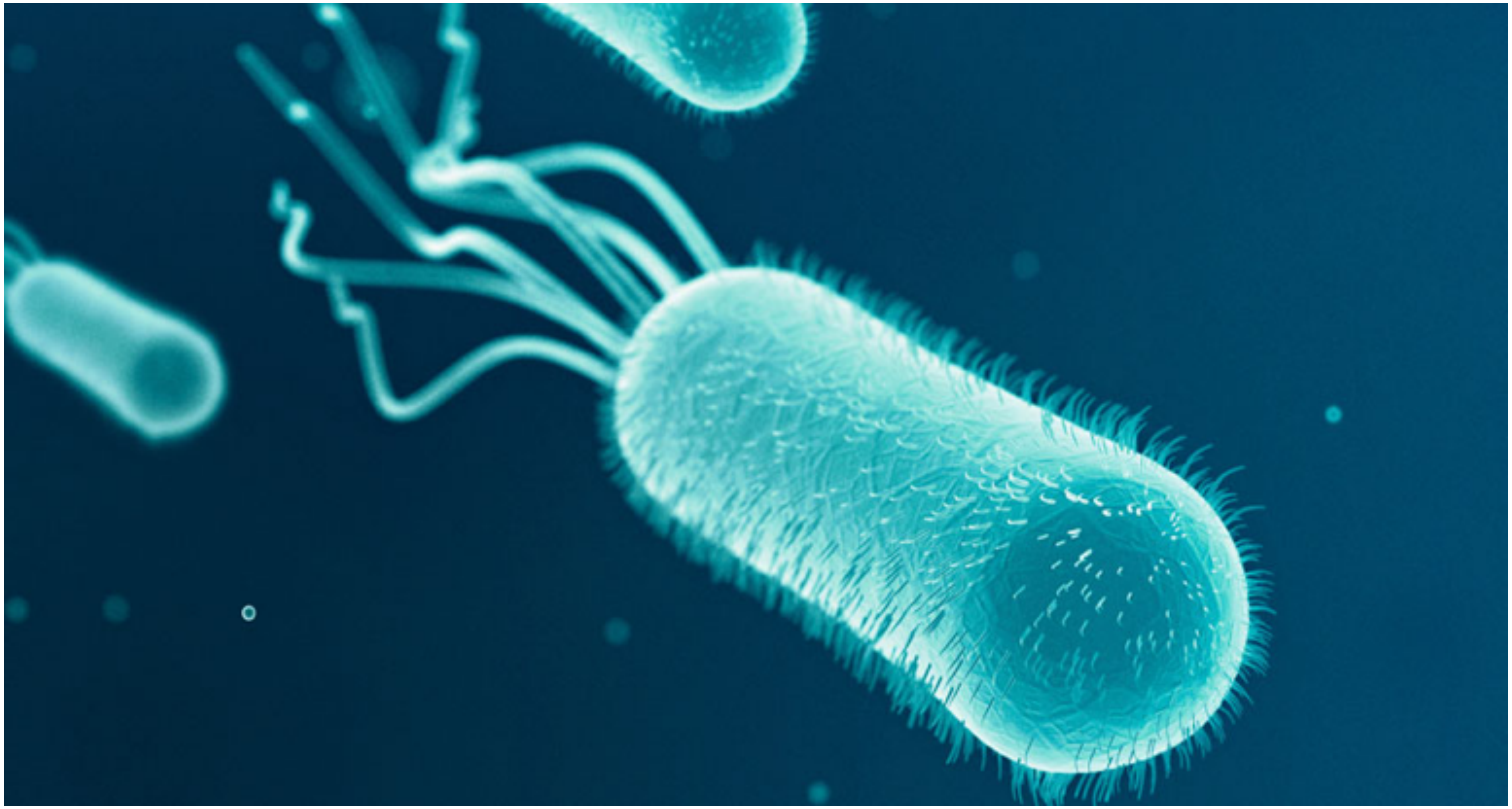
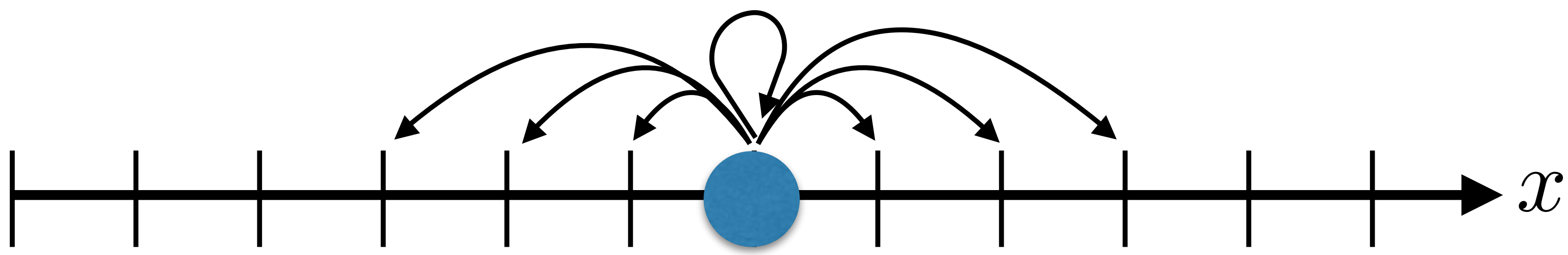
MAE 545: Lecture 2 (9/22)

E. coli chemotaxis



Recap from Lecture 1

Fokker-Planck equation



In general the probability distribution Π of jump lengths *s* can depend on the particle position *x*. $\Pi(s|x)$

Assume that jumps occur in regular small time intervals Δt

$$\frac{\partial p(x,t)}{\partial t} = -\frac{\partial}{\partial x}\Big[v(x)p(x,t)\Big] + \frac{\partial^2}{\partial x^2}\Big[D(x)p(x,t)\Big]$$

drift velocity (external fluid flow, external potential)

$$v(x) = \sum_s \frac{s}{\Delta t}\Pi(s|x) = \frac{\langle s(x)\rangle}{\Delta t}$$

diffusion coefficient (e.g. position dependent temperature)

$$D(x) = \sum_s \frac{s^2}{2\Delta t}\Pi(s|x) = \frac{\langle s^2(x)\rangle}{2\Delta t}$$

Lévy flights

Probability of jump lengths in D dimensions

$$p(|\vec{s}|) = \begin{cases} C|\vec{s}|^{-\alpha}, & |\vec{s}| > s_0 \\ 0, & |\vec{s}| < s_0 \end{cases}$$

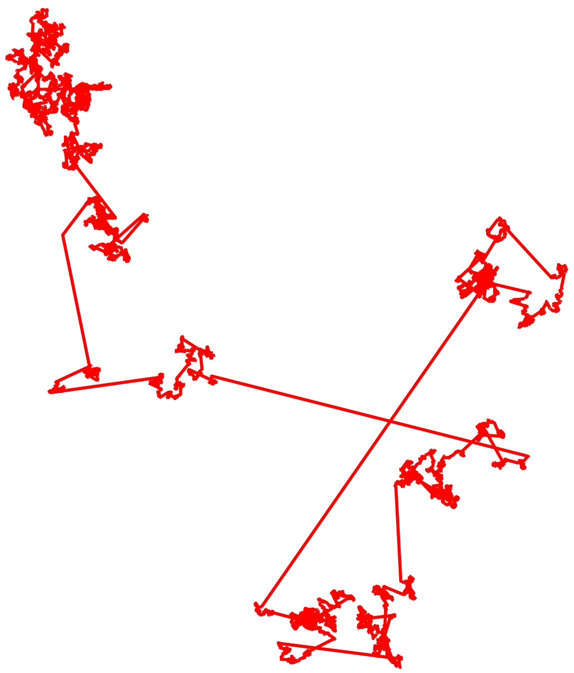
Normalization condition

$$\int d^D\vec{s}\; p(|\vec{s}|) = 1 \longrightarrow \alpha > D$$

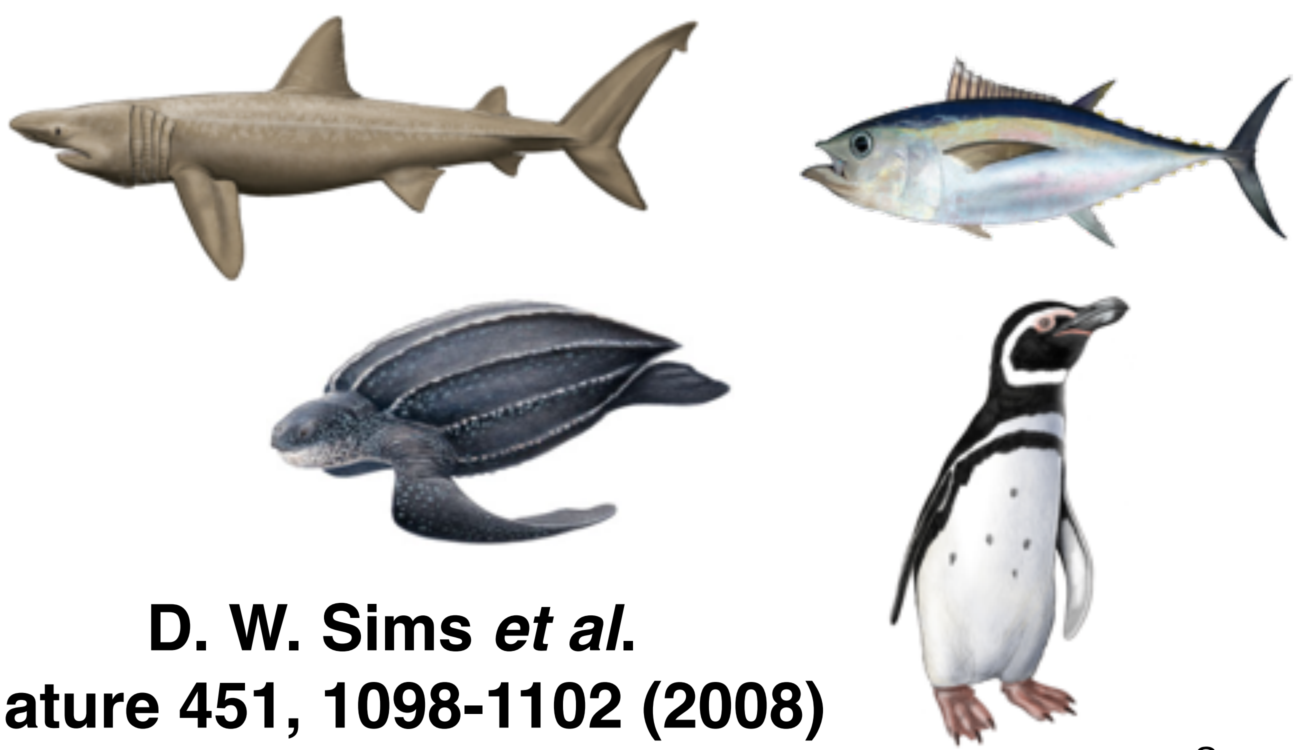
Moments of distribution

$$\langle \vec{s} \rangle = 0 \qquad \langle |\vec{s}|^2 \rangle = \begin{cases} A_D s_0^2, & \alpha > D+2 \\ \infty, & \alpha < D+2 \end{cases}$$

