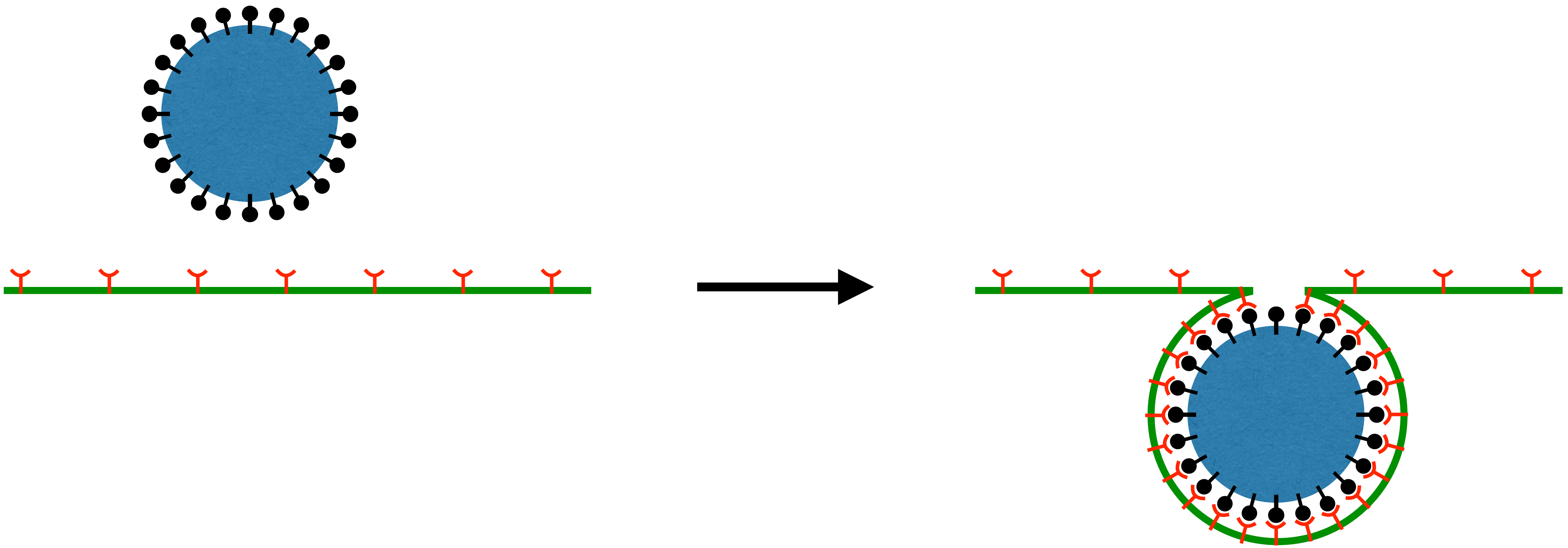
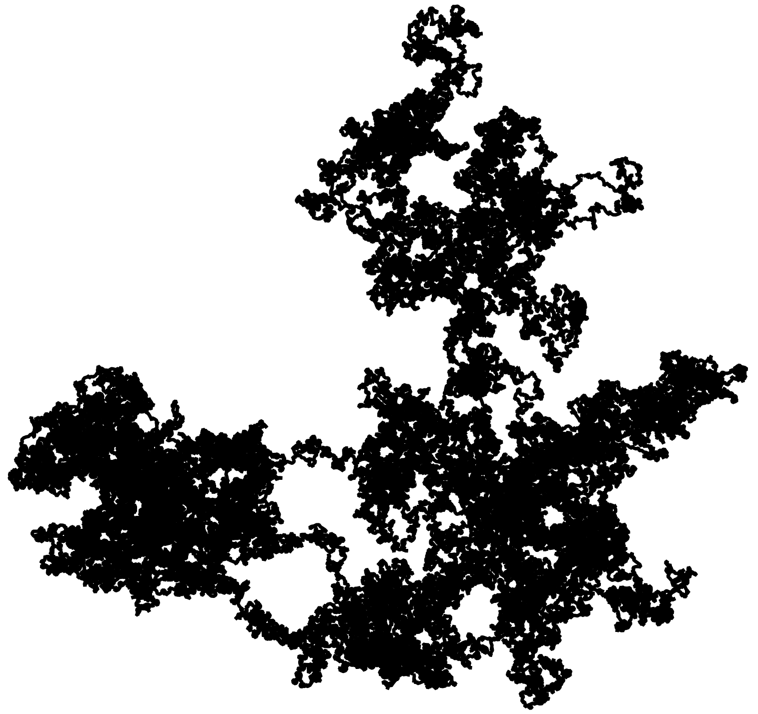
MAE 545: Lecture 17 (4/20)

Receptor mediated endocytosis

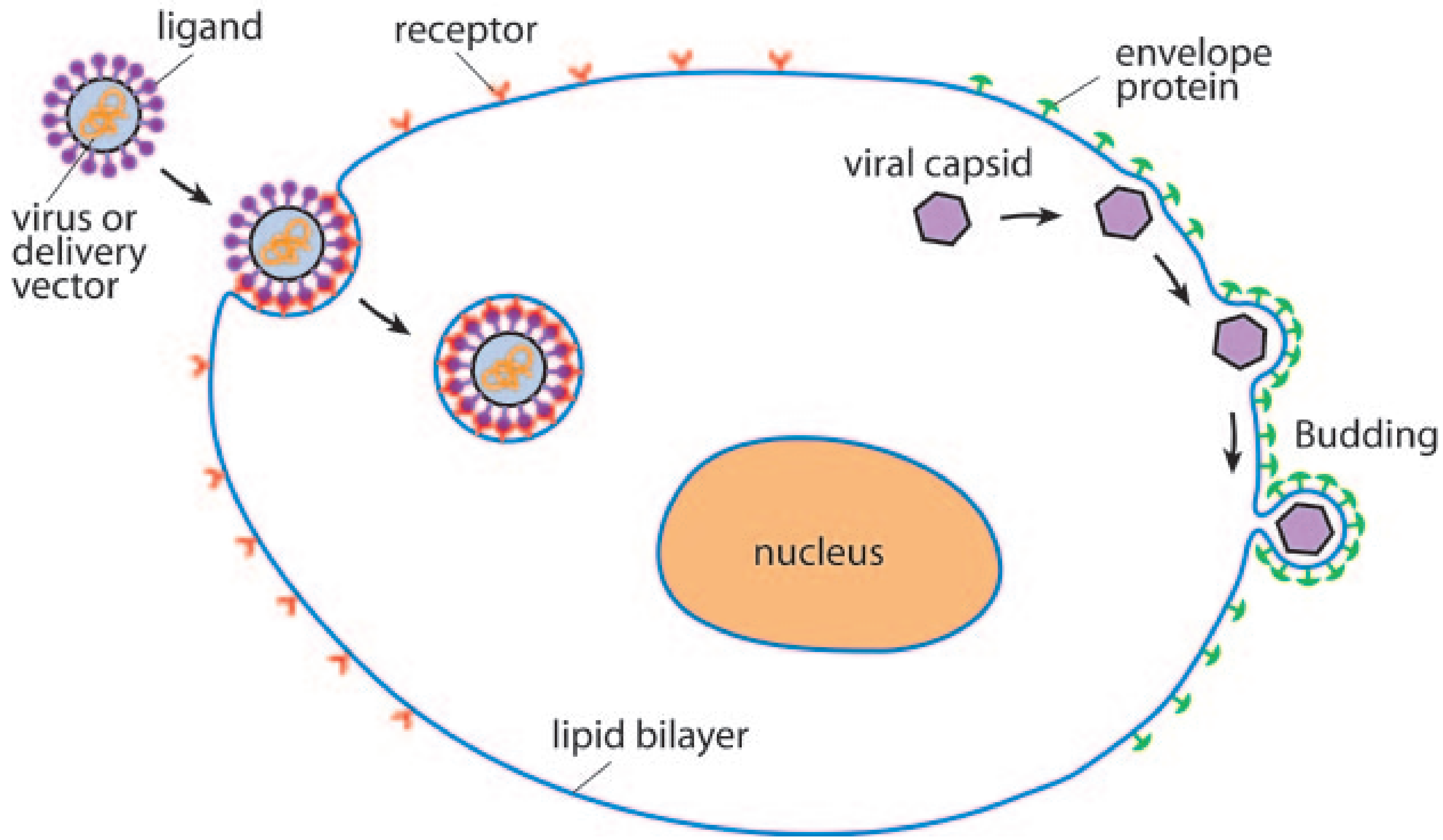


Random walks



Viral entry to cell via receptor mediated endocytosis

(density n_L) **(density n_0)**

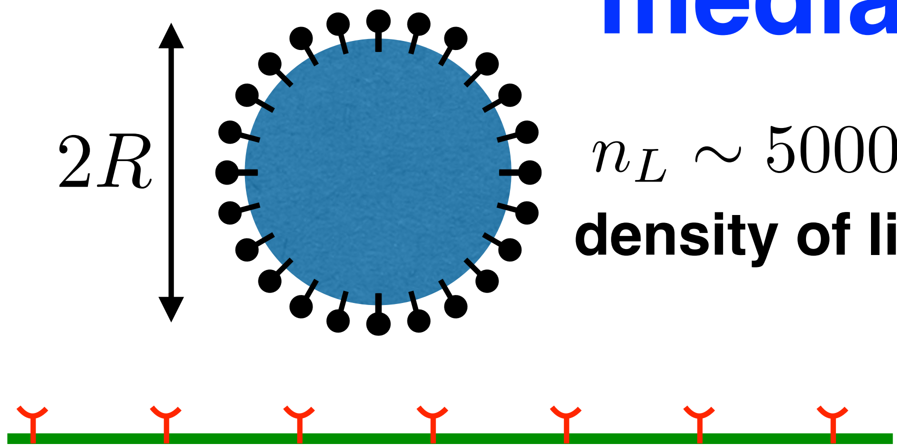


(similar process may help during budding of enveloped viruses)

Bending energy cost and loss of entropy for receptors is compensated by the binding energy between cell receptors and ligands on the surface of viral capsid.

G. Bao and X.R. Bao, PNAS 102, 9997 (2005)

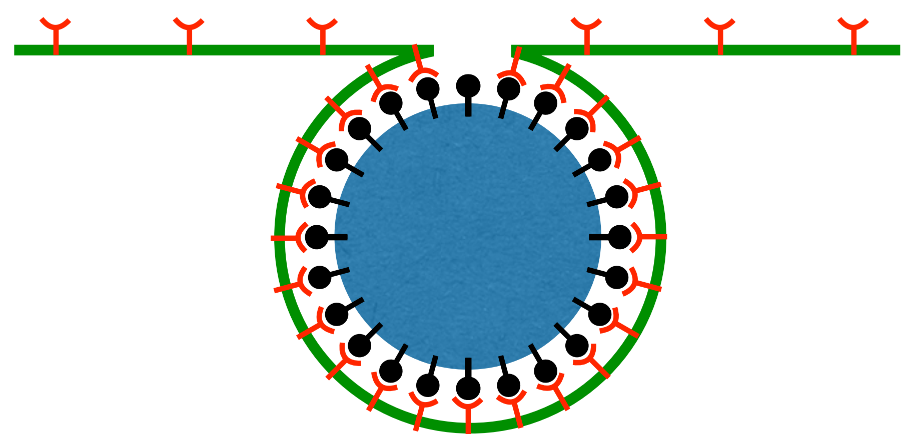
Viral entry to cell via receptor mediated endocytosis



