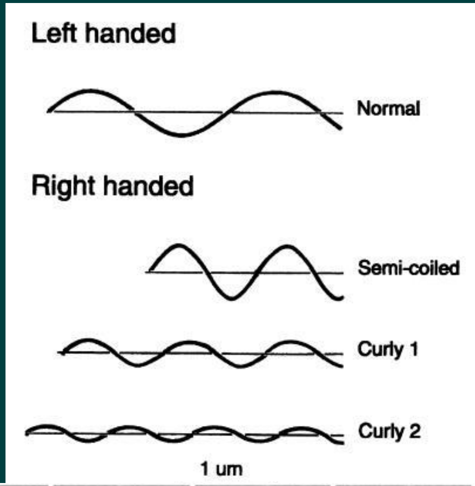


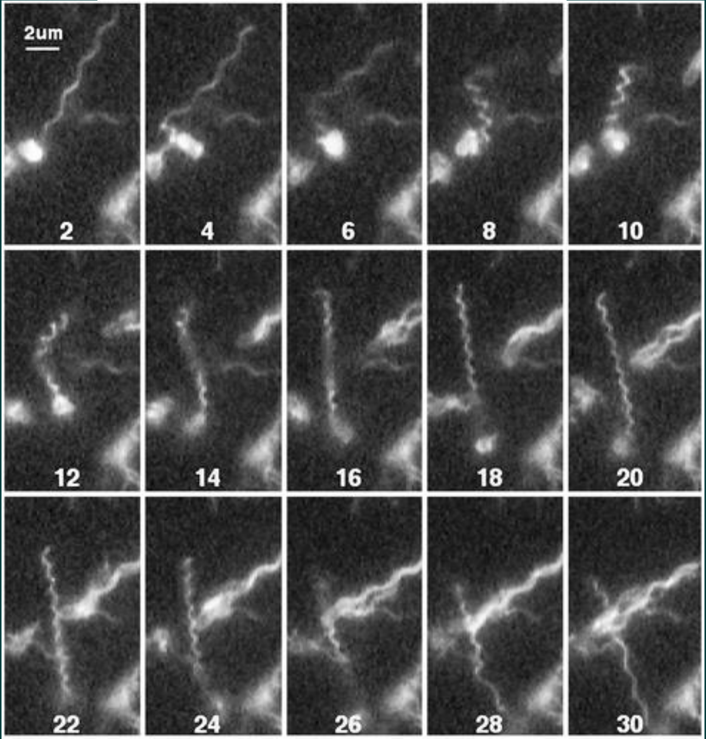




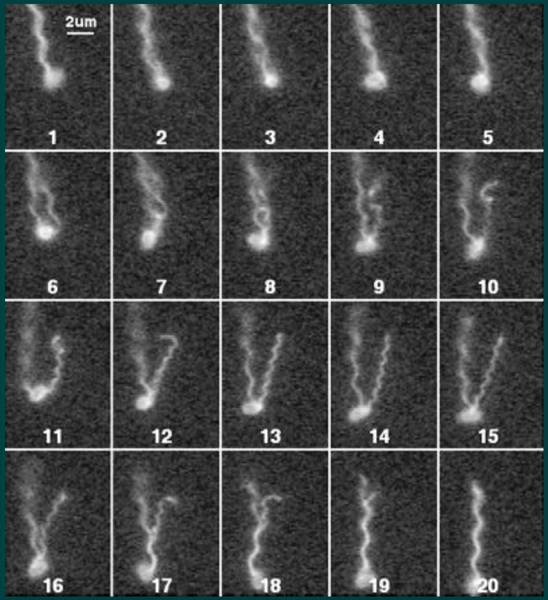
Morimoto and Minamino, Biomolecules, 2014