$\alpha = 3.5, D = 2$



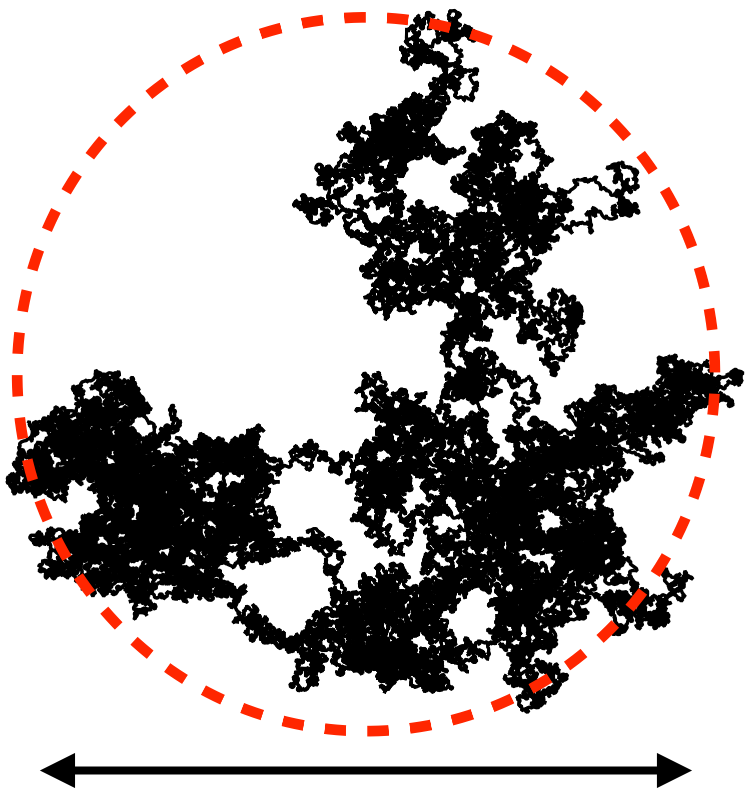
Lévy flights are better strategy than random walk for finding prey that is scarce



D. W. Sims *et al.*
Nature 451, 1098-1102 (2008)

2D random walk

Number of distinct sites visited by random walk



Total number of sites inside explored region after *N* steps

1D	$N_{\mathrm{tot}} \propto \sqrt{N}$
2D	$N_{\mathrm{tot}} \propto N$
3D	$N_{\mathrm{tot}} \propto N\sqrt{N}$

In 1D and 2D every site gets visited after a long time

In 3D not every site is visited even after a very long time!

Shizuo Kakutani: "A drunk man will find his way home, but a drunk bird may get lost forever."

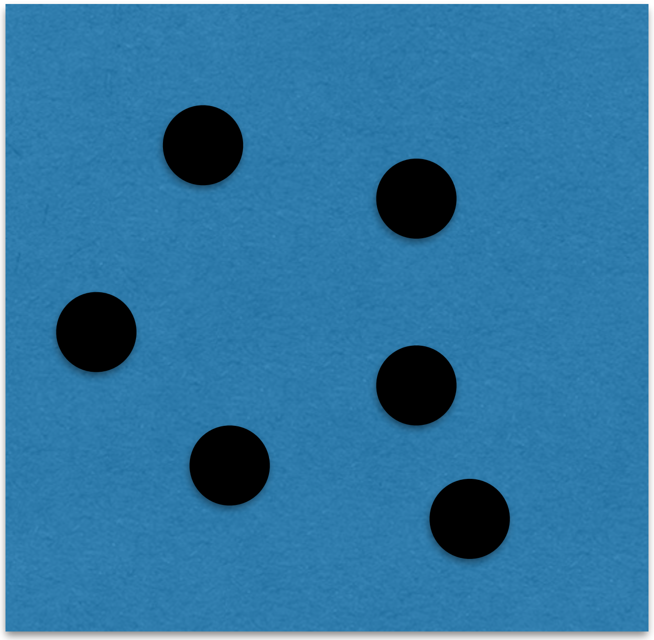
Number of distinct visited sites after *N* steps

1D	$N_{\mathrm{vis}} \approx \sqrt{8N/\pi}$
2D	$N_{\mathrm{vis}} \approx \pi N/\ln(8N)$
3D	$N_{\mathrm{vis}} \approx 0.66N$

Fick's laws

Adolf Fick 1855

N noninteracting Brownian particles



Local concentration $c(x,t) = Np(x,t)$

Fick's laws below follow from Fokker-Plank equations

First Fick's law

Flux of particles $J = vc - D\frac{\partial c}{\partial x}$

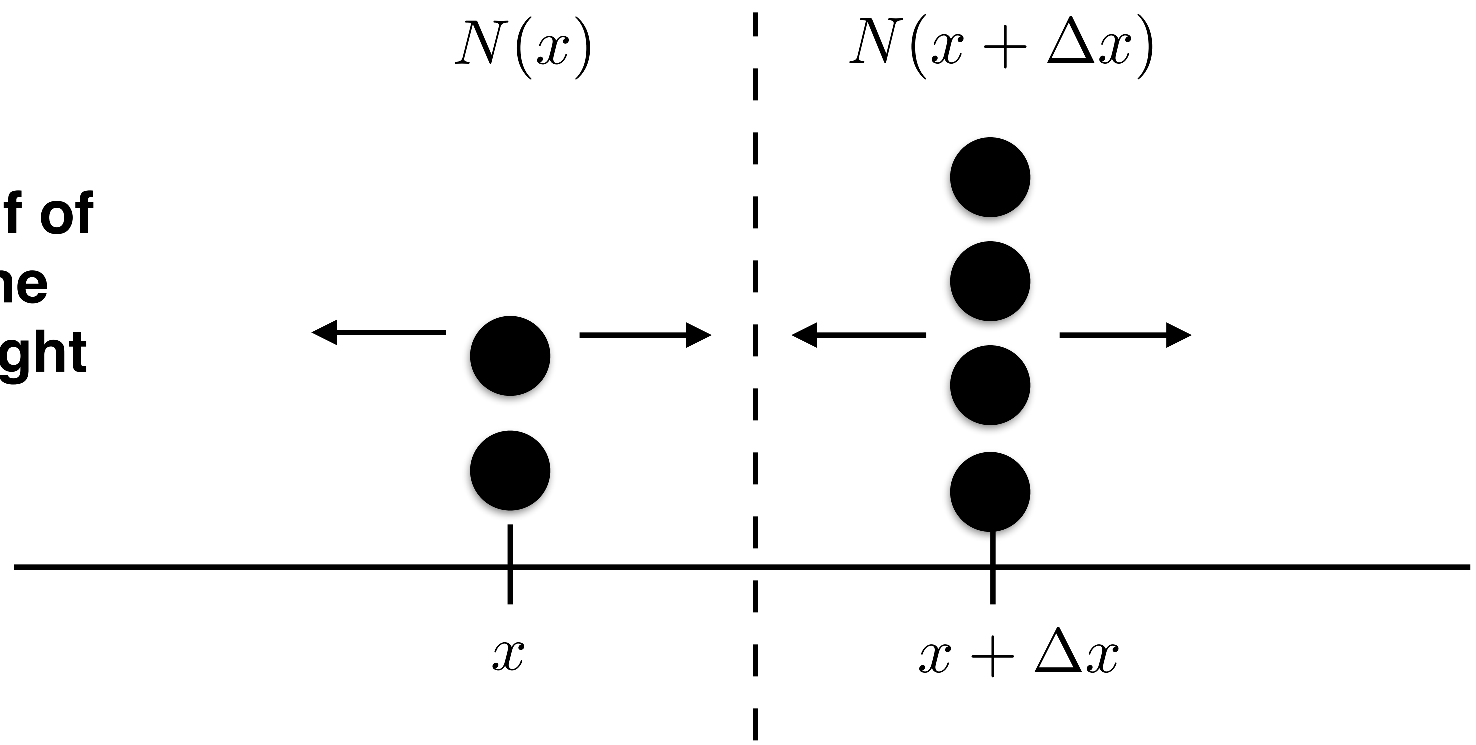
Second Fick's law

Diffusion of particles $\frac{\partial c}{\partial t} = -\frac{\partial J}{\partial x} = -\frac{\partial}{\partial x}\left[vc\right] + \frac{\partial}{\partial x}\left[D\frac{\partial c}{\partial x}\right]$

First Fick's laws

Estimate flow of particles due to concentration gradient

At next time step half of particles jump to the left and half to the right



Net flux

$$J = -\frac{1}{2}\frac{[N(x+\Delta x) - N(x)]}{\Delta t} \times \frac{\Delta x^2}{\Delta x^2} = -\frac{\Delta x^2}{2\Delta t} \times \frac{1}{\Delta x}\left[\frac{N(x+\Delta x)}{\Delta x} - \frac{N(x)}{\Delta x}\right]$$

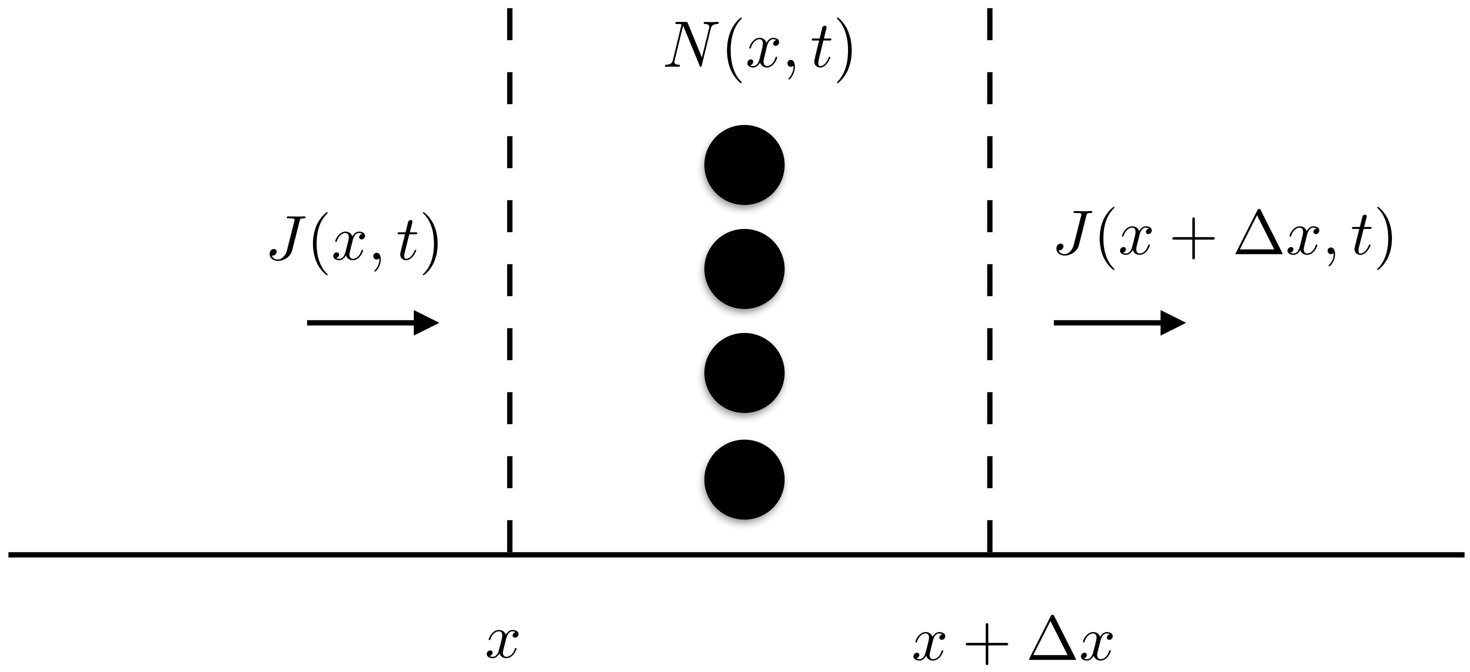
$$J = -D \times \frac{1}{\Delta x}\left[c(x+\Delta x) - c(x)\right] = -D\frac{\partial c}{\partial x}$$