$n_L \sim 5000\mu\text{m}^{-2}$
density of ligands

$n_0 \sim 50\text{-}500\mu\text{m}^{-2}$
density of receptors

total number of ligands
$N_L = 4\pi R^2 n_L$



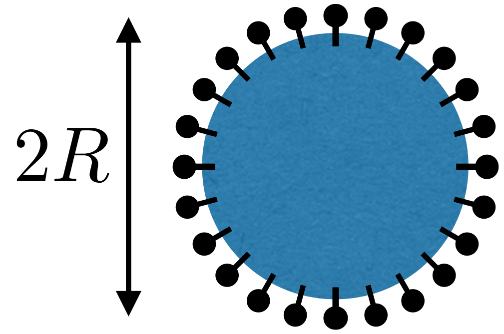
bending energy	$E_{\text{bend}} = 0$	$E_{\text{bend}} = 8\pi\kappa$
binding energy of ligand-receptor pairs	$E_{\text{bind}} = 0$	$E_{\text{bind}} = -N_L U_b$
free energy due to mixing of receptors	$G_{\text{mix}} = N k_B T \ln(n_0 A_0)$	$G_{\text{mix}} = (N - N_L) k_B T \ln(n_0 A_0) + N_L k_B T \ln(n_L A_0)$

total change of free energy

$$\Delta G = 8\pi\kappa - N_L U_b + N_L k_B T \ln(n_L / n_0)$$

H. Gao *et al.*, PNAS **102**, 9469 (2005)

Viral entry to cell via receptor mediated endocytosis

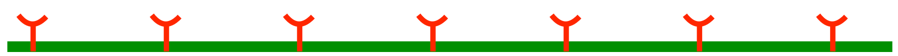


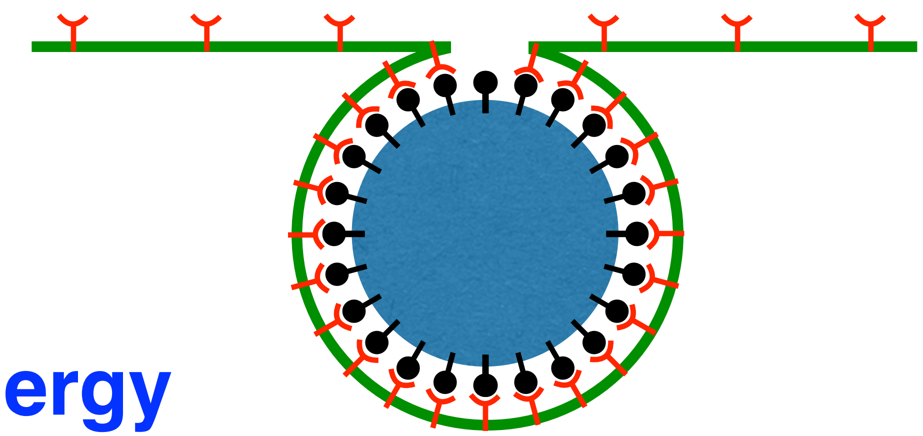
$n_L \sim 5000 \mu\text{m}^{-2}$

density of ligands

total number of ligands

$N_L = 4\pi R^2 n_L$





$n_0 \sim$ 50-500μm^{-2}

density of receptors

receptor-ligand binding energy

$U_b \sim 15 k_B T$

bending rigidity

$\kappa \sim 20 k_B T$

total change of free energy

$$\Delta G = 8\pi\kappa - 4\pi R^2 n_L U_b + 4\pi R^2 k_B T n_L \ln(n_L/n_0)$$

Receptor mediated endocytosis is thermodynamically favorable when $\Delta G < 0$

$$R > \sqrt{\frac{2\kappa}{n_L\left(U_b - k_B T \ln(n_L/n_0)\right)}} \sim 30\,\text{nm}$$

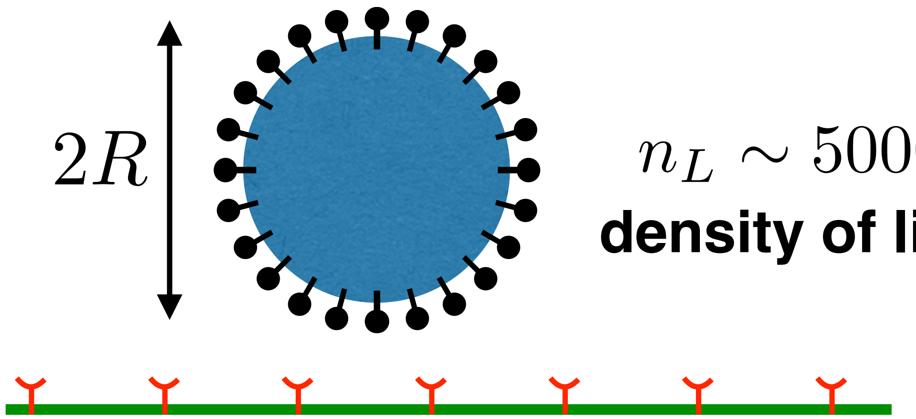
H. Gao *et al.*, PNAS **102**, 9469 (2005)

How fast is this process?

Viral entry to cell via receptor mediated endocytosis

H. Gao *et al.*, PNAS **102**, 9469 (2005)

Side view:



$n_L \sim 5000 \mu\text{m}^{-2}$
density of ligands

$n_0 \sim$ 50-500μm^{-2}
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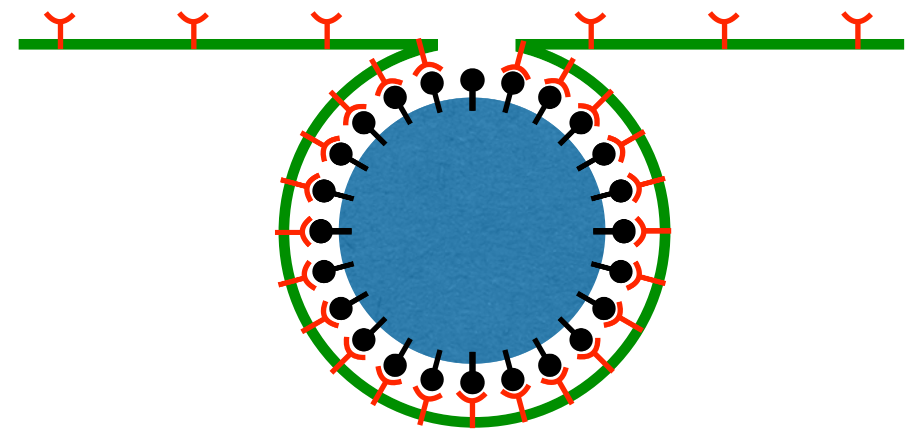
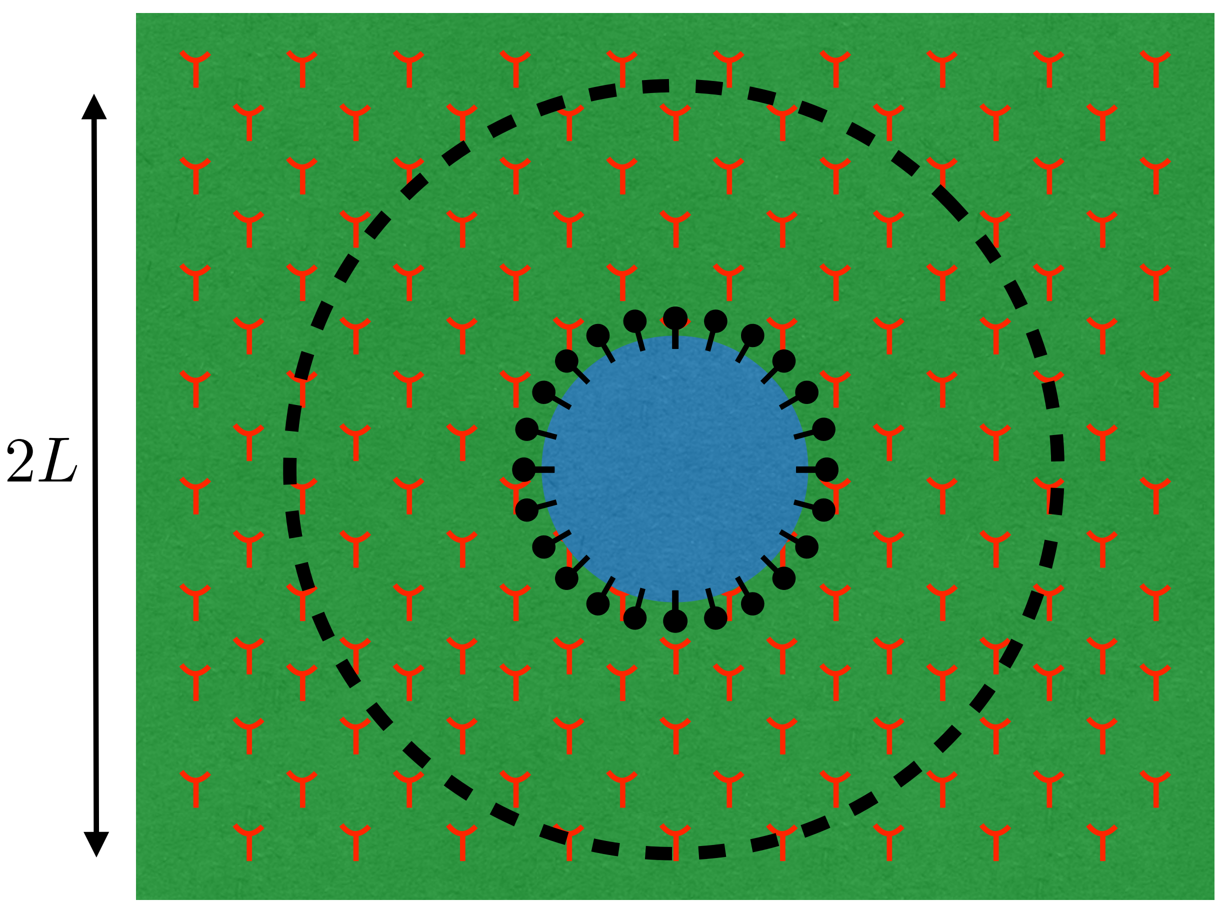


$$R > \sqrt{\frac{2\kappa}{n_L\left(U_b - k_B T \ln(n_L/n_0)\right)}} \sim 30\,\text{nm}$$

Top view:



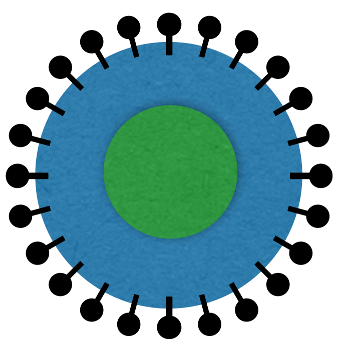
Need to recruit N_L receptors from circular region of radius L via diffusion

$$N_L = \pi L^2 n_0 = 4\pi R^2 n_L$$

$$t \sim \frac{L^2}{D} \sim \frac{R^2 n_L}{D n_0} \gtrsim 10\text{s}$$

Use of magnetic nanoparticles for diagnostic and treatment of tumors

Receptors for LHRH hormone are over-expressed in breast, ovarian, and prostate cancer cells

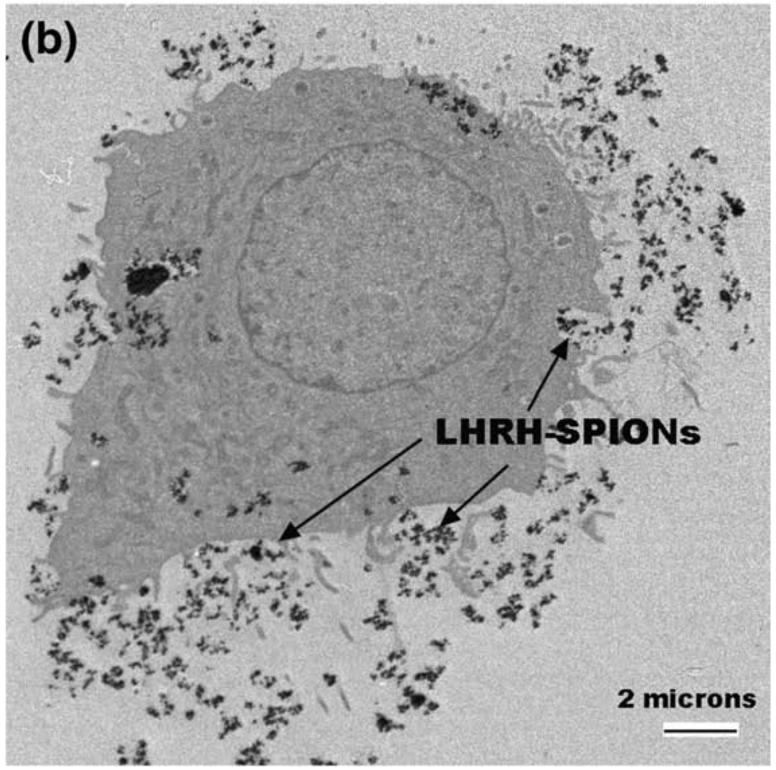


LHRH hormone
PEG coating
magnetic core

Magnetic particles enter only cancer cells via LHRH-receptor mediated endocytosis

PEG coating shields nanoparticles from immune system and prevents macro-clustering of nanoparticles.

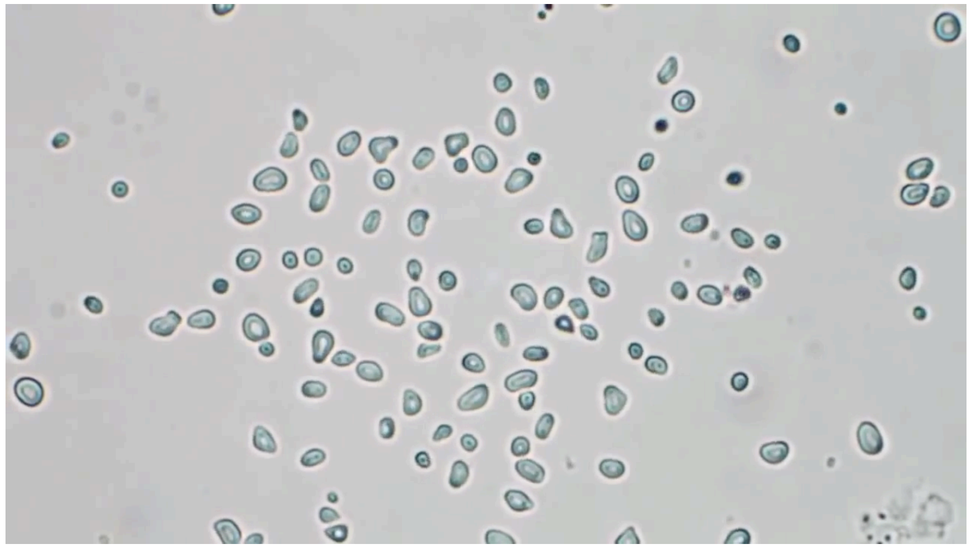
Cancer cells containing magnetic nanoparticles can be detected with MRI (magnetic resonance imaging). Then magnetic particles can be heated via magnetic field to destroys cancer cells.