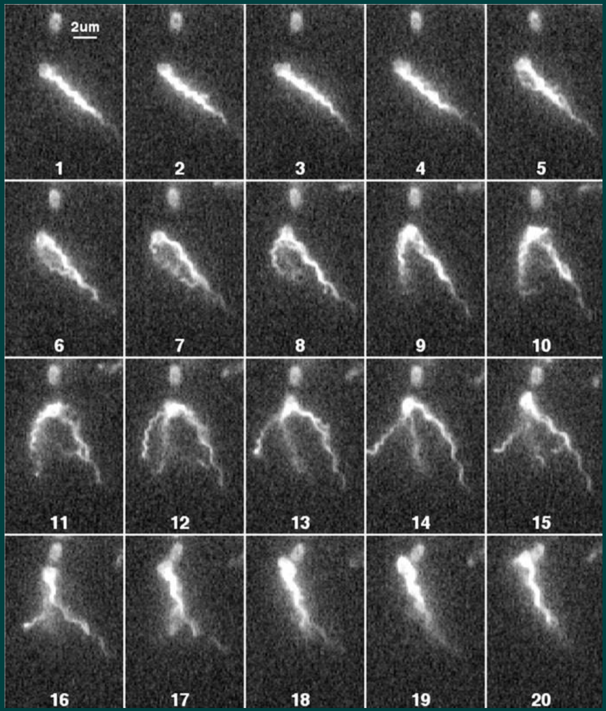
change of twist in a single flagellum



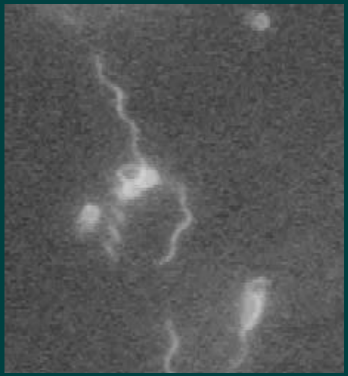