In the presence of flow we need to add transport of molecules

$$J = vc - D\frac{\partial c}{\partial x}$$

Second Fick's laws

Estimate change in concentration due to gradient in flow



$$\frac{1}{\Delta t \Delta x}\left[N(x,t+\Delta t) - N(x,t)\right] = -\frac{1}{\Delta t \Delta x} \times \left[J(x+\Delta x,t) - J(x,t)\right] \times \Delta t$$

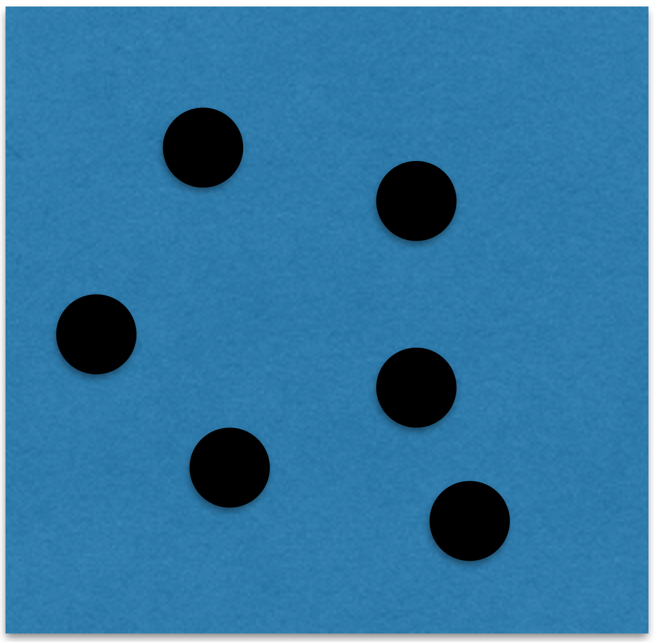
$$\frac{1}{\Delta t}\left[c(x,t+\Delta t) - c(x,t)\right] = -\frac{1}{\Delta x} \times \left[J(x+\Delta x,t) - J(x,t)\right]$$

$$\frac{\partial c}{\partial t} = -\frac{\partial J}{\partial x}$$

Fick's laws

Adolf Fick 1855

N noninteracting Brownian particles



Local concentration $c(x,t) = Np(x,t)$

Fick's laws below follow from Fokker-Plank equations

First Fick's law

Flux of particles $J = vc - D\dfrac{\partial c}{\partial x}$

Second Fick's law

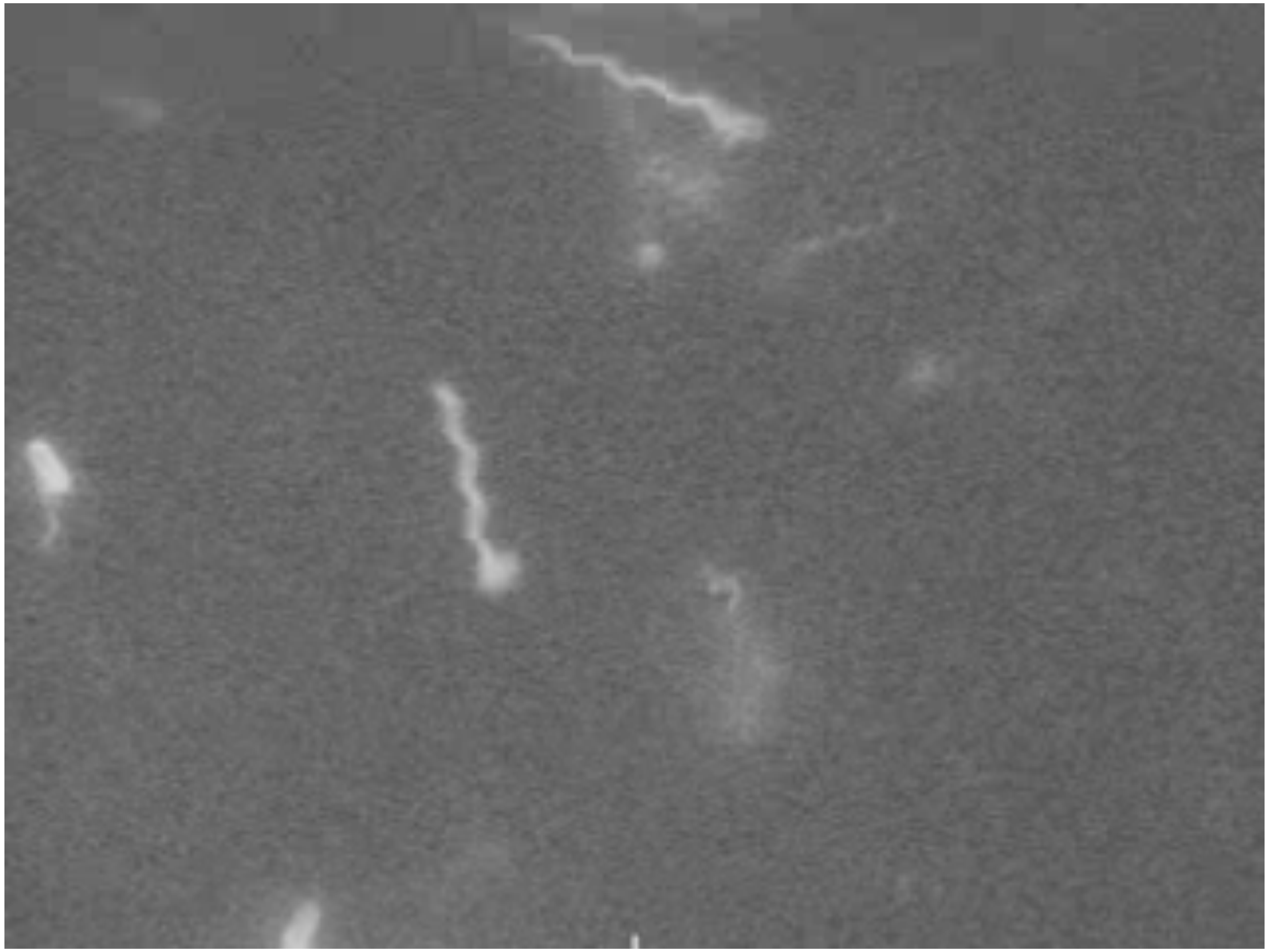
Diffusion of particles $\dfrac{\partial c}{\partial t} = -\dfrac{\partial J}{\partial x} = -\dfrac{\partial}{\partial x}\left[vc\right] + \dfrac{\partial}{\partial x}\left[D\dfrac{\partial c}{\partial x}\right]$

Generalization to higher dimensions

$$\vec{J} = \vec{v}c - \vec{\nabla}(Dc)$$

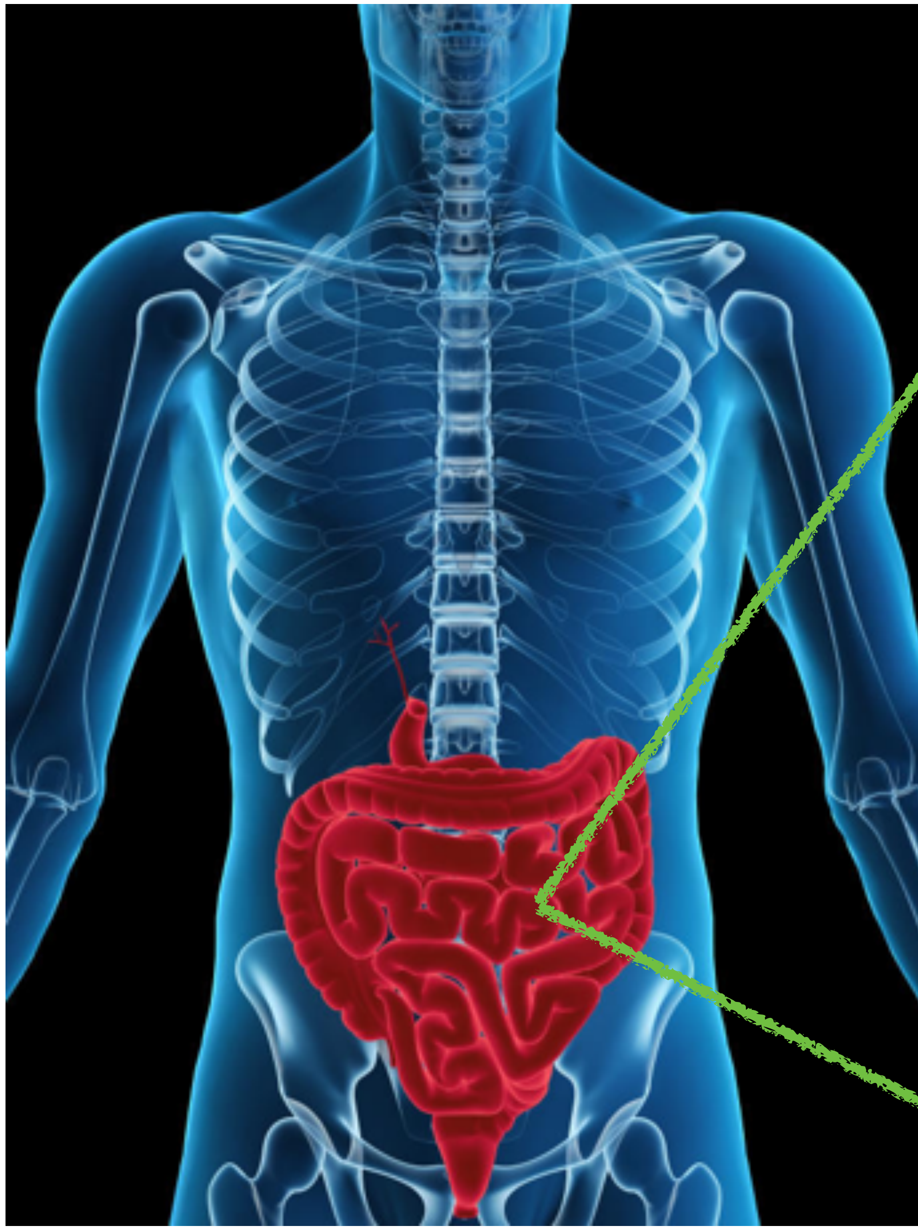
$$\frac{\partial c}{\partial t} = -\vec{\nabla}\cdot(\vec{v}c) + \vec{\nabla}^2(Dc)$$