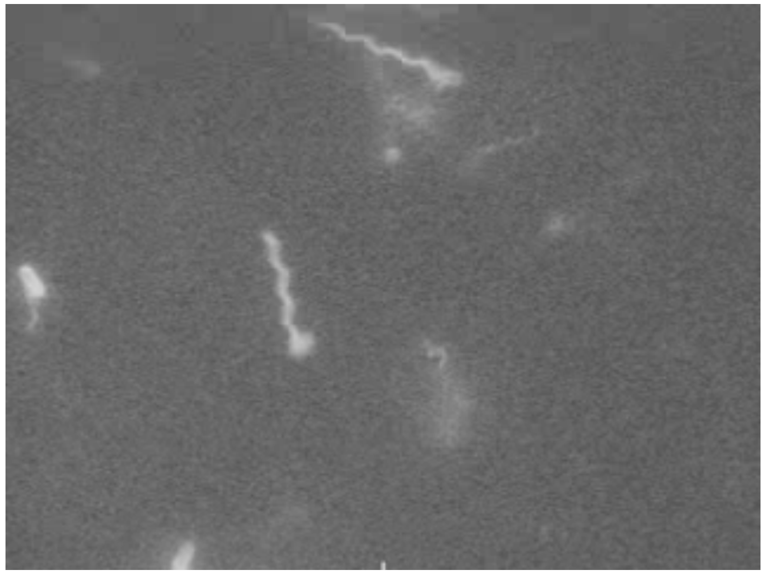
J. Meng *et al.*, Mater. Sci. Eng. C **29,** 1467 (2009)

Random walks

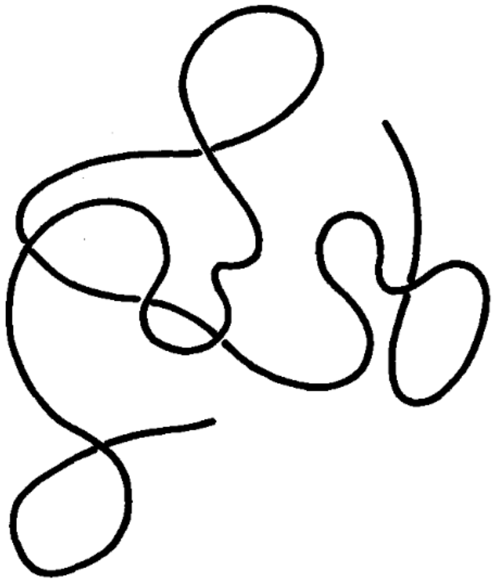
Brownian motion



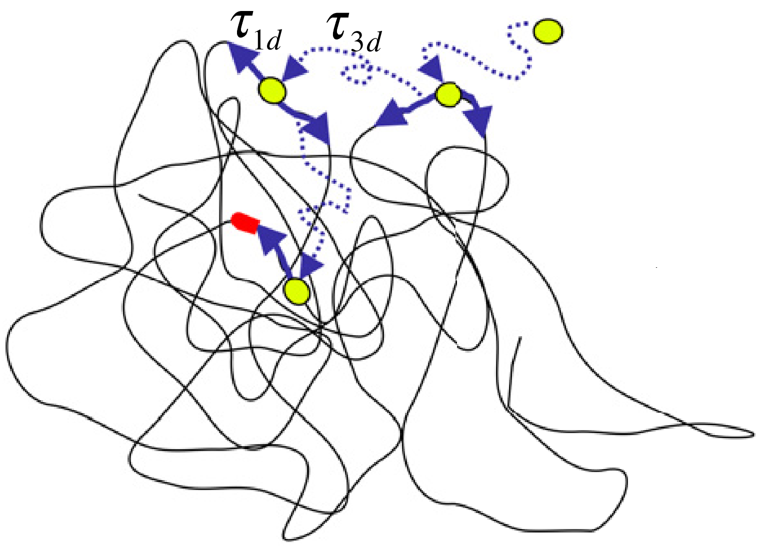
Swimming of E. coli



Polymer random coils

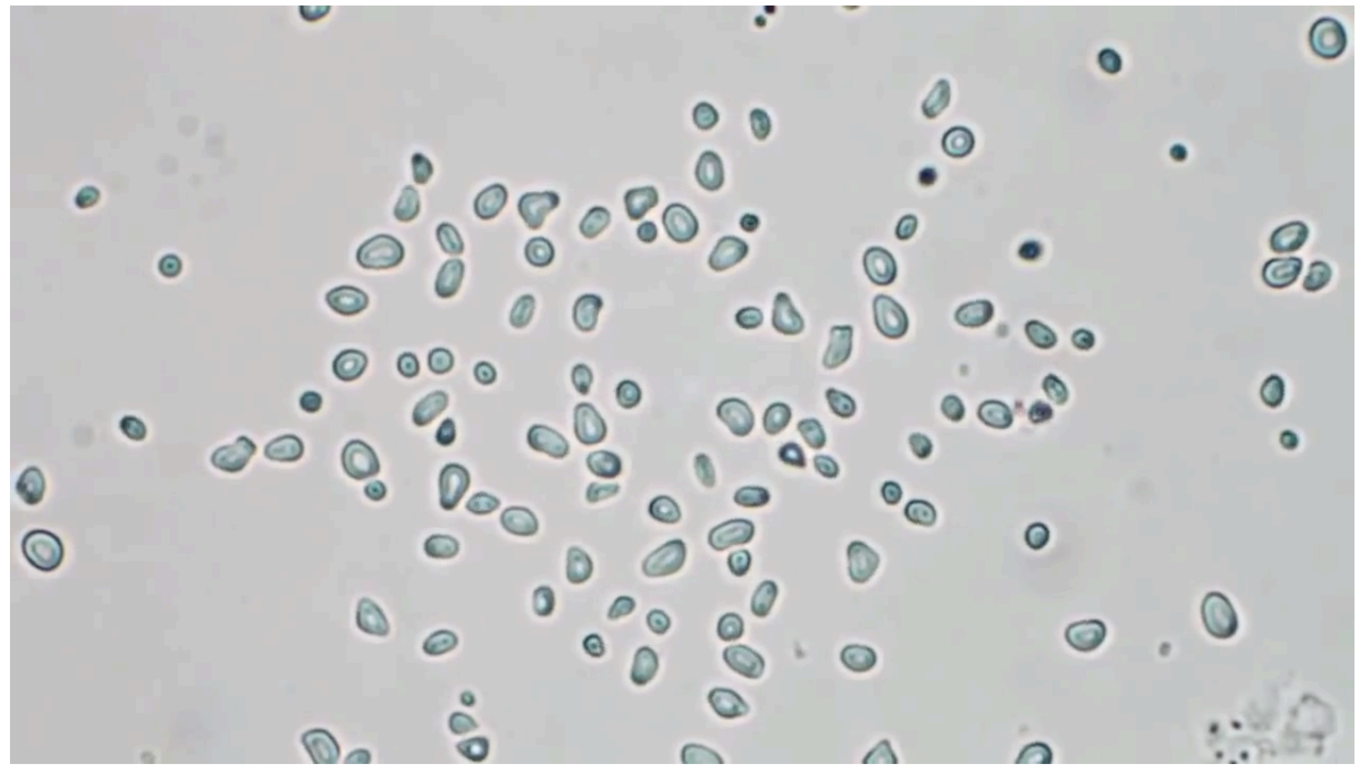


Protein search for a binding site on DNA



Brownian motion of small particles

1827 Robert Brown: observed irregular motion of small pollen grains suspended in water

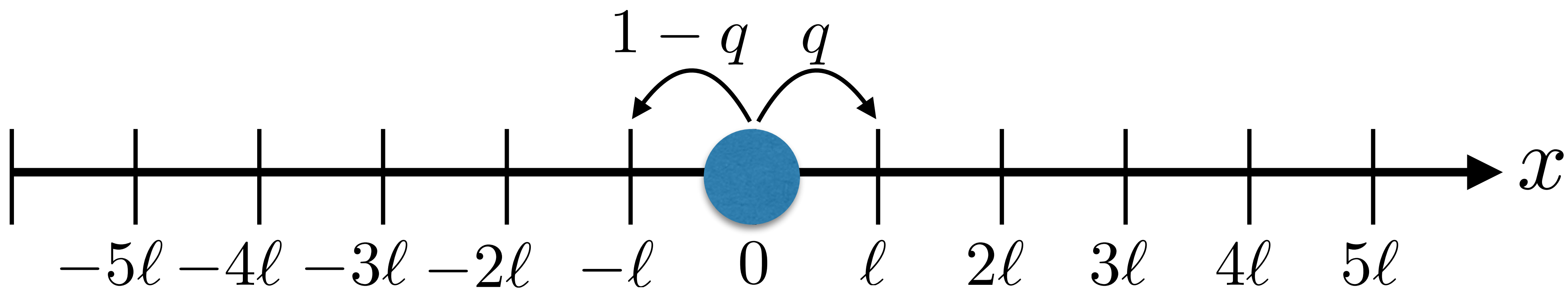


$| \approx 10\mu\text{m}$

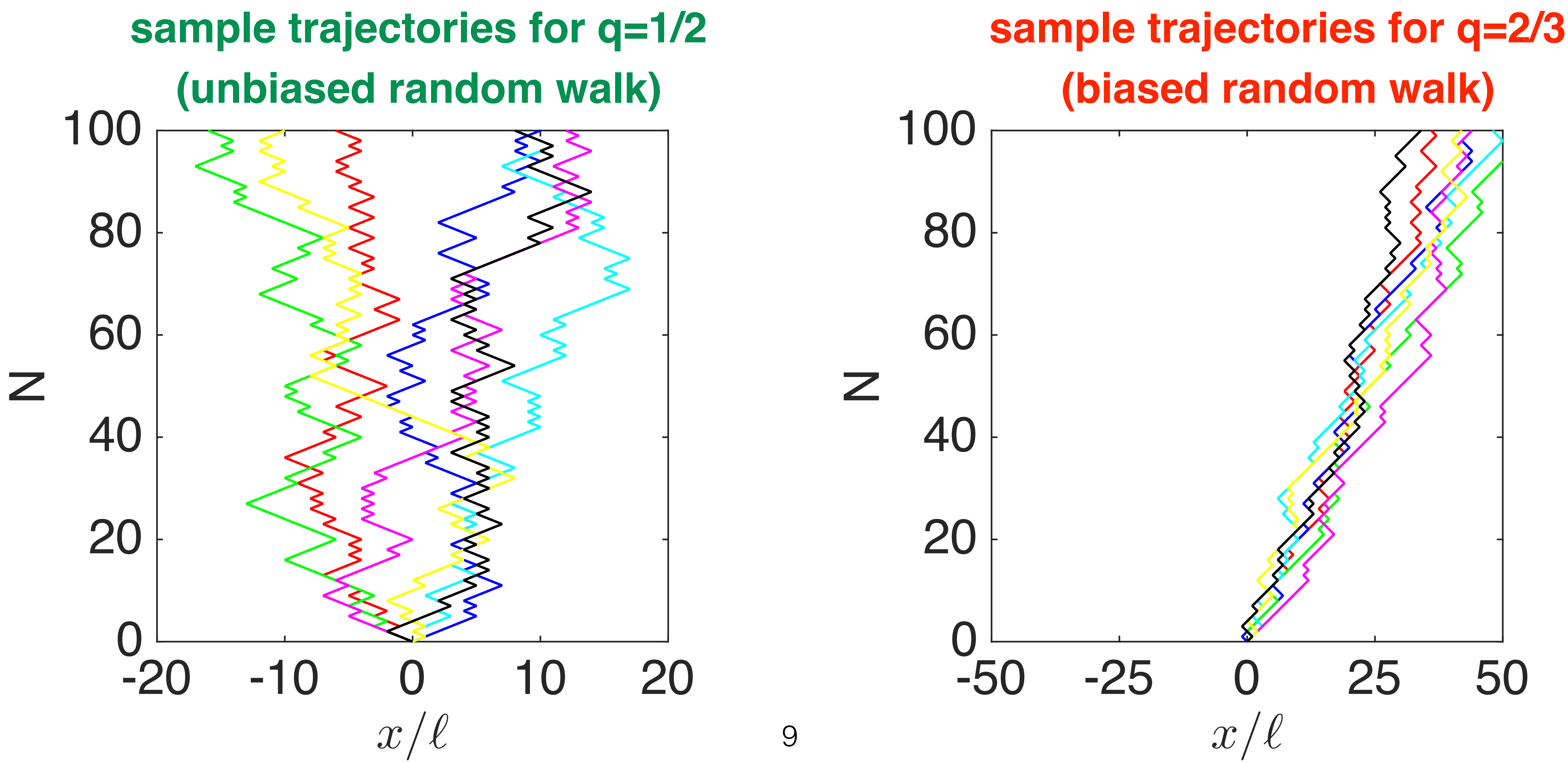
https://www.youtube.com/watch?v=R5t-oA796to