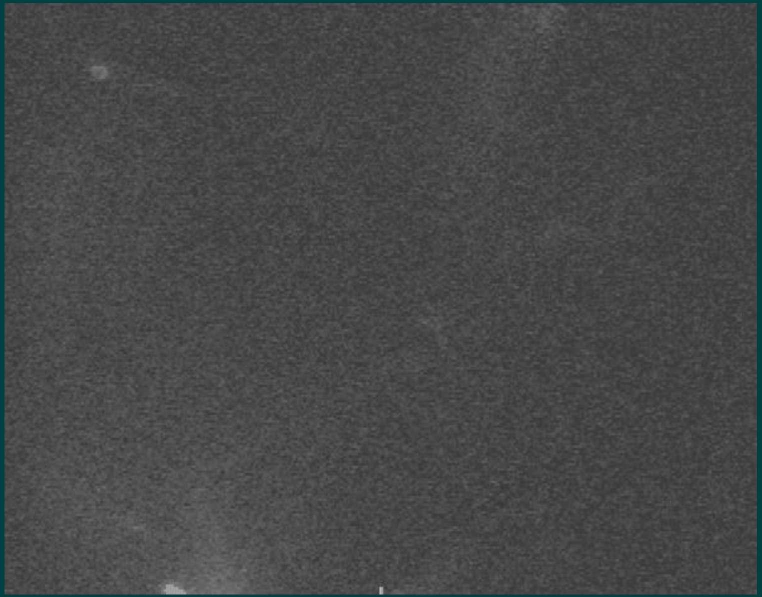
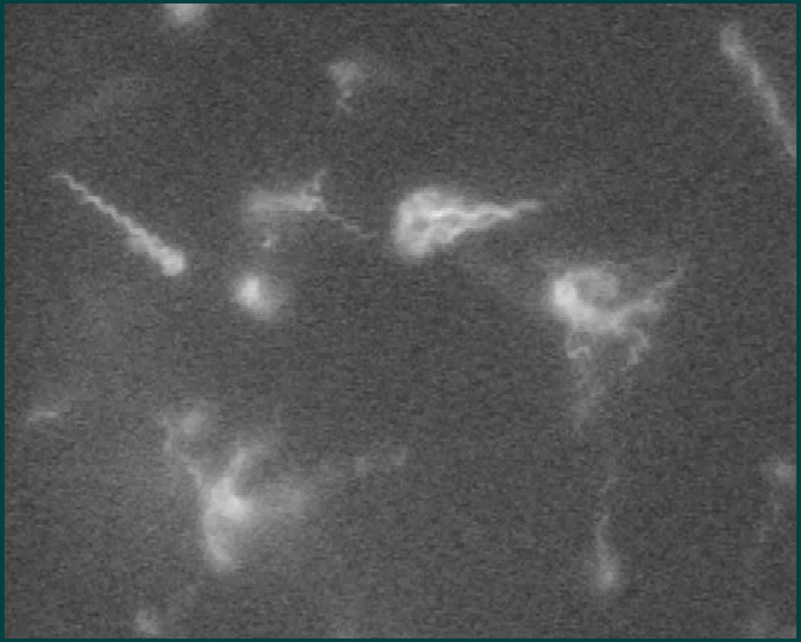
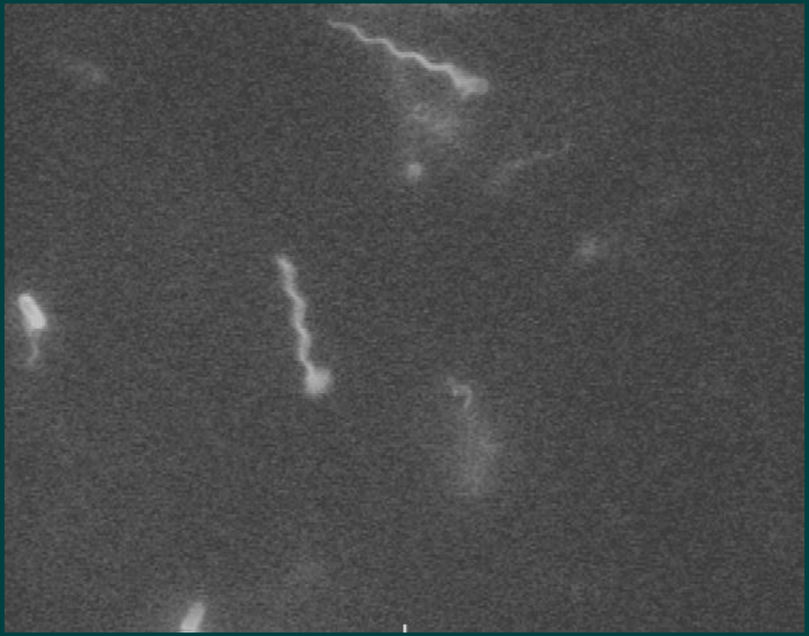
swim - tumble -swim