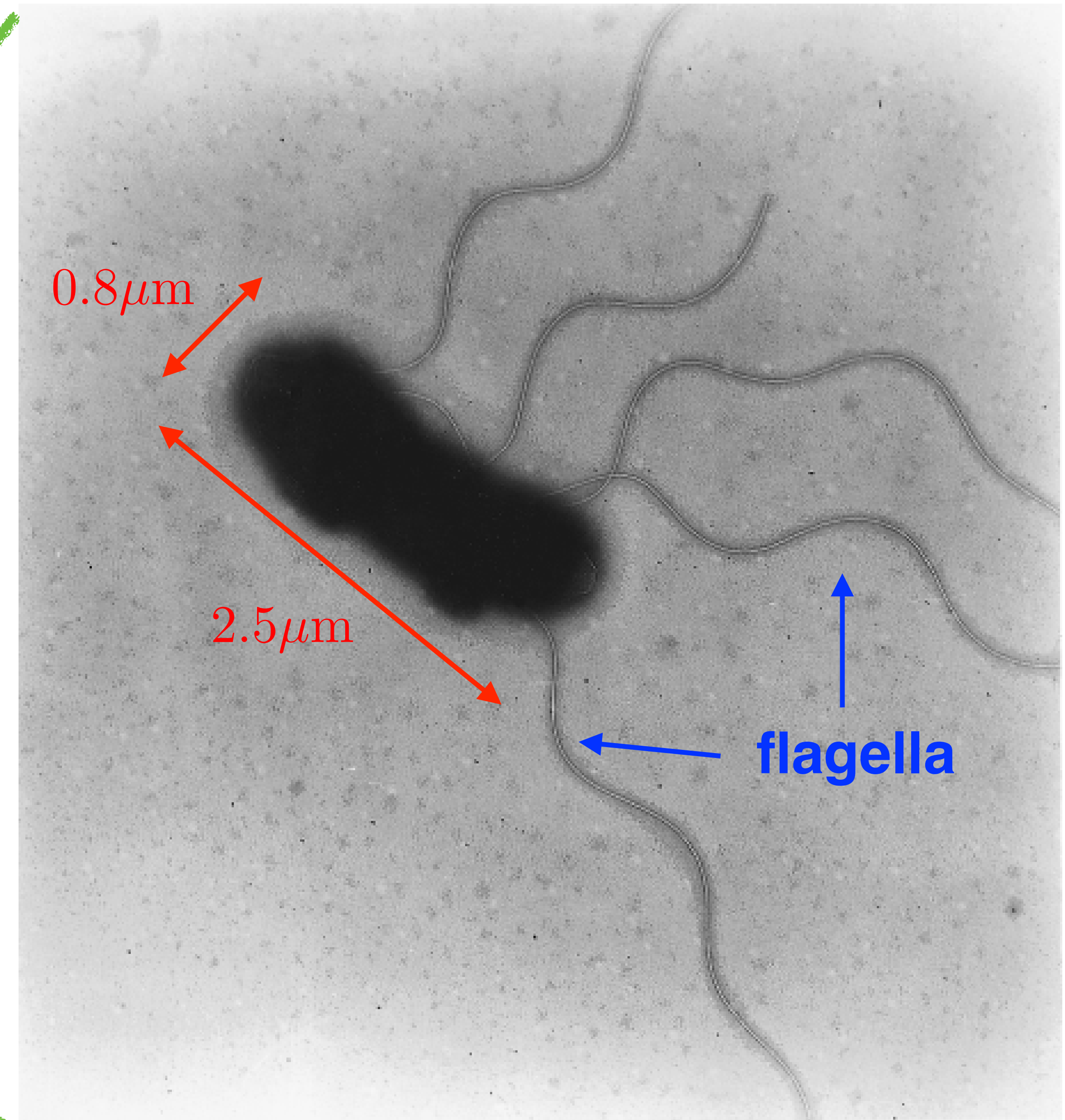
E. coli chemotaxis



L. Turner, W.S. Ryu, H.C. Berg, J. Bacteriol. 182, 2793-2801 (2000)

Escherichia coli





E. coli is a part of gut flora that helps us digest food.

Concentration of E. coli $\sim 10^9 \mathrm{cm}^{-3}$

Total concentration of bacteria $\sim 10^{11} \mathrm{cm}^{-3}$

In normal conditions E. coli divide and produce 2 daughter cells every ~20min.

In one day one E. coli could produce ~7x10^{10} new cells!