1905-06 Albert Einstein, Marian Smoluchowski: microscopic description of Brownian motion and relation to diffusion equation

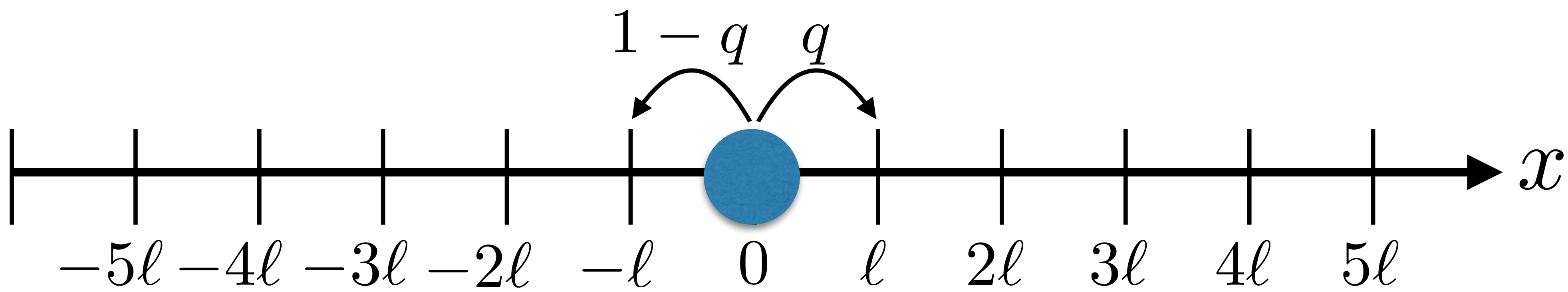
Random walk on a 1D lattice



At each step particle jumps to the right with probability q and to the left with probability 1-q.



Random walk on a 1D lattice



At each step particle jumps to the right with probability q and to the left with probability 1-q.

What is the probability *p(x,N)* that we find particle at position *x* after *N* jumps?

Probability that particle makes *k* jumps to the right and *N-k* jumps to the left obeys the binomial distribution

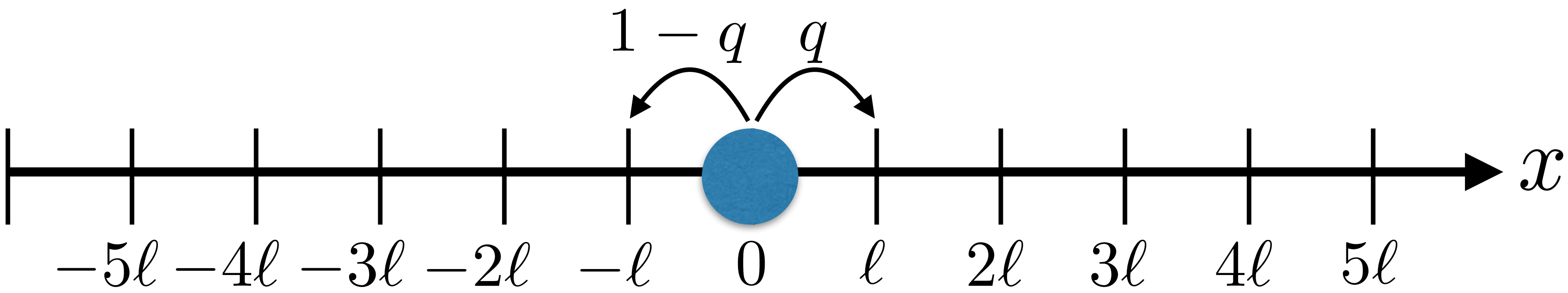
$$p(k,N) = \binom{N}{k} q^k (1-q)^{N-k}$$

Relation between *k* and particle position *x*:

$$x = k\ell - (N-k)\ell = (2k-N)\ell$$

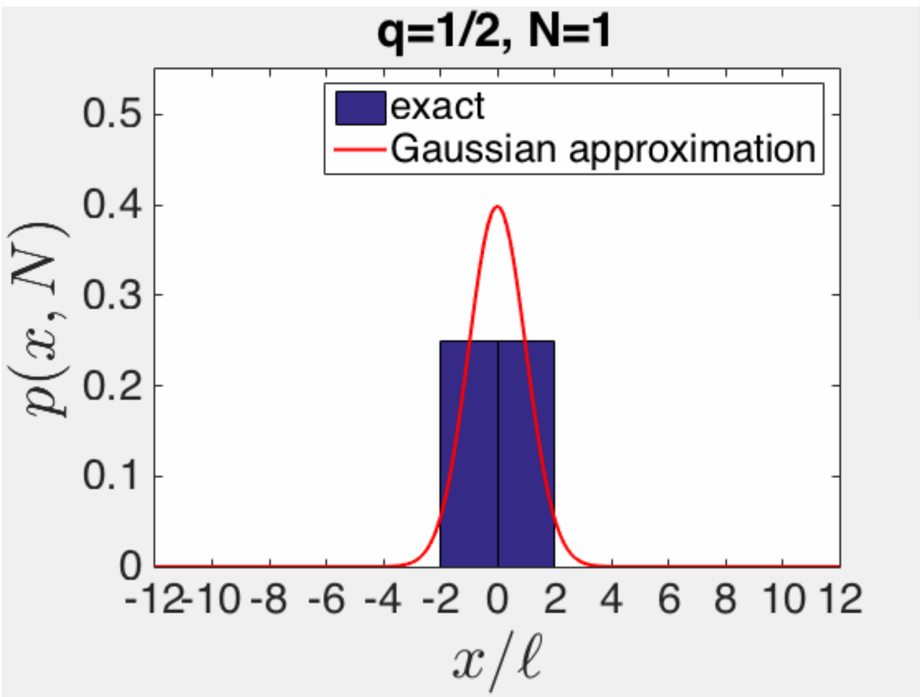
$$k = \frac{1}{2}\left(N + \frac{x}{\ell}\right)$$

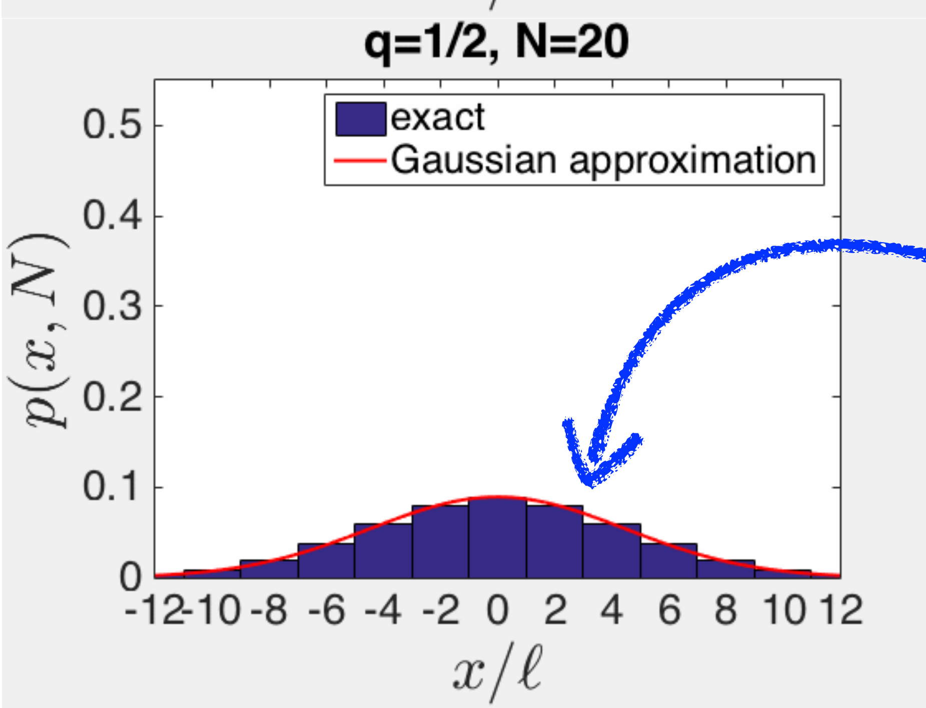
Random walk on a 1D lattice



unbiased random walk

biased random walk



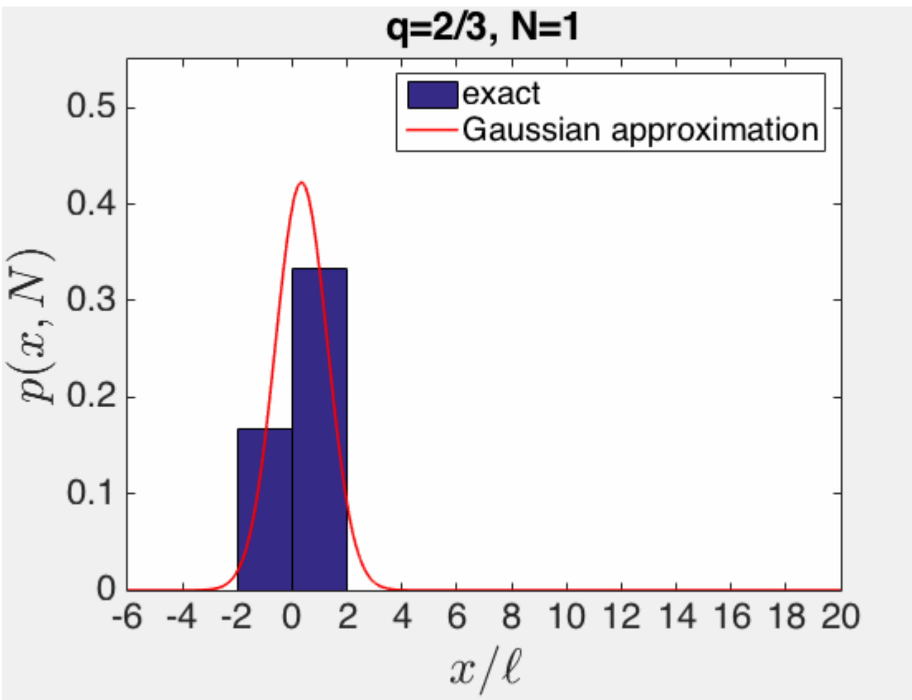


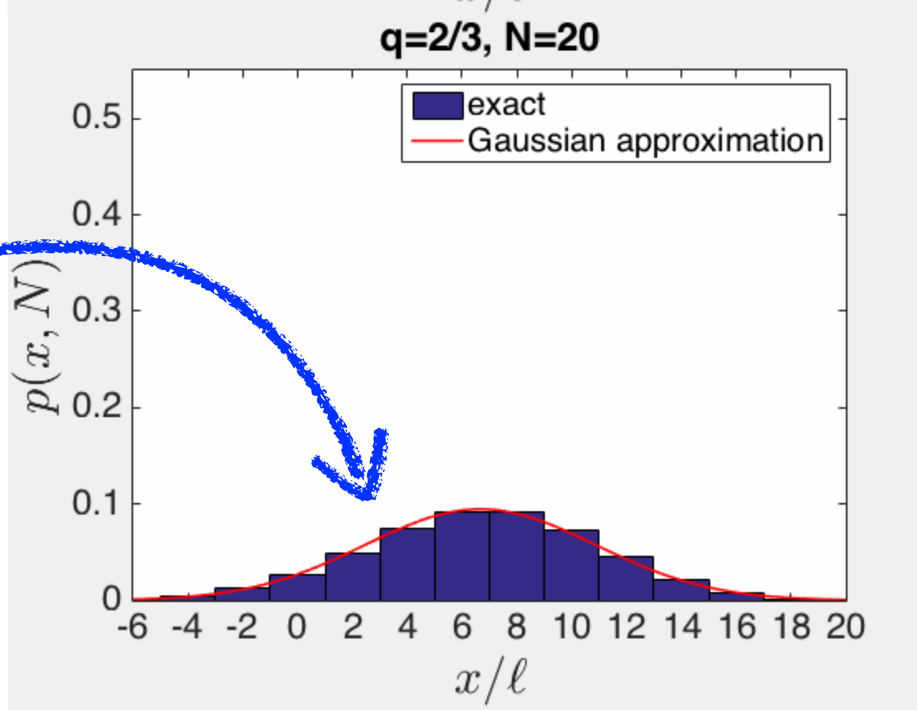
$$p(k,N) = \binom{N}{k} q^k (1-q)^{N-k}$$

$$k = \frac{1}{2}\left(N + \frac{x}{\ell}\right)$$

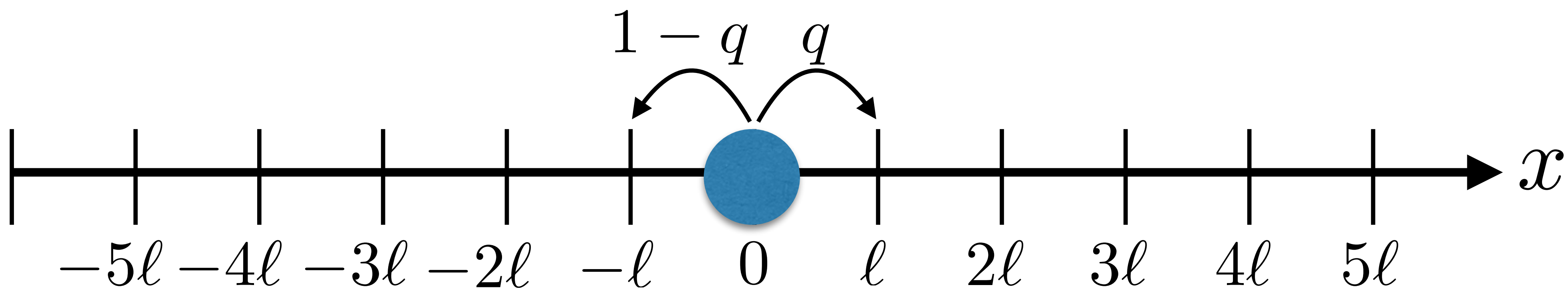
Note: exact discrete distribution has been made continuous by replacing discrete peaks with boxes whose area corresponds to the same probability.