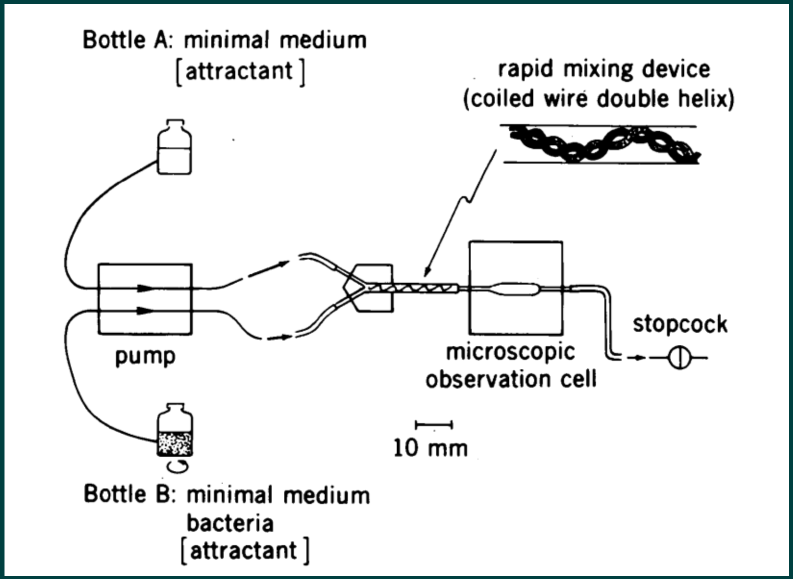
Twist and un-twist visualized

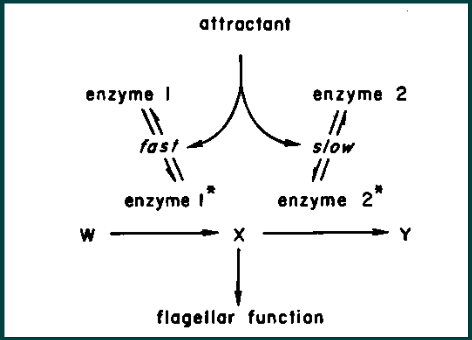


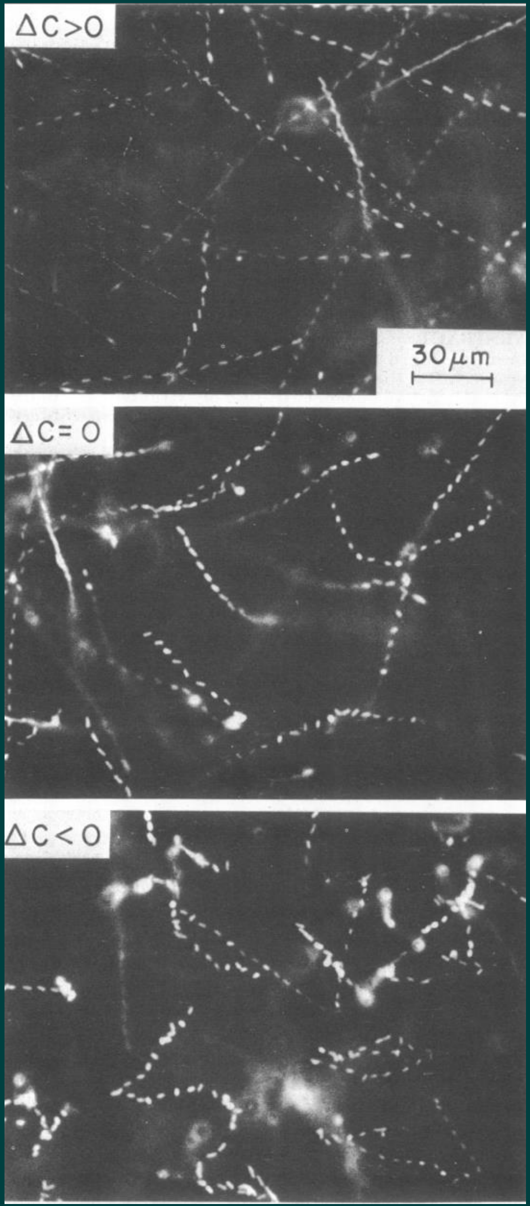




Howard Berg lab at Rowland Inst., Harvard Univ.
http://www.rowland.org/labs/bacteria/index_movies.html