Flagella filaments and rotary motors

Flagellum filament

left handed helix

helix diameter

$d \approx 0.4\mu\text{m}$

filament diameter

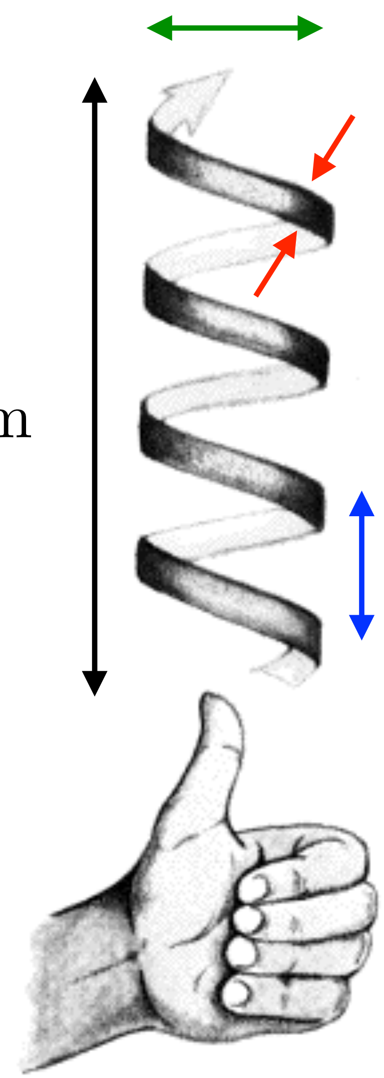
$\approx 20\text{nm}$

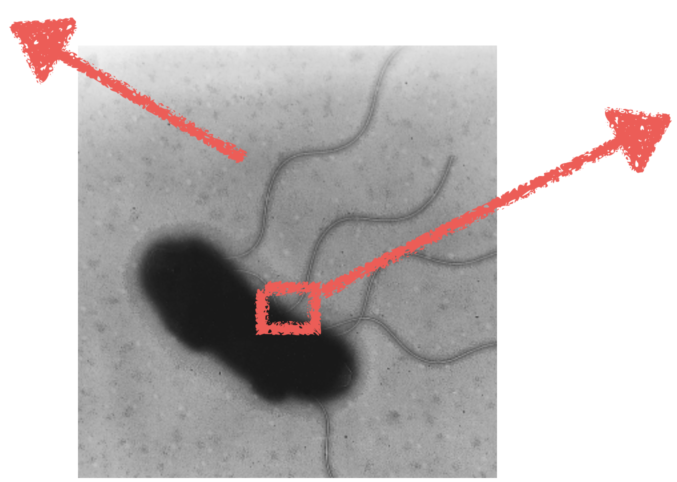
length

$L \lesssim 10\mu\text{m}$

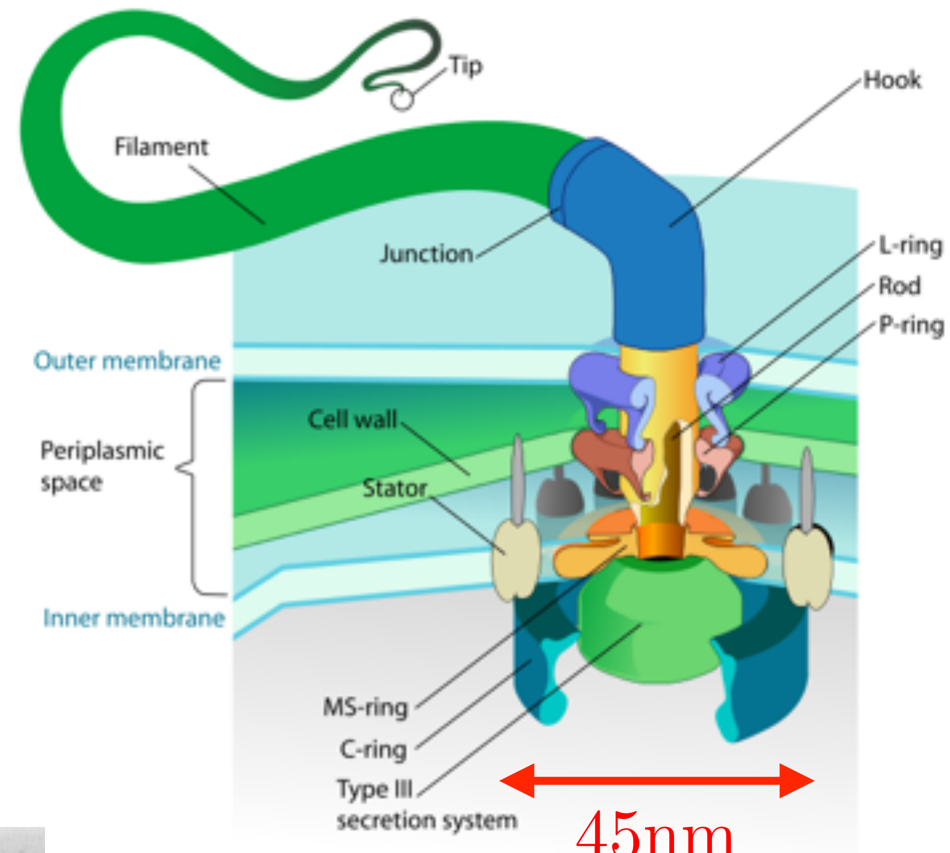
pitch

$p \approx 2.3\mu\text{m}$

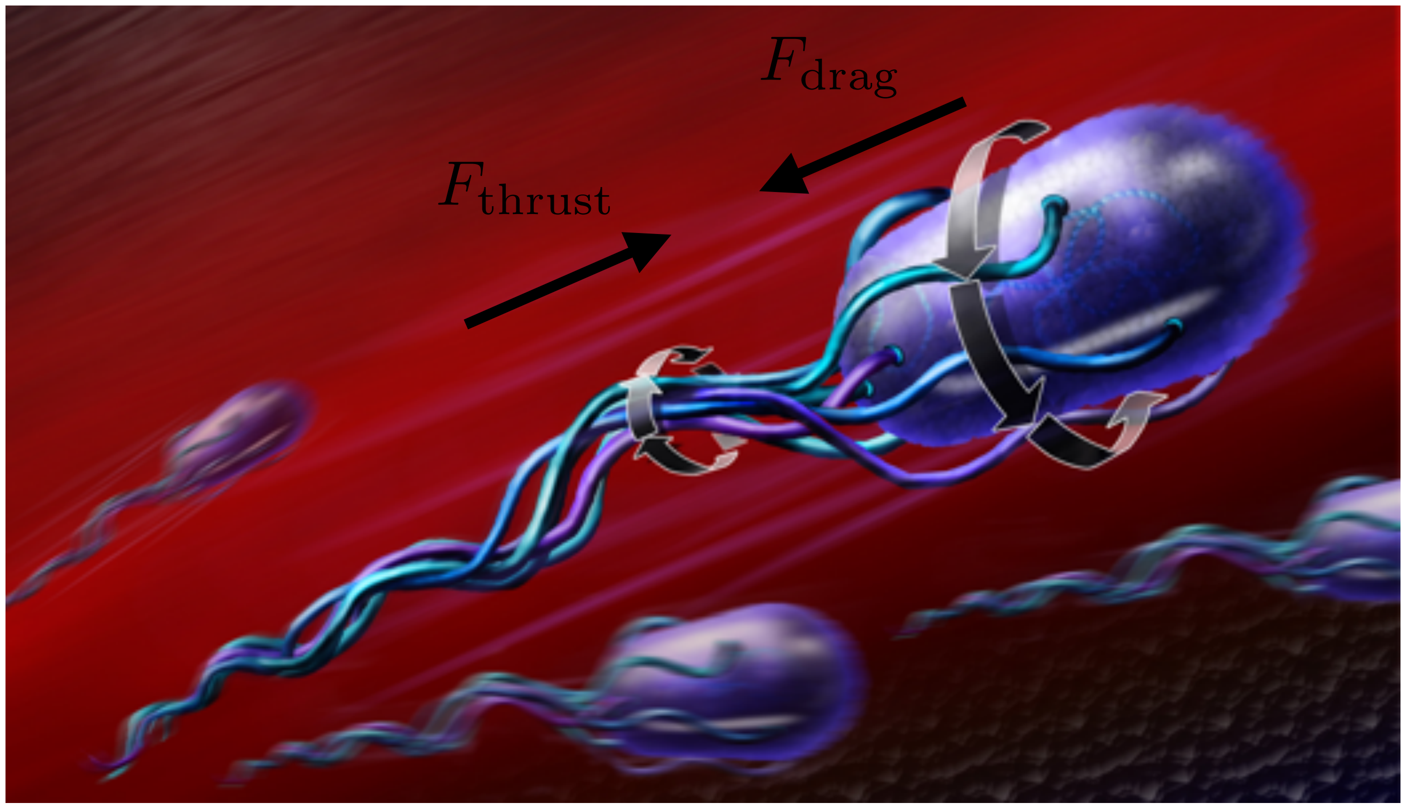




Rotary motor



Swimming of E. coli



swimming speed $v_s \sim 20\mu\text{m/s}$

body spinning frequency $f_b \sim 10\text{Hz}$

spinning frequency of flagellar bundle $f_r \sim 100\text{Hz}$

Thrust force generated by spinning flagellar bundle

$$F_{\text{thrust}} = F_{\text{drag}} \approx 6\pi\eta R v_s$$

$$F_{\text{thrust}} \sim 0.4\text{pN} = 4 \times 10^{-13}\text{N}$$

Torque generated by spinning flagellar bundle

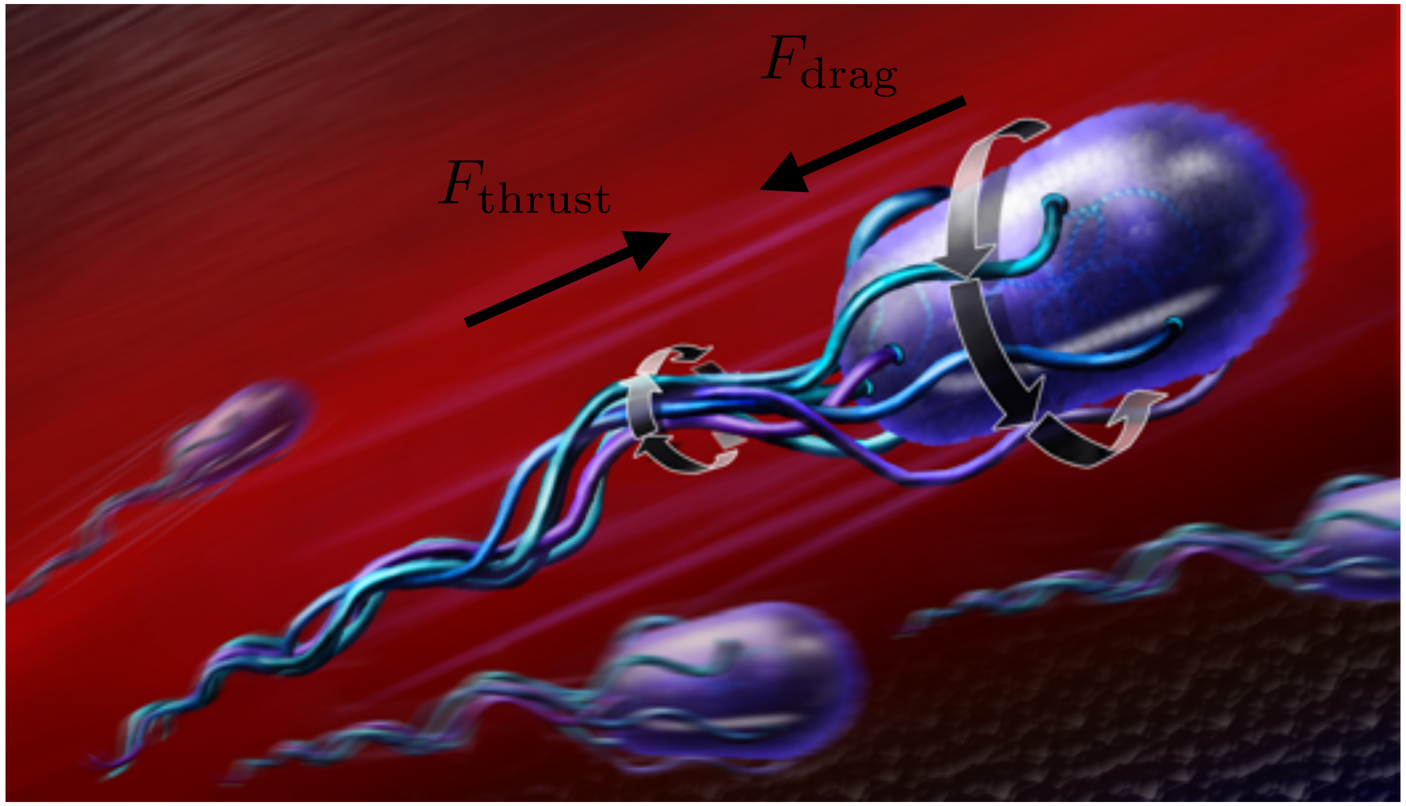
$$N = N_{\text{drag}} \approx 8\pi\eta R^3 \omega_b$$

$$N \sim 2\text{pN}\,\mu\text{m} = 2 \times 10^{-18}\text{Nm}$$

size of E. coli $R \approx 1\mu\text{m}$

water viscosity $\eta \approx 10^{-3}\text{kg}\,\text{m}^{-1}\text{s}^{-1}$

How quickly E. coli stops if motors shut off?



swimming speed $v_s \sim 20\mu\text{m/s}$

size of E. coli $R \approx 1\mu\text{m}$

water viscosity $\eta \approx 10^{-3}\text{kg}\,\text{m}^{-1}\text{s}^{-1}$

mass of E. coli $m \sim \frac{4\pi R^3 \rho}{3} \sim 4\text{pg}$

Newton's law

$$ma = -6\pi\eta R v$$

$$x = x_0 \left[1 - e^{-t/\tau}\right]$$

$$\tau \approx \frac{m}{6\pi\eta R} \approx \frac{2\rho R^2}{9\eta} \sim 0.2\mu\text{s}$$