after several steps the probability distribution spreads out and becomes approximately Gaussian





Gaussian approximation for p(x,N)



Position *x* after *N* jumps can be expressed as the sum of individual jumps $x_i \in \{-\ell, \ell\}$.

$$x = \sum_{i=1}^{N} x_i$$

Mean value averaged over all possible random walks

$$\langle x \rangle = \sum_{i=1}^{N} \langle x_i \rangle = N \langle x_1 \rangle = N\left(q\ell - (1-q)\ell\right)$$

$$\boxed{\langle x \rangle = N\ell\,(2q-1)}$$

Variance averaged over all possible random walks

$$\sigma^2 = \langle x^2 \rangle - \langle x \rangle^2 = N\sigma_1^2 = N\left(\langle x_1^2 \rangle - \langle x_1 \rangle^2\right)$$

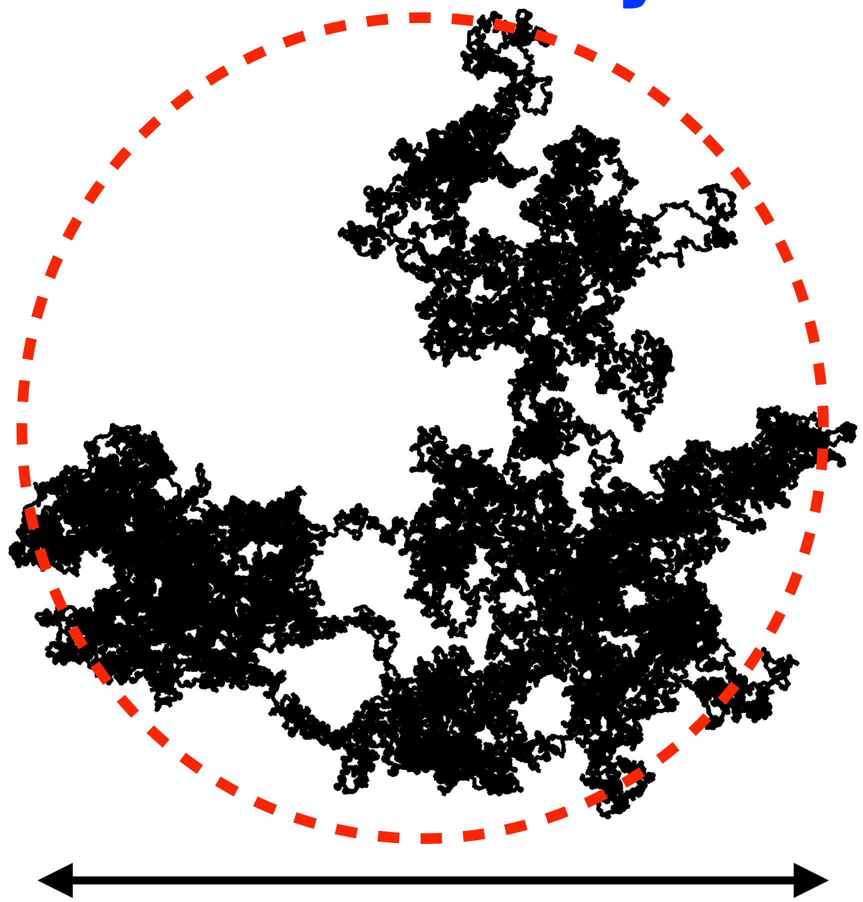
$$\sigma^2 = N\left(q\ell^2 + (1-q)\ell^2 - \langle x_1 \rangle^2\right)$$

$$\boxed{\sigma^2 = 4N\ell^2 q(1-q)}$$

According to the central limit theorem p(x,N) approaches Gaussian distribution for large N:

$$\boxed{p(x,N) \approx \frac{1}{\sqrt{2\pi\sigma^2}} e^{-(x-\langle x \rangle)^2/(2\sigma^2)}}$$

Number of distinct sites visited by unbiased random walks



$2r \propto \sqrt{N}$

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

1D $N_{\text{tot}} \propto \sqrt{N}$

2D $N_{\text{tot}} \propto N$

3D $N_{\text{tot}} \propto N\sqrt{N}$

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

In 3D some sites are never 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."

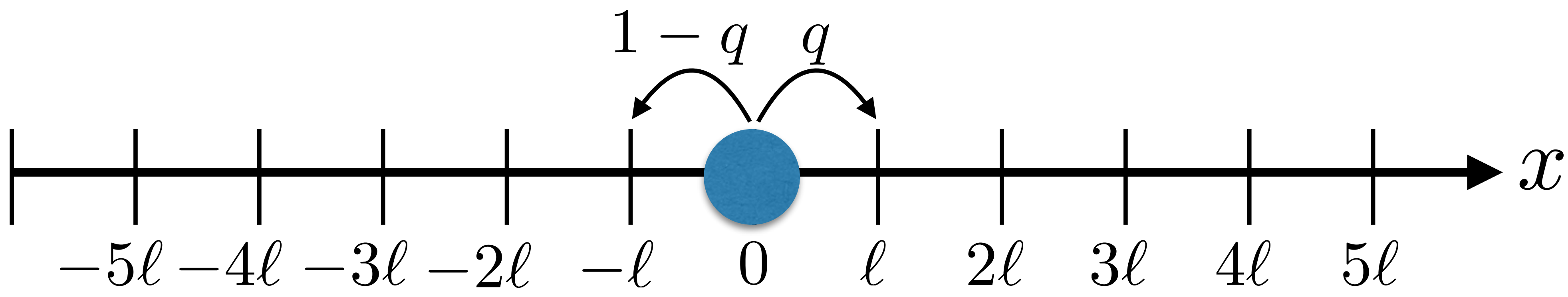
Number of distinct visited sites after *N* steps

1D $N_{\text{vis}} \approx \sqrt{8N/\pi}$

2D $N_{\text{vis}} \approx \pi N/\ln(8N)$

3D $N_{\text{vis}} \approx 0.66N$

Master equation



Master equation provides recursive relation for the evolution of probability distribution, where $\Pi(x,y)$ describes probability for a jump from *y* to *x*.

$$p(x, N+1) = \sum_y \Pi(x,y) p(y,N)$$

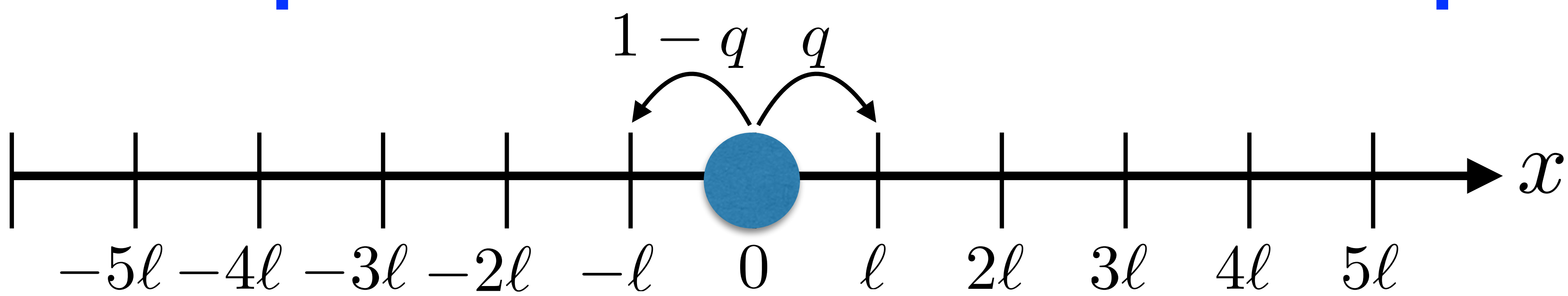
For our example the master equation reads:

$$p(x, N+1) = q\, p(x-\ell, N) + (1-q)\, p(x+\ell, N)$$

Initial condition: $p(x,0) = \delta(x)$

Probability distribution *p*(*x*,*N*) can be easily obtained numerically by iteratively advancing the master equation.

Master equation and Fokker-Planck equation



Assume that jumps occur in regular small time intervals: Δt

Master equation:

$$p(x, t + \Delta t) = q\, p(x - \ell, t) + (1 - q)\, p(x + \ell, t)$$

In the limit of small jumps and small time intervals, we can Taylor expand the master equation to derive an approximate drift-diffusion equation:

$$p + \Delta t \frac{\partial p}{\partial t} = q \left(p - \ell \frac{\partial p}{\partial x} + \frac{1}{2} \ell^2 \frac{\partial^2 p}{\partial x^2} \right) + (1 - q) \left(p + \ell \frac{\partial p}{\partial x} + \frac{1}{2} \ell^2 \frac{\partial^2 p}{\partial x^2} \right)$$

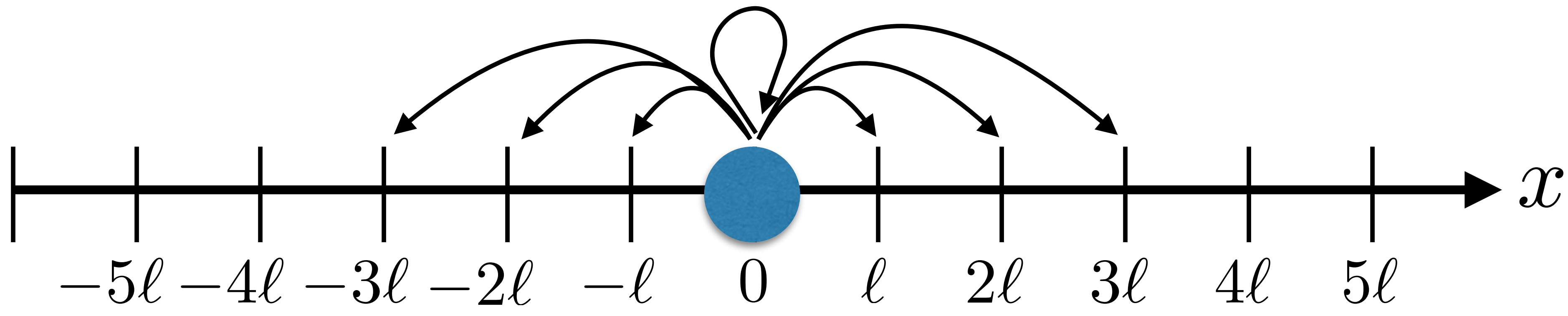
Fokker-Planck equation:

$$\frac{\partial p}{\partial t} = -v \frac{\partial p}{\partial x} + D \frac{\partial^2 p}{\partial x^2}$$

drift velocity $v = (2q - 1) \dfrac{\ell}{\Delta t}$

diffusion coefficient $D = \dfrac{\ell^2}{2 \Delta t}$

Fokker-Planck equation



In general the probability distribution Π of jump lengths *s* can depend on the particle position *x*

$$\Pi(s|x)$$

Generalized master equation:

$$p(x, t + \Delta t) = \sum_s \Pi(s|x - s)p(x - s, t)$$

Again Taylor expand the master equation above to derive the Fokker-Planck equation:

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

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

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

Normalization condition

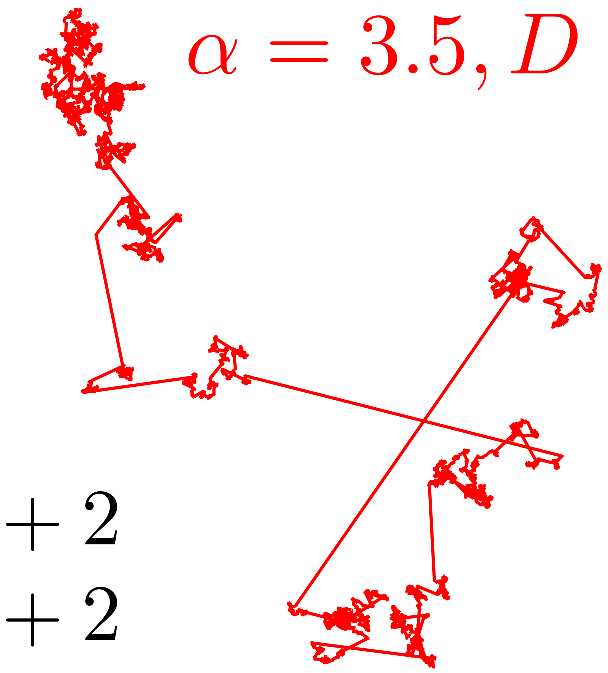
$$\int d^D\vec{s}\,\Pi(\vec{s}) = 1 \longrightarrow \alpha > D$$

Moments of distribution

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

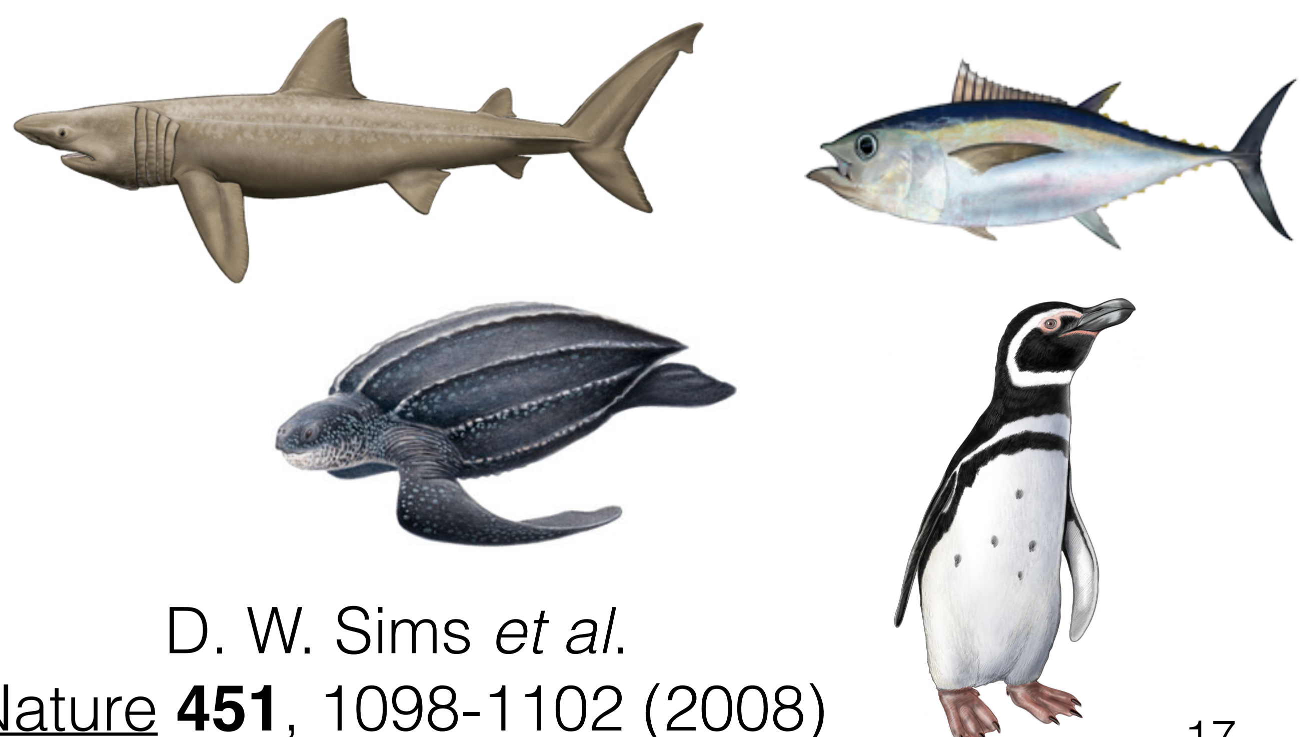
Lévy flight trajectory

$\alpha = 3.5, D = 2$



2D random walk trajectory

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



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

Probability current

Fokker-Planck equation

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

Conservation law of probability (no particles created/removed)

$$\frac{\partial p(x,t)}{\partial t} = -\frac{\partial J(x,t)}{\partial x}$$

Probability current:

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

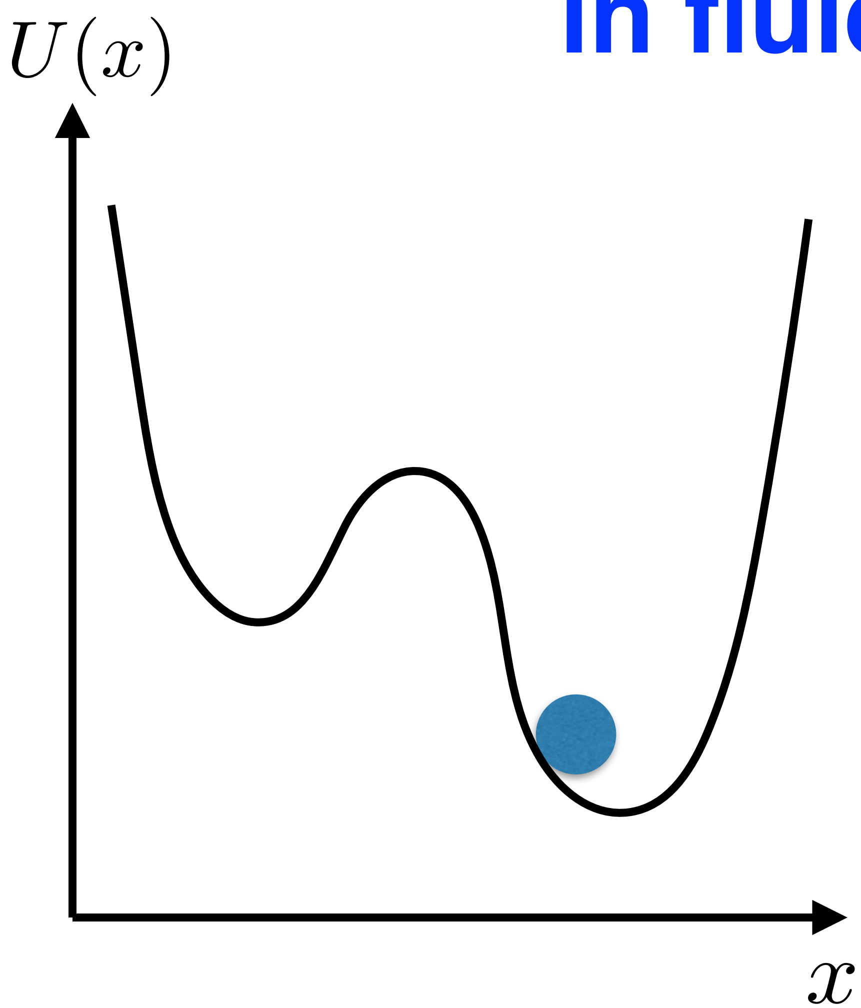
Note that for the steady state distribution, where $\partial p^*(x,t)/\partial t \equiv 0$ **the steady state current is constant and independent on *x***

$$J^* \equiv v(x)p^*(x) - \frac{\partial}{\partial x}\Big[D(x)p^*(x)\Big] = \text{const}$$

If we don't create/remove particles at boundaries then *J=0** → **Equilibrium probability distribution:**

$$p^*(x) \propto \frac{1}{D(x)} \exp\left[\int_{-\infty}^{x} dy \frac{v(y)}{D(y)}\right]$$

Spherical particle suspended in fluid in external potential



Newton's law:

$$m\frac{\partial^2 x}{\partial t^2} = -\lambda v(x) - \frac{\partial U(x)}{\partial x} + F_r$$

fluid drag — external potential force — random Brownian force

For simplicity assume overdamped regime: $\frac{\partial^2 x}{\partial t^2} \approx 0$

Drift velocity averaged over time $\langle v(x)\rangle = -\frac{1}{\lambda}\frac{\partial U(x)}{\partial x}$

R	**particle radius**
η	**fluid viscosity**
$\lambda = 6\pi\eta R$	**Stokes drag coefficient**
k_B	**Boltzmann constant**
T	**temperature**
D	**diffusion constant**

Equilibrium probability distribution

$$p^*(x) = Ce^{-U(x)/\lambda D} = Ce^{-U(x)/k_B T}$$

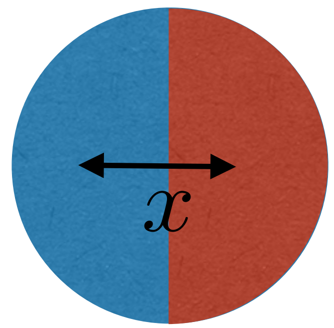
(see previous slide) **(equilibrium physics)**

Einstein - Stokes equation

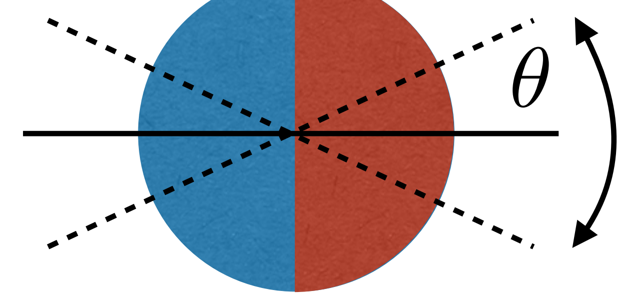
$$D = \frac{k_B T}{\lambda} = \frac{k_B T}{6\pi\eta R}$$

Translational and rotational diffusion for particles suspended in liquid

Translational diffusion



Rotational diffusion



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

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

Stokes viscous drag: $\lambda_T = 6\pi\eta R$

Stokes viscous drag: $\lambda_R = 8\pi\eta R^3$

Einstein - Stokes relation

$$D_T = \frac{k_B T}{6\pi\eta R}$$

Einstein - Stokes relation

$$D_R = \frac{k_B T}{8\pi\eta R^3}$$

Time to move one body length in water at room temperature

$$\langle x^2 \rangle \sim R^2 \longrightarrow t \sim \frac{3\pi\eta R^3}{k_B T}$$

$$R \sim 1\mu\text{m} \longrightarrow t \sim 1\text{s}$$

$$R \sim 1\text{mm} \longrightarrow t \sim 100\,\text{years}$$

Time to rotate by 90⁰ in water at room temperature

$$\langle \theta^2 \rangle \sim 1 \longrightarrow t \sim \frac{4\pi\eta R^3}{k_B T}$$

Boltzmann constant $k_B = 1.38 \times 10^{-23}\text{J/K}$

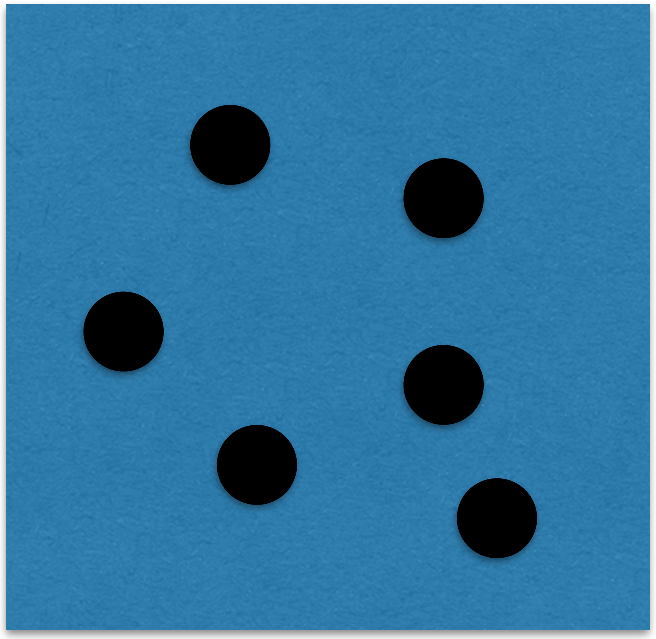
water viscosity $\eta \approx 10^{-3}\text{kg}\,\text{m}^{-1}\text{s}^{-1}$