Experimental proof of temporal gradient sensing in bacteria

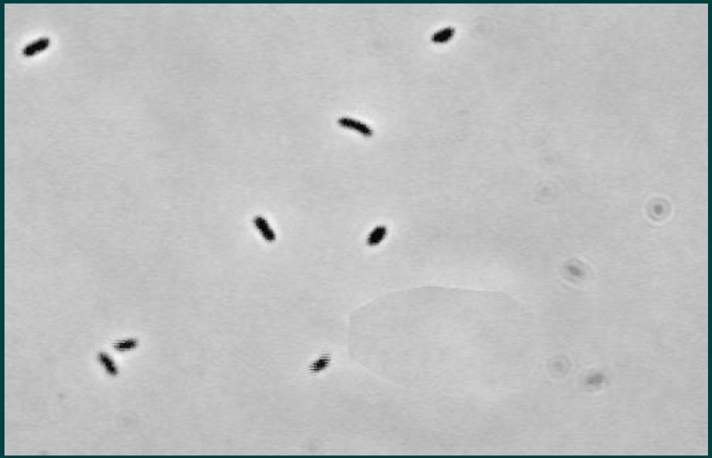


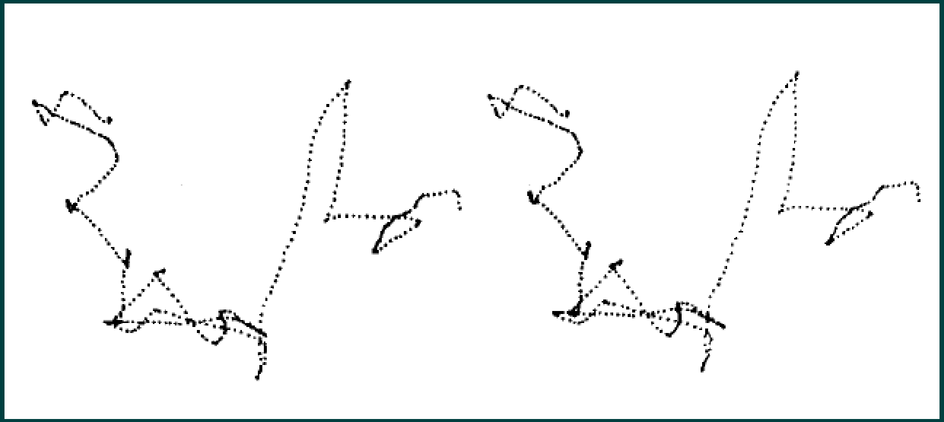




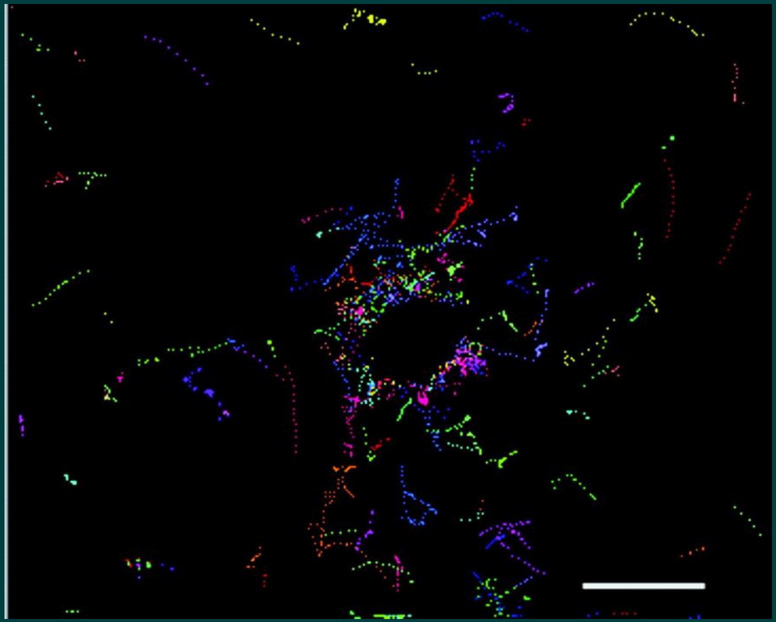
Macnab and Koshland, PNAS, 1972

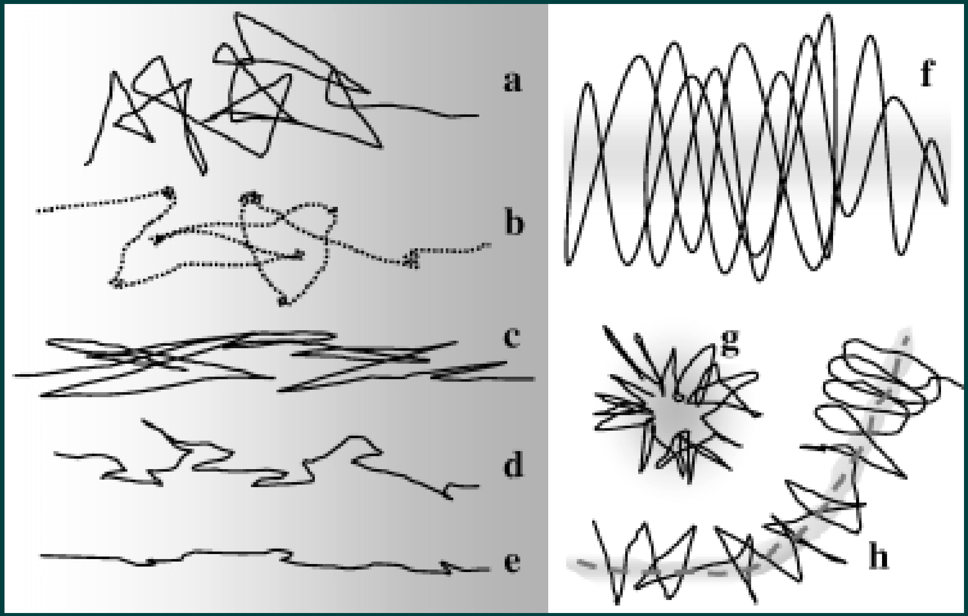
Bacterial trajectories





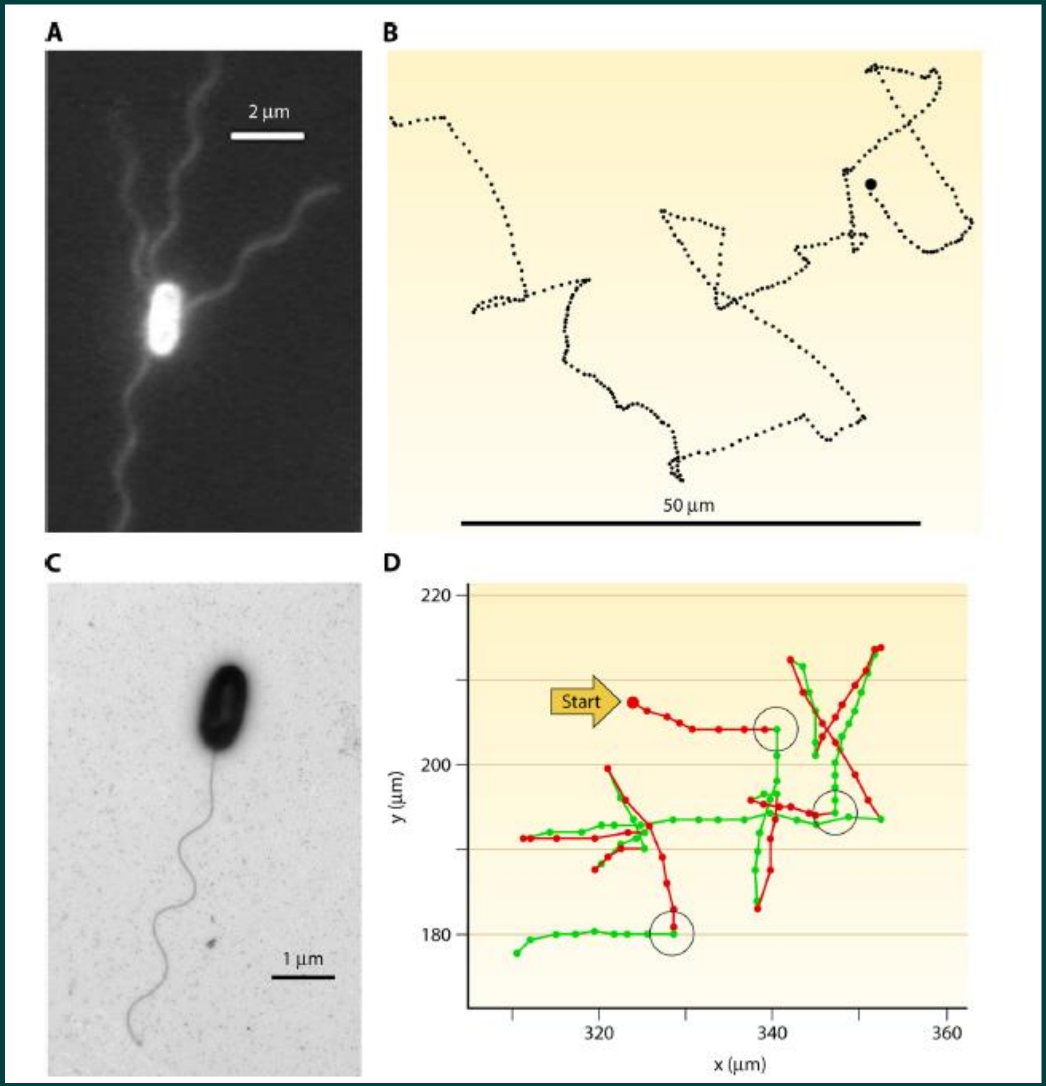
Berg, Physics Today, 2000

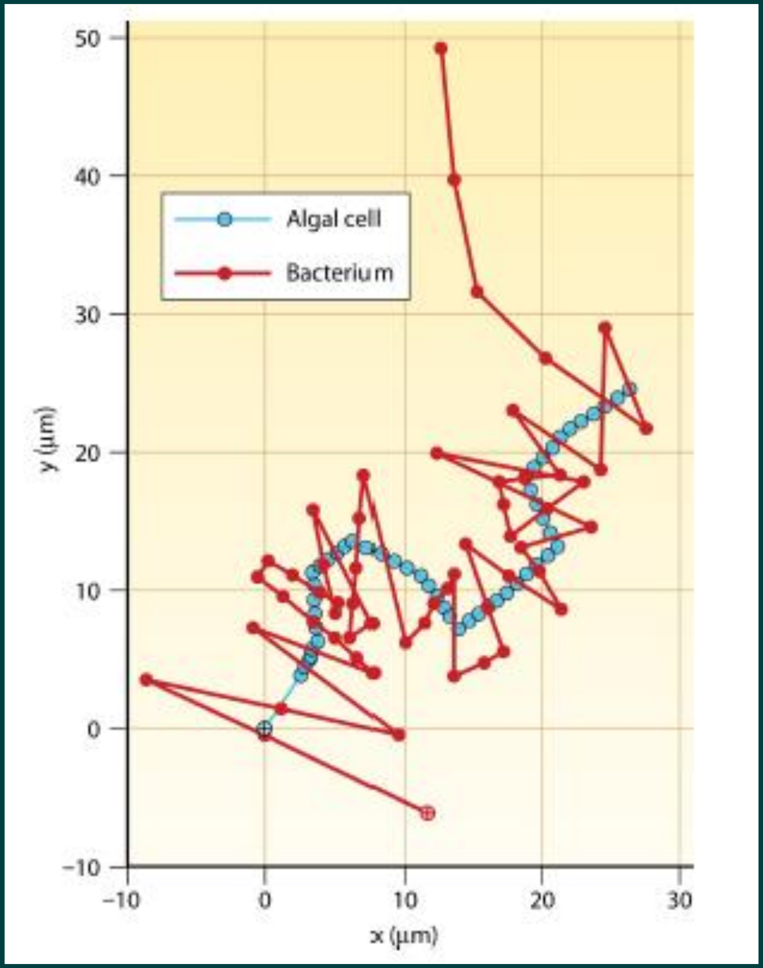




Fenchel, Science, 2002

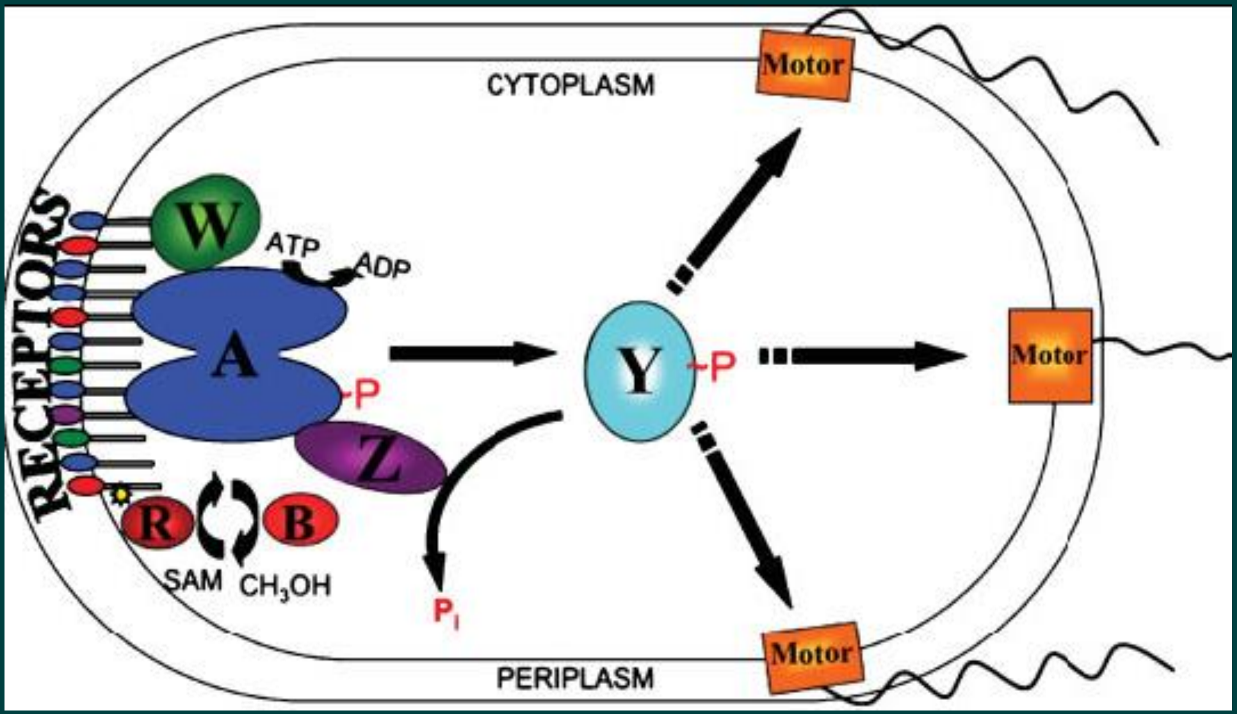