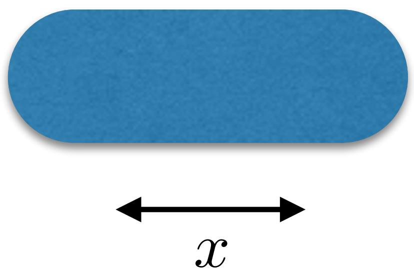
$$x_0 = v_s \tau \sim 0.1\text{Å}$$

E. coli stops almost instantly!

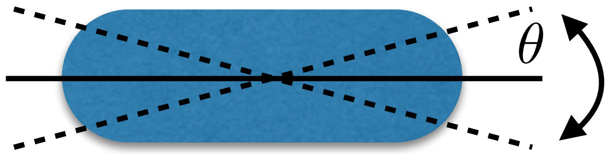
signature of low Reynolds numbers

$$\text{Re} = \frac{R v_s \rho}{\eta} \sim 2 \times 10^{-5}$$

Translational and rotational diffusion



$$\langle x^2 \rangle = 2D_T t$$



$$\langle \theta^2 \rangle = 2D_R t$$

Einstein - Stokes relation

$$D_T \approx \frac{k_B T}{6\pi\eta R} \approx 0.2\mu\mathrm{m}^2/s$$

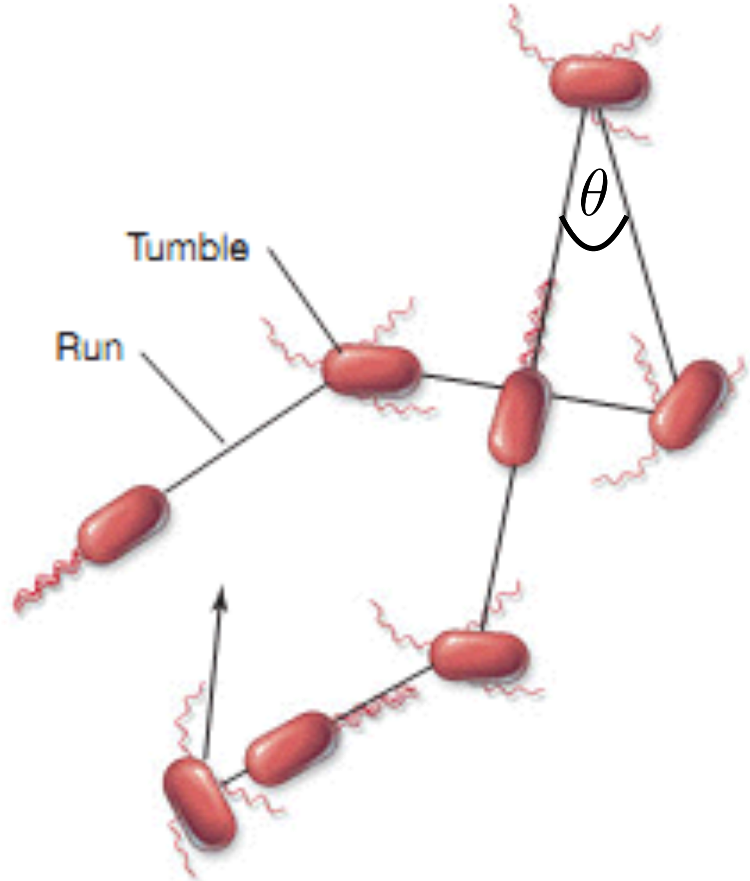
Einstein - Stokes relation

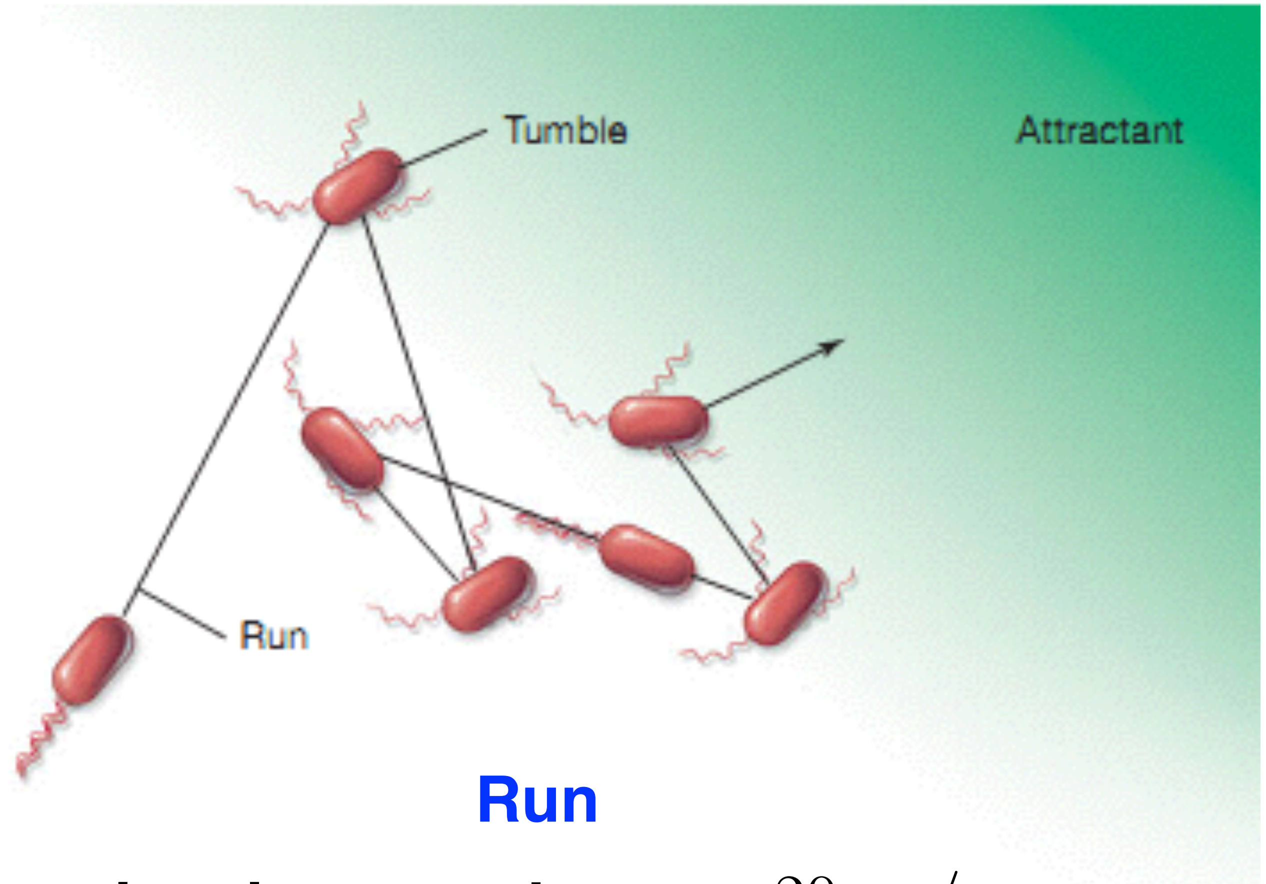
$$D_R \approx \frac{k_B T}{8\pi\eta R^3} \sim 0.2\,\mathrm{rad}^2/\mathrm{s}$$

After ~10s orientation changes by 90 degrees due to Brownian motion!

size of E. coli	$R \approx 1\mu\mathrm{m}$
water viscosity	$\eta \approx 10^{-3}\mathrm{kg\,m^{-1}s^{-1}}$
temperature	$T = 300\mathrm{K}$
Boltzmann constant	$k_B = 1.38 \times 10^{-23}\mathrm{J/K}$

E. coli chemotaxis





Run

swimming speed: $v_s \sim 20\mu\mathrm{m/s}$

typical duration: $t_r \sim 1\mathrm{s}$

all motors turning counter clockwise

Increase (Decrease) run durations, when swimming towards good (harmful) environment.

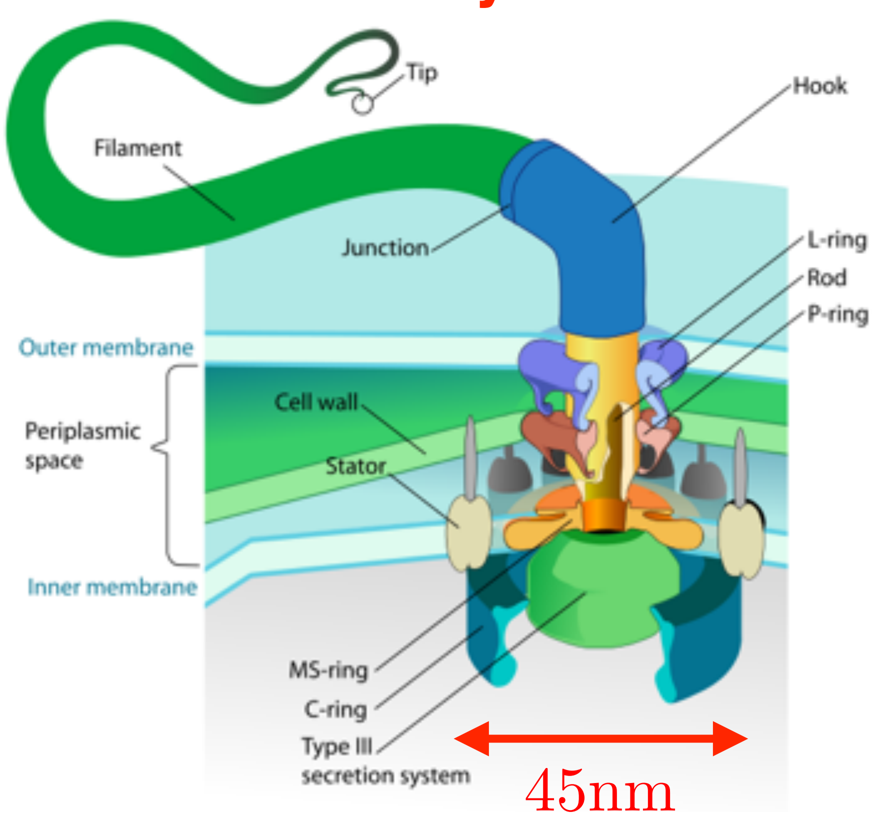
Tumble

random change in orientation $\langle\theta\rangle = 68^\circ$

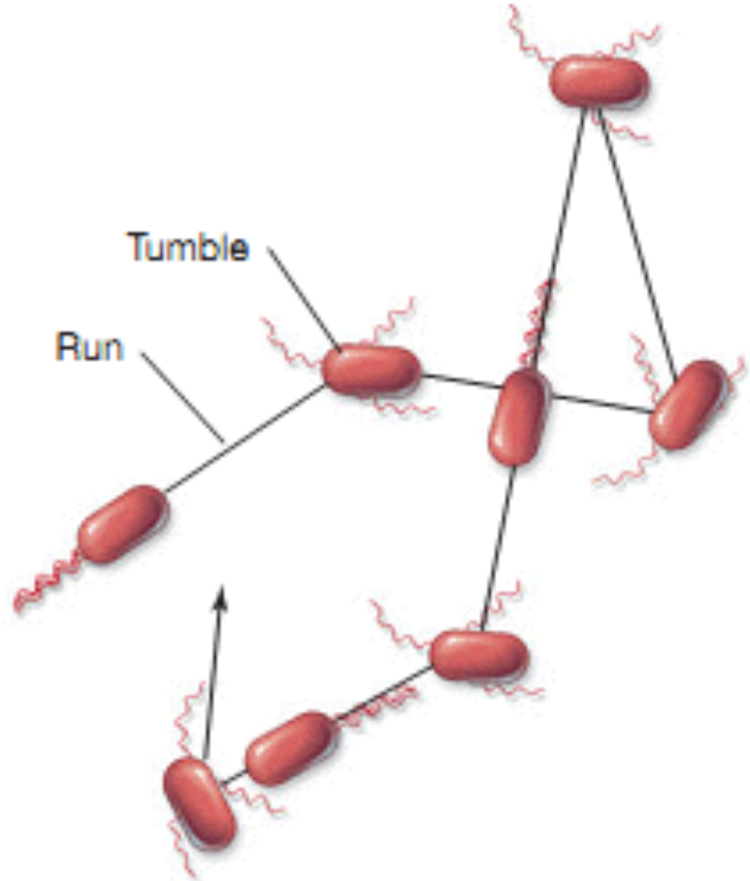
typical duration: $t_t \sim 0.1\mathrm{s}$

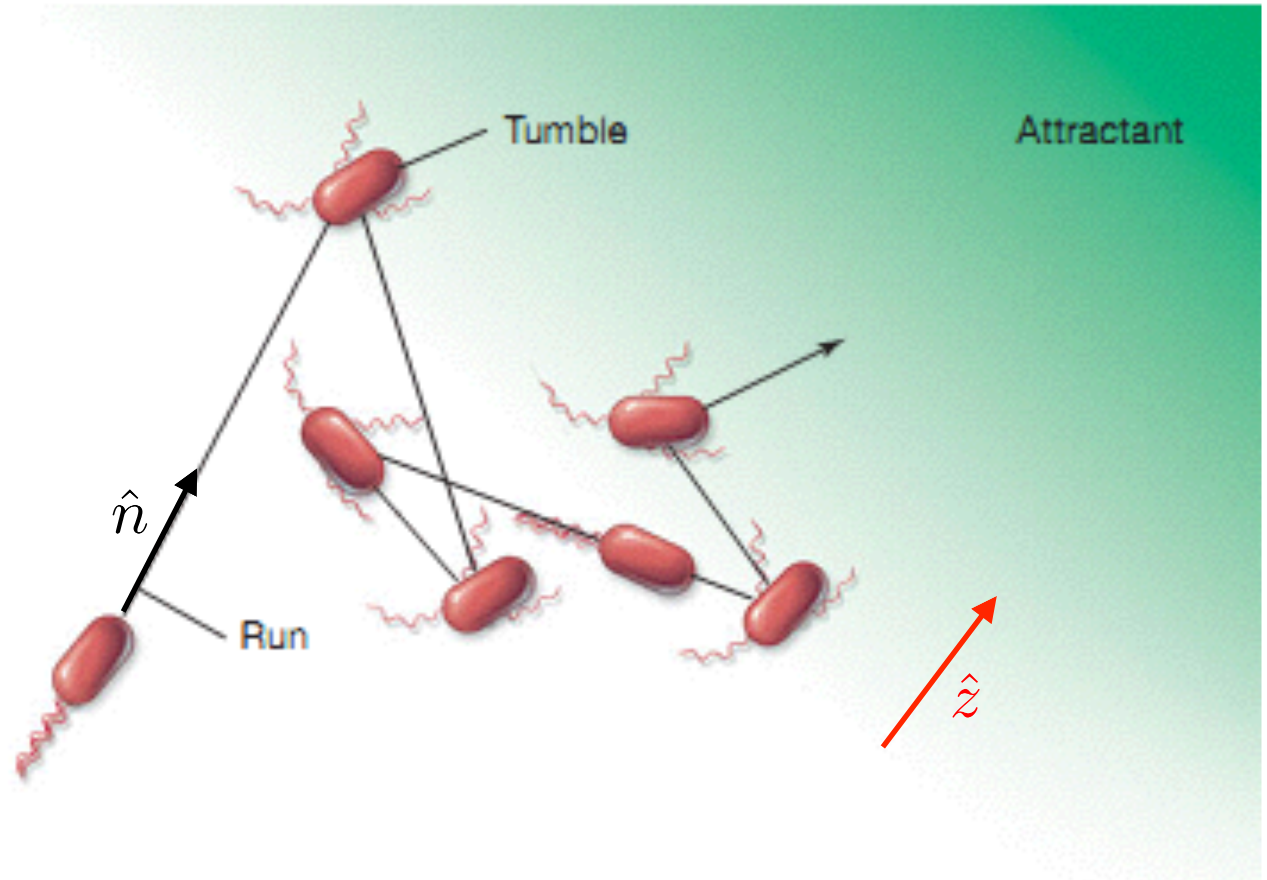
one or more motors turning clockwise

Rotary motor



E. coli chemotaxis





Homogeneous environment

run duration: $t_r \sim 1\mathrm{s}$

tumble duration: $t_t \sim 0.1\mathrm{s}$

swimming speed: $v_s \sim 20\mu\mathrm{m/s}$

drift velocity

$$v_d = 0$$

effective diffusion

$$D_{\mathrm{eff}} = \frac{\langle \Delta \ell^2 \rangle}{6 \langle \Delta t \rangle}$$

$$D_{\mathrm{eff}} \approx \frac{v_s^2 t_r^2}{6(t_r + t_t)} \sim 60\mu\mathrm{m}^2/\mathrm{s}$$