room temperature $T = 300\text{K}$

Fick's laws

Adolf Fick 1855

N noninteracting Brownian particles



Local concentration of particles

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

Fick's laws are equivalent to Fokker-Plank equation

First Fick's law

Flux of particles

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

Second Fick's law

Diffusion of particles

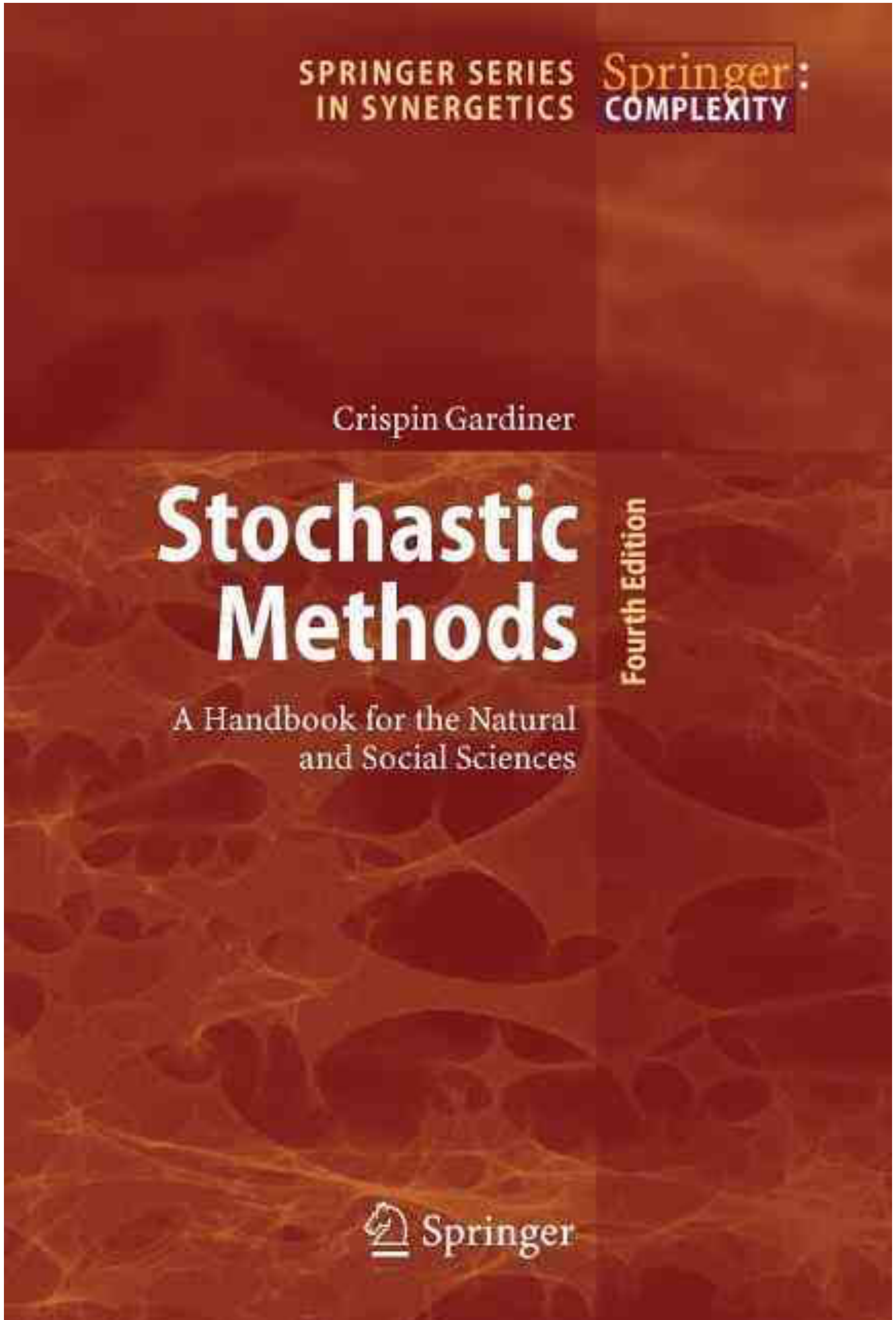
$$\frac{\partial c}{\partial t} = -\frac{\partial J}{\partial x} = -\frac{\partial}{\partial x}\Big[vc\Big] + \frac{\partial}{\partial x}\Big[D\frac{\partial c}{\partial x}\Big]$$

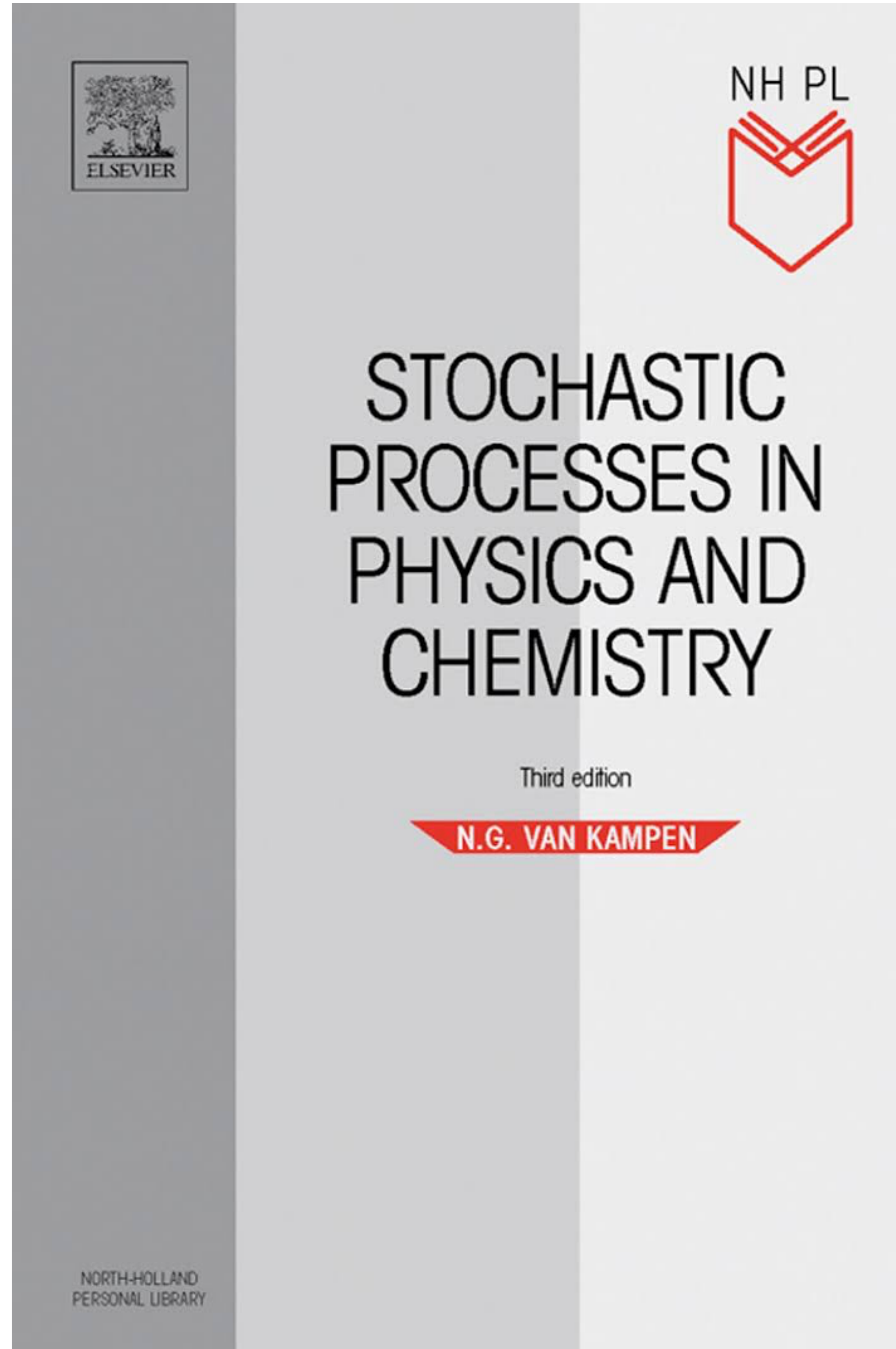
Generalization to higher dimensions

$$\vec{J} = c\vec{v} - D\vec{\nabla}c$$

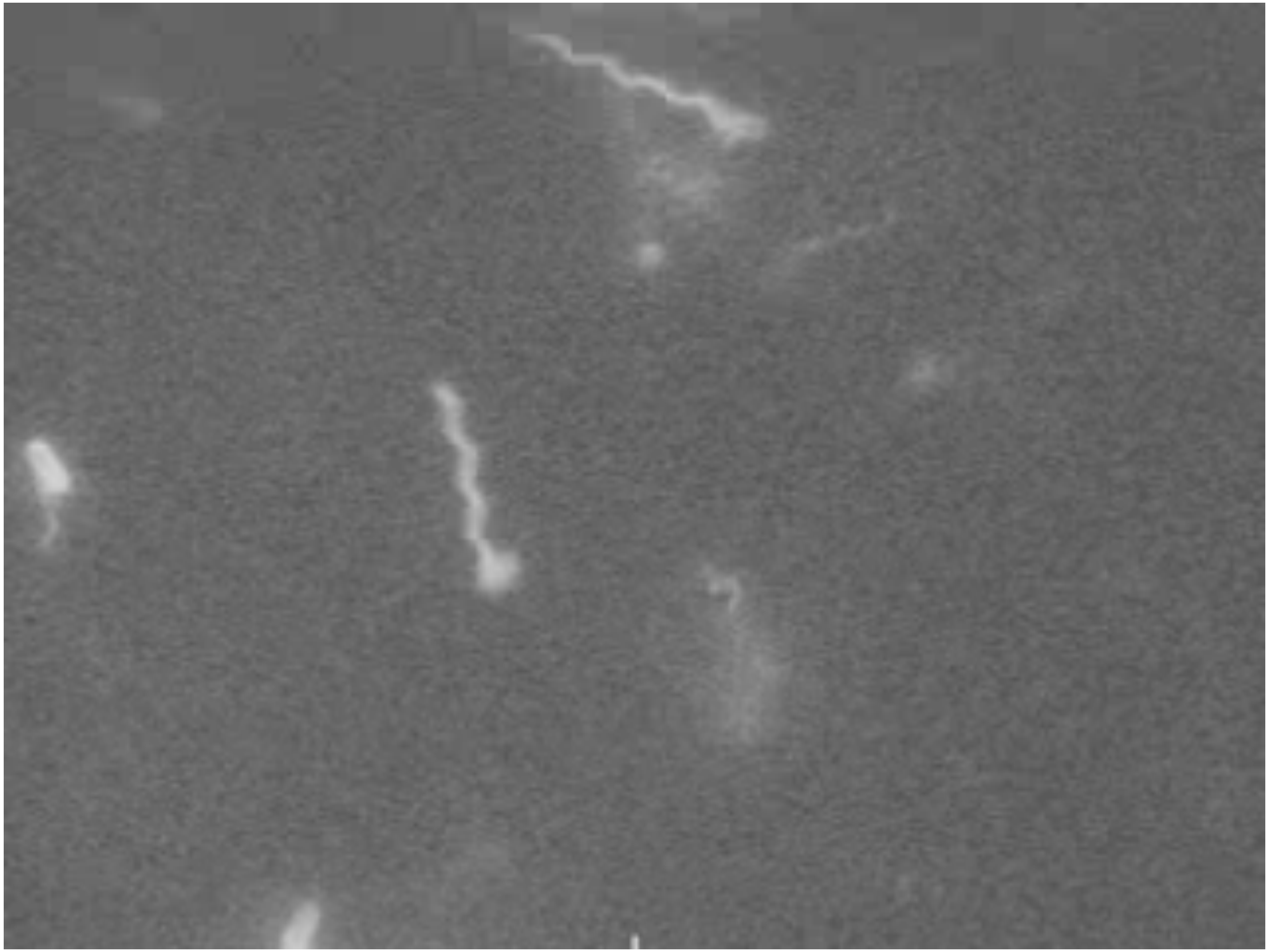
$$\frac{\partial c}{\partial t} = -\vec{\nabla}J = -\vec{\nabla}\cdot(c\vec{v}) + \vec{\nabla}\cdot(D\vec{\nabla}c)$$