Single-flagellated bacteria reverse their motion and can pursue algae cells





Stocker and Seymour, 2015

How the external signals lead to motor reversal:
Chemotactic signaling chain in E. coli



Baker et al., Bioessays, 2006

adaptation:
paper for presentation Barkai and Leibner, Nature, 1997

optional problems

1. From PBOC, chapter 12

12.5 Life at low *Re*

(a) *E.coli* swims at about 20 μm/s by rotating a bundle of helical flagella. If the motors were to turn 10 times faster than normal, what would their swimming speed be? If their fluid environment was made 10 times more viscous, but the motors were to turn at the same rate, what would the swimming speed be? How does the power output of the motor change in these two hypothetical situations?

(b) Two micron-sized spheres, one made of silver and the other gold, sediment (that is, fall under gravity) in a viscous fluid. The silver sphere has twice the radius of the gold one. Which sediments faster?

(c) The left ventricle of the human heart expels about 50 cc of blood per heartbeat. Assuming a pulse rate of 1 heartbeat per second and a diameter of the aorta of about 2 cm, what is the mean velocity of blood in the aorta? What is the Reynolds number?

(d) What is the Reynolds number of a swimming bacterium? A tadpole? A blue whale?

(Adapted from a problem courtesy of H. C. Berg and D. Nelson.)

next time: energy for electric motor
active collective behavior
start eukaryotic motility and cytoskeleton