Gradient in "food" concentration

run duration increases (decreases) when swimming towards (away) from "food"

$$t_r(\hat{n}) = \bar{t}_r + \alpha(\hat{n} \cdot \hat{z})(\partial c/\partial z)$$

drift velocity

$$v_d = \frac{\langle \Delta z \rangle}{\langle \Delta t \rangle} \approx \frac{v_s \alpha (\partial c/\partial z)}{3(\bar{t}_r + t_t)}$$

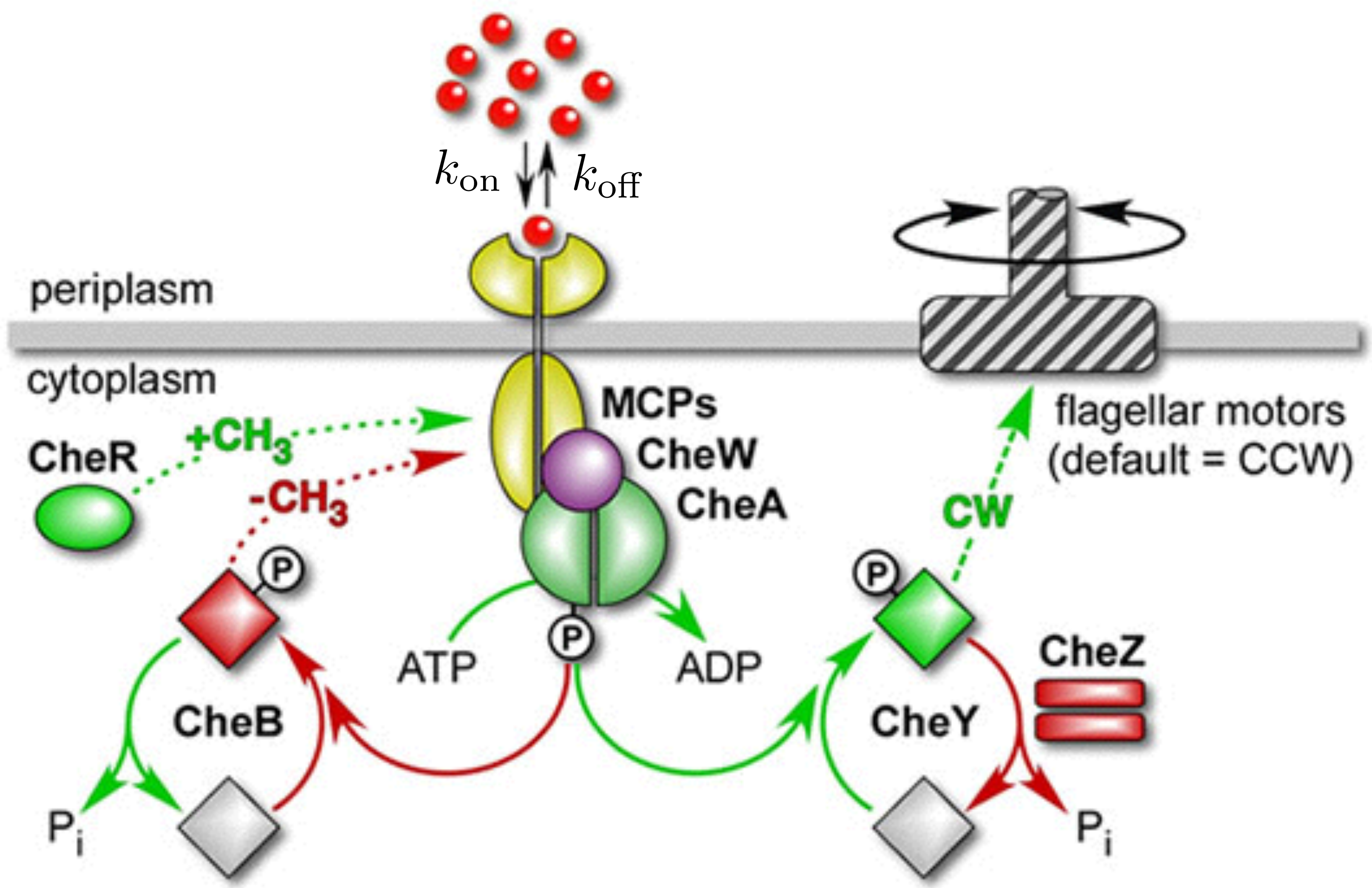
Sensing of environment

E. coli surface is covered with receptors, which can bind specific molecules.

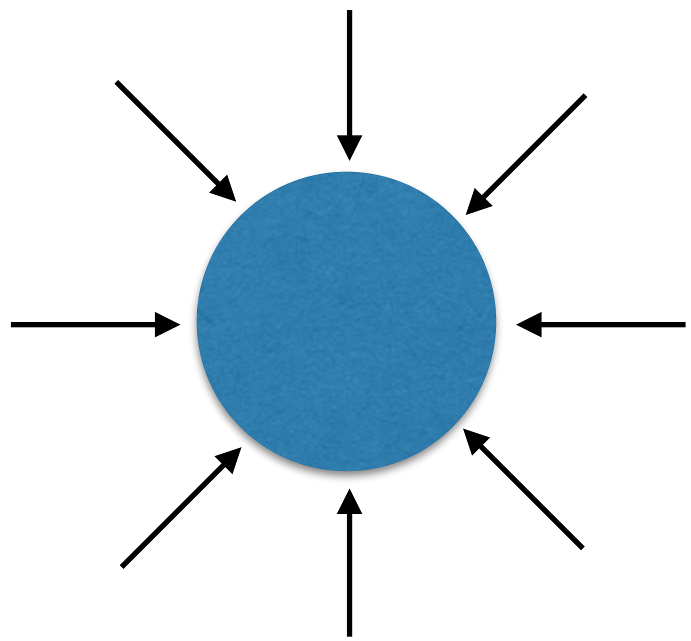
Average fraction of bound receptors p_B is related to concentration c of molecules.

$$p_B = \frac{c}{c + c_0} \qquad c_0 = \frac{k_{\text{off}}}{k_{\text{on}}}$$

Singling network inside E. coli analyzes state of receptors and gives direction to rotary motor.



Diffusion limited flux of molecules to E. coli



absorbing sphere

Fick's law

$$\frac{\partial c}{\partial t} = D\nabla^2 c = D\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial c}{\partial r}\right)$$

boundary conditions

$$c(r \to \infty) = c_\infty$$
$$c(R) = 0$$

steady state

$$c(r) = c_\infty\left[1 - \frac{R}{r}\right]$$

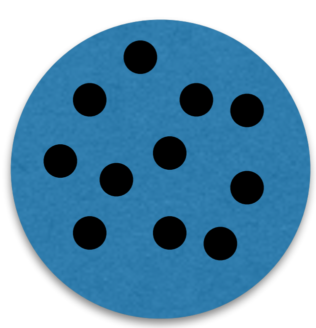
flux of molecules

$$J(r) = -D\frac{\partial c(r)}{\partial r} = -\frac{Dc_\infty R}{r^2}$$

rate of absorbing molecules

$$I(r) = J(r) \times 4\pi r^2 = -4\pi DRc_\infty = I_0 = -k_{\text{on}}c_\infty$$

diffusion constant for small molecules $D \approx 10^3 \mu\text{m}^2/s$ $\qquad k_{\text{on}} \sim 10^4 \mu\text{m}^3/s$



N* absorbing disks of radius *s

$$I = \frac{I_0}{1 + \pi R/Ns}$$

example $R \sim 1\mu\text{m} \quad s \sim 1\text{nm}$

flux drops by factor 2 for

$$N = \pi R/s \sim 3000$$

fractional area covered by these receptors

$$(N\pi s^2)/(4\pi R^2) \sim 10^{-3}$$

→ **E. coli can use many types of receptors specific for different molecules, without significantly affecting the diffusive flux**

Accuracy of concentration measurement

How many molecules do we expect inside a volume occupied by E. coli?

$$\overline{N} \sim R^3 c$$

Probability *p(N)* that cell measures *N* molecules follows Poisson distribution

$$p(N) = \frac{\overline{N}^N E^{-\overline{N}}}{N!}$$

mean $\overline{N}$

standard deviation $\sigma_N = \sqrt{\overline{N}}$

Error in measurement

$$\mathrm{Err} \sim \frac{\sigma_N}{\overline{N}} \sim (R^3 c)^{-1/2}$$

for $c = 1\mu\mathrm{M} = 6 \times 10^{20}\mathrm{m}^{-3} \Rightarrow \mathrm{Err} \sim 4\%$

**E.coli can be more precise by counting molecules for longer time *t*.
However, they need to wait some time t_0 in order for the original molecules to diffuse away to prevent double counting of the same molecules!**

$$t_0 \sim R^2/D \sim 10^{-3} s$$

$$\overline{N} \sim R^3 ct/t_0 \sim DRct$$

$$\mathrm{Err} \sim (DRct)^{-1/2}$$

for *t*=1s, precision improves to Err~0.1%

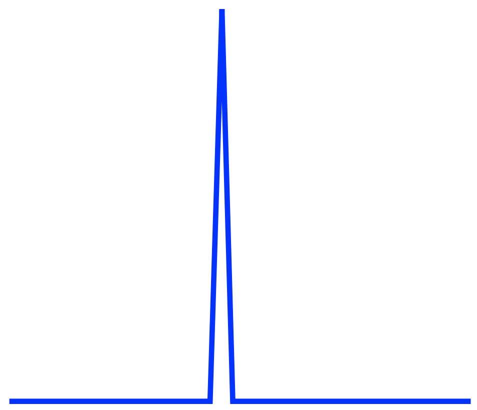
When E. coli is swimming, it wants to swim faster than the diffusion of small molecules

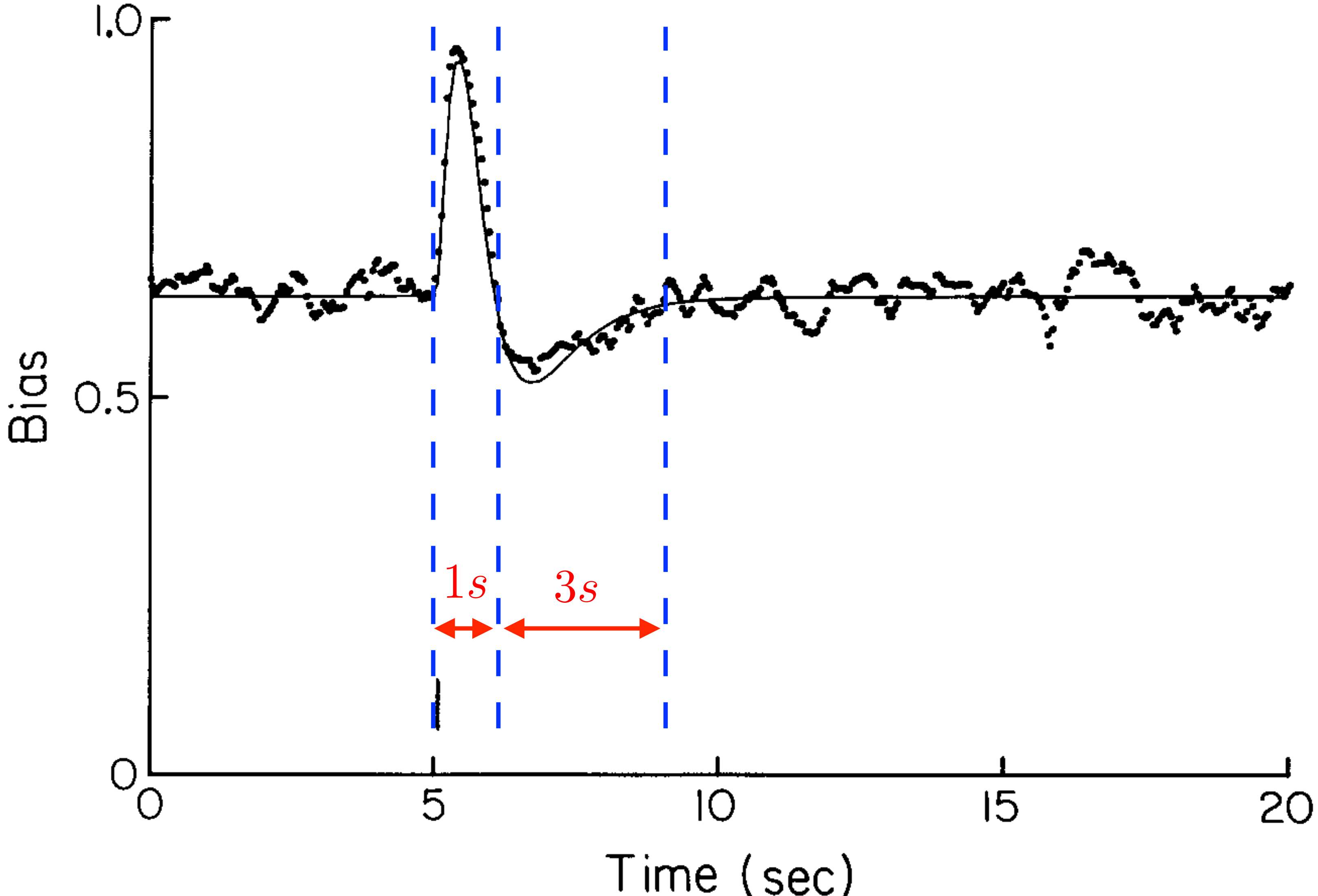
$$v_s t \gtrsim (Dt)^{1/2} \Rightarrow t \gtrsim D/v_s^2 \sim 1s$$

How E. coli actually measures concentration?

Probability for motor to rotate in CCW direction (runs) as a function of time in response to short pulse in external molecular concentration

Input concentration





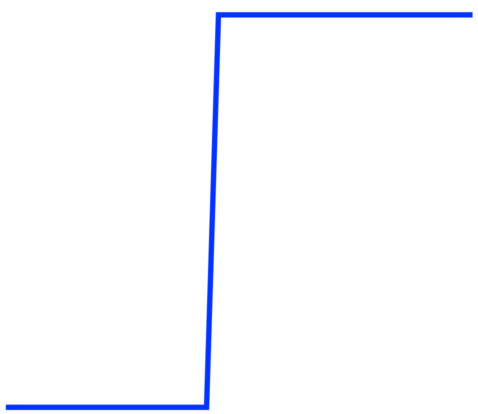
E. coli integrates measured concentration observed during the last second and compare this with measured concentration during the previous 3 seconds. If difference is positive then increase the probability of runs, otherwise increase the probability of tumbles.

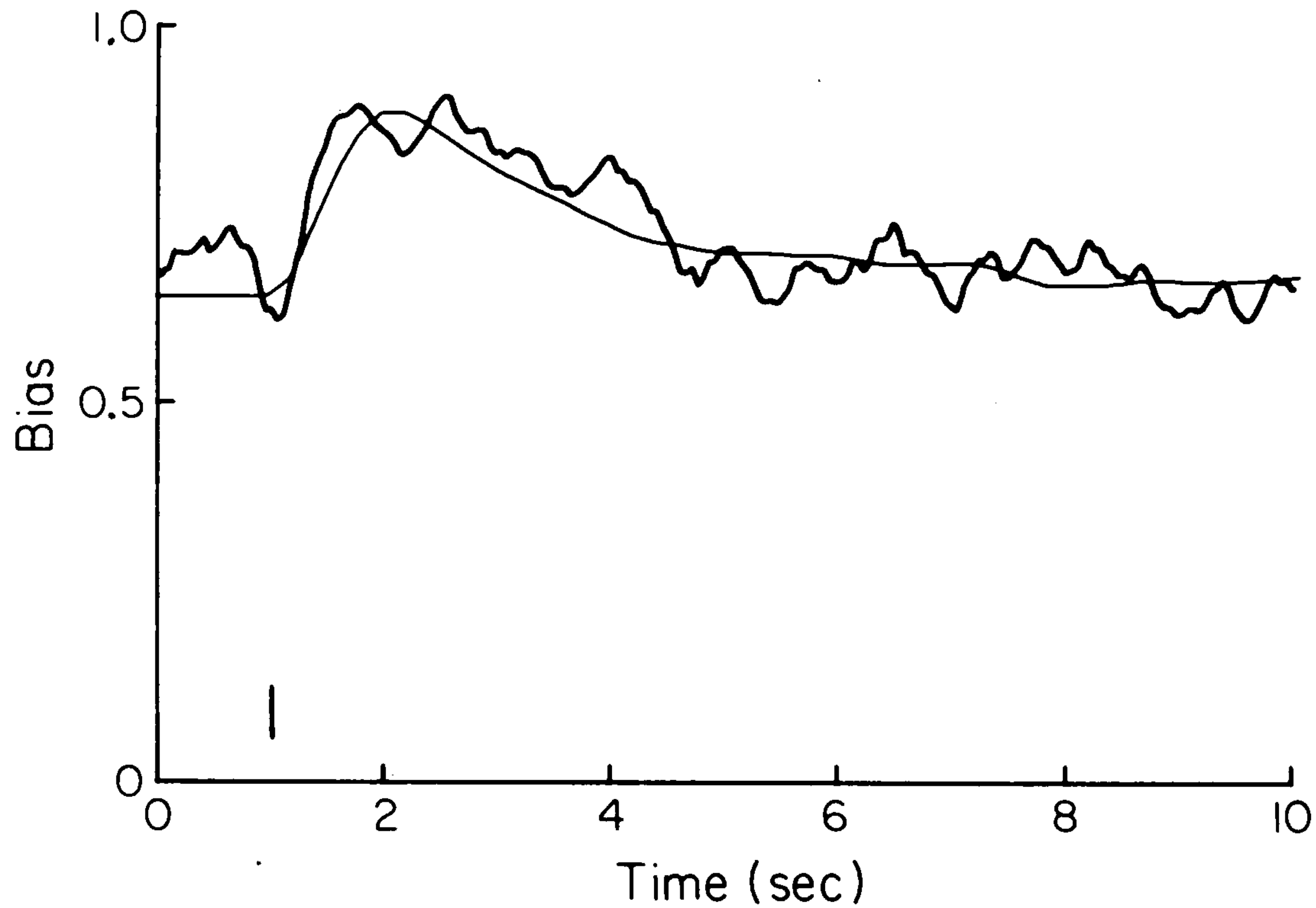
J. E. Segall, S. M. Block, and H. C. Berg, PNAS 83, 8987–8991 (1986)

Adaptation

Probability for motor to rotate in CCW direction (runs) as a function of time in response to a sudden increase in external molecular concentration

Input concentration





E. coli adapts to the new level of concentration in about 4 seconds.
This enables E. coli to be very sensitive to changes in concentration over a very broad range of concentrations!

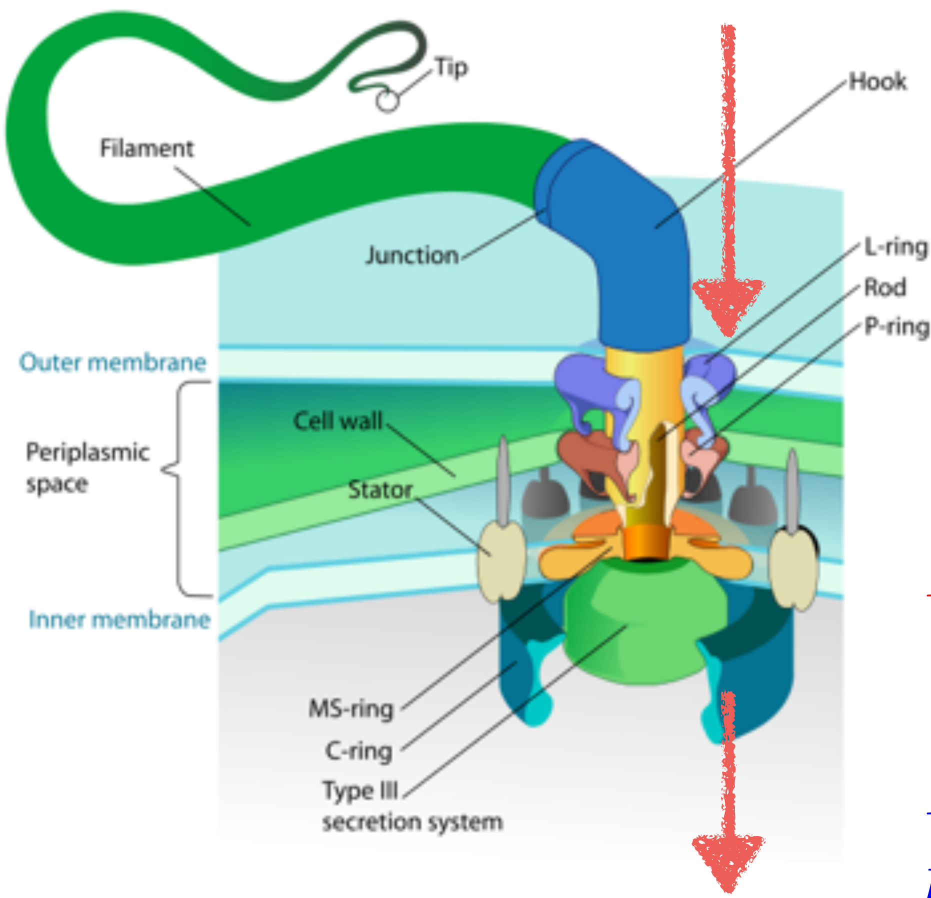
J. E. Segall, S. M. Block, and H. C. Berg, PNAS 83, 8987–8991 (1986)

How efficient is motor of E. coli?

Energy source for rotary motor are charged protons

$pH = 7.0$

H^+



H^+

$pH \approx 7.8$

Each proton gains energy due to

Transmembrane electric potential difference

$$\delta\psi \approx -120\mathrm{mV}$$

Change in pH

$$\delta U = (-2.3k_BT/e)\Delta pH \approx -50mV$$

Total protonmotive force

$$\Delta p = \delta\psi + \delta U \approx -170\mathrm{mV}$$

Need 1200 protons per one revolution

Input power

$$P_{\mathrm{in}} = e\Delta p \times f = 170\mathrm{meV} \times 10\mathrm{Hz} \approx 3.2 \times 10^5 \mathrm{pN\ nm/s}$$

Power loss due to stokes drag

$$P_{\mathrm{rot}} = N \times (2\pi f) \approx 4600\mathrm{pN\ nm} \times (20\pi\mathrm{Hz}) \approx 2.9 \times 10^5 \mathrm{pN\ nm/s}$$

$$P_{\mathrm{trans}} = F \times v \approx 0.4\mathrm{pN} \times 20000\mathrm{nm/s} \approx 8 \times 10^3 \mathrm{pN\ nm/s}$$

Motor efficiency

$$\frac{P_{\mathrm{trans}} + P_{\mathrm{rot}}}{P_{\mathrm{in}}} \approx 90\%$$

Further reading