Further reading



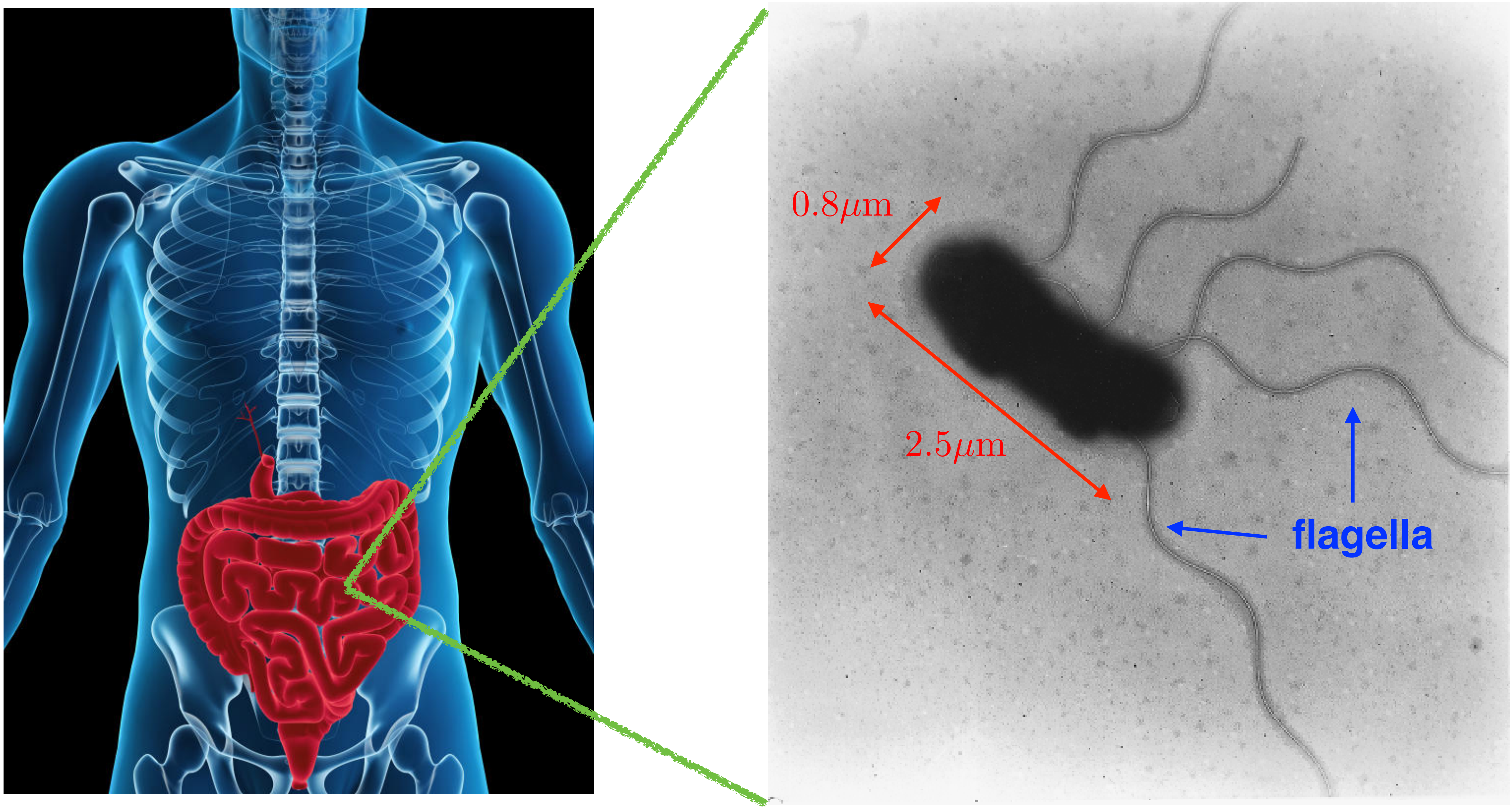


E. coli chemotaxis



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.

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

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

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

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

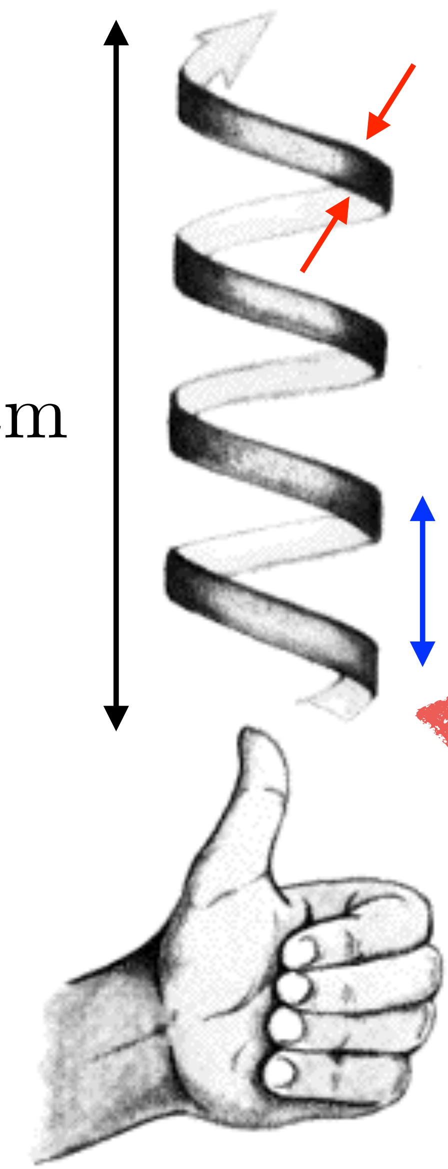
$\approx 20\text{nm}$

length

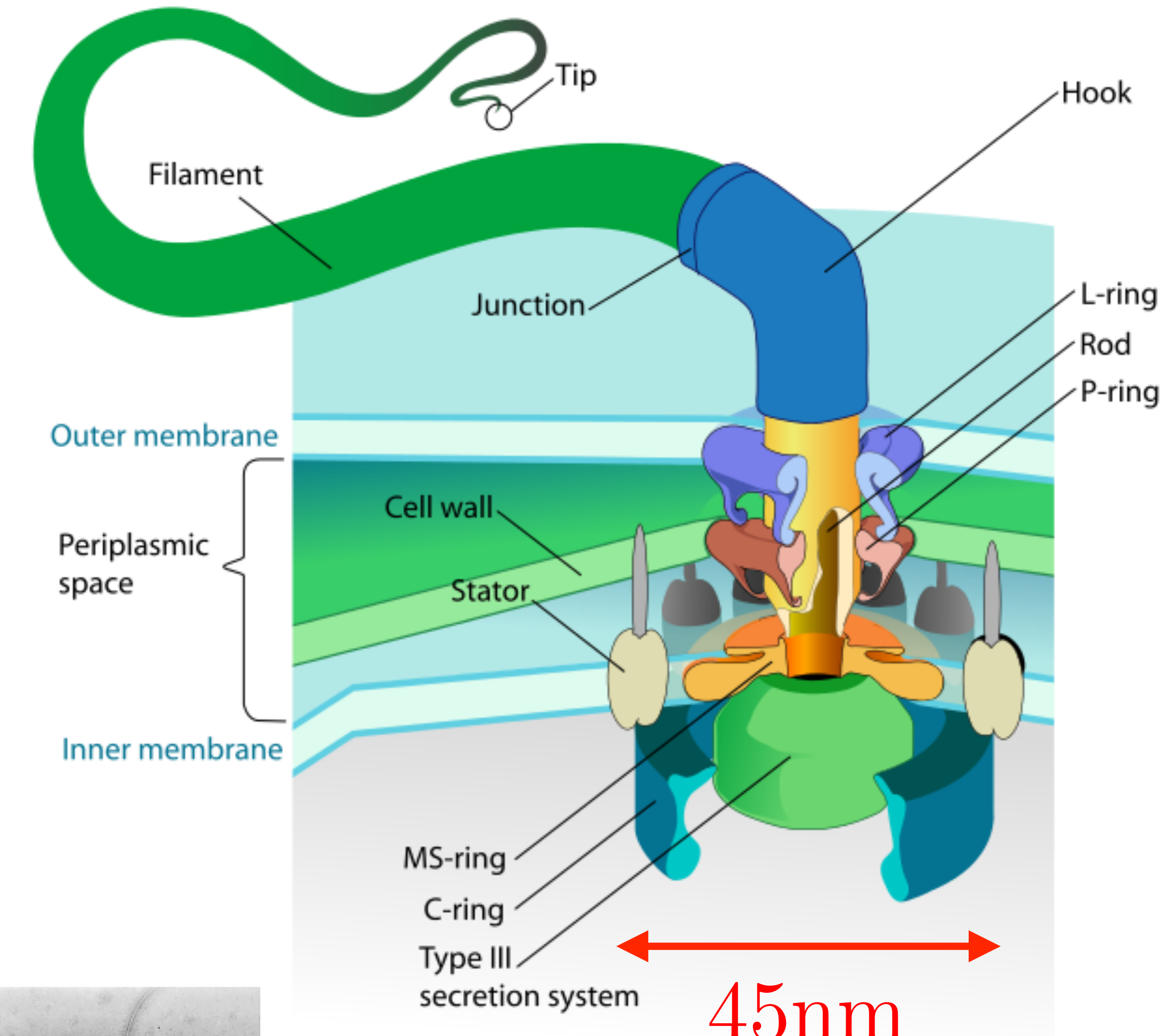
$L \lesssim 10\mu\text{m}$

pitch

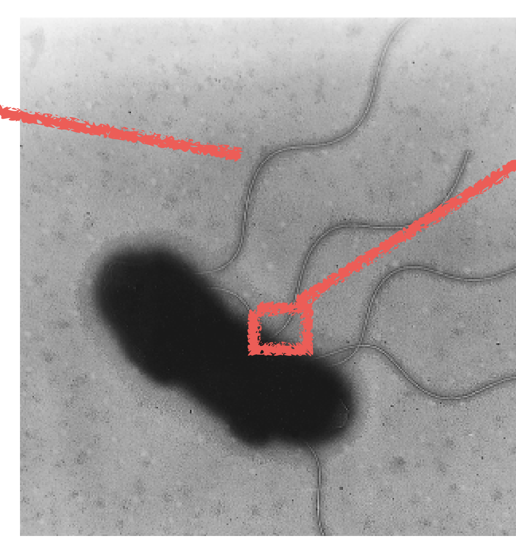
$p \approx 2.3\mu\text{m}$



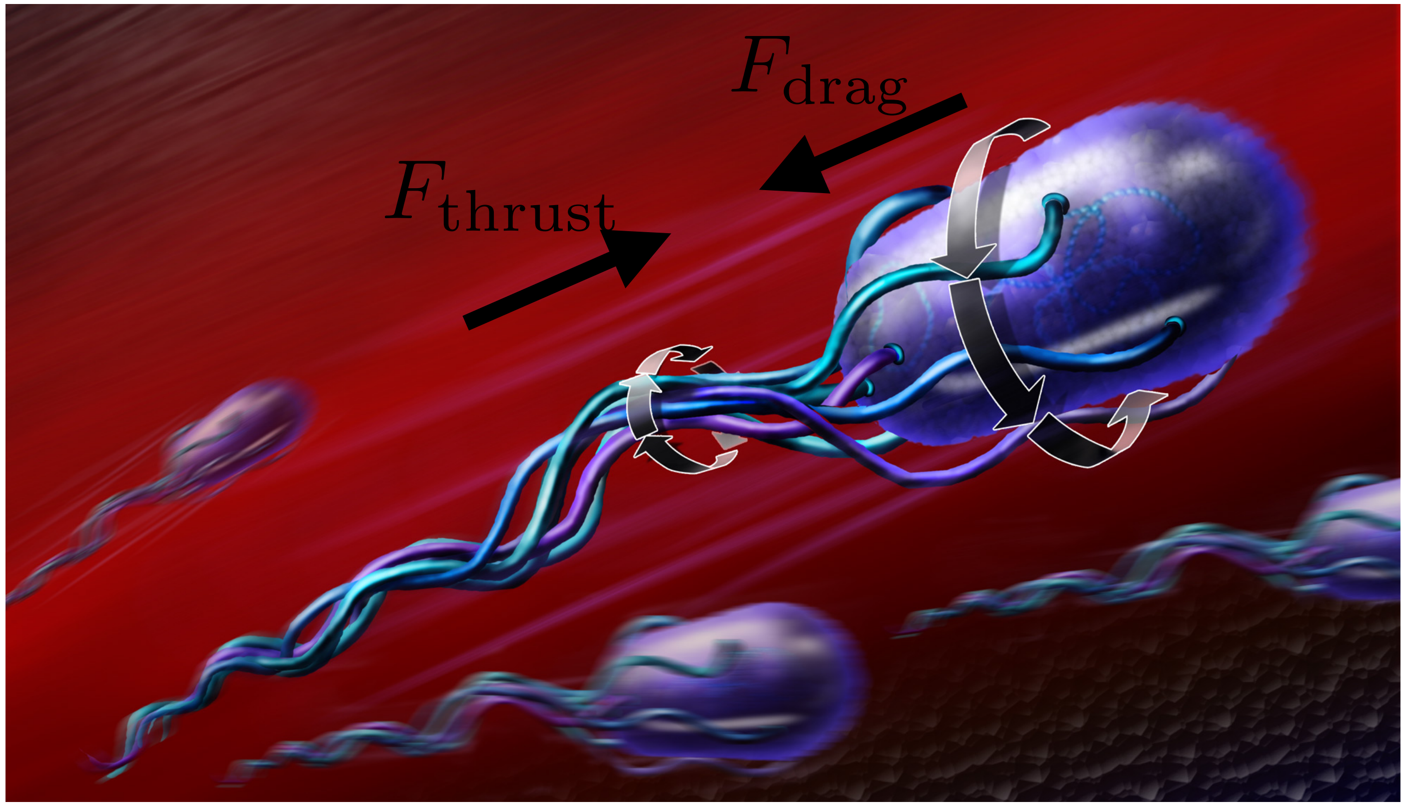
Rotary motor



45nm



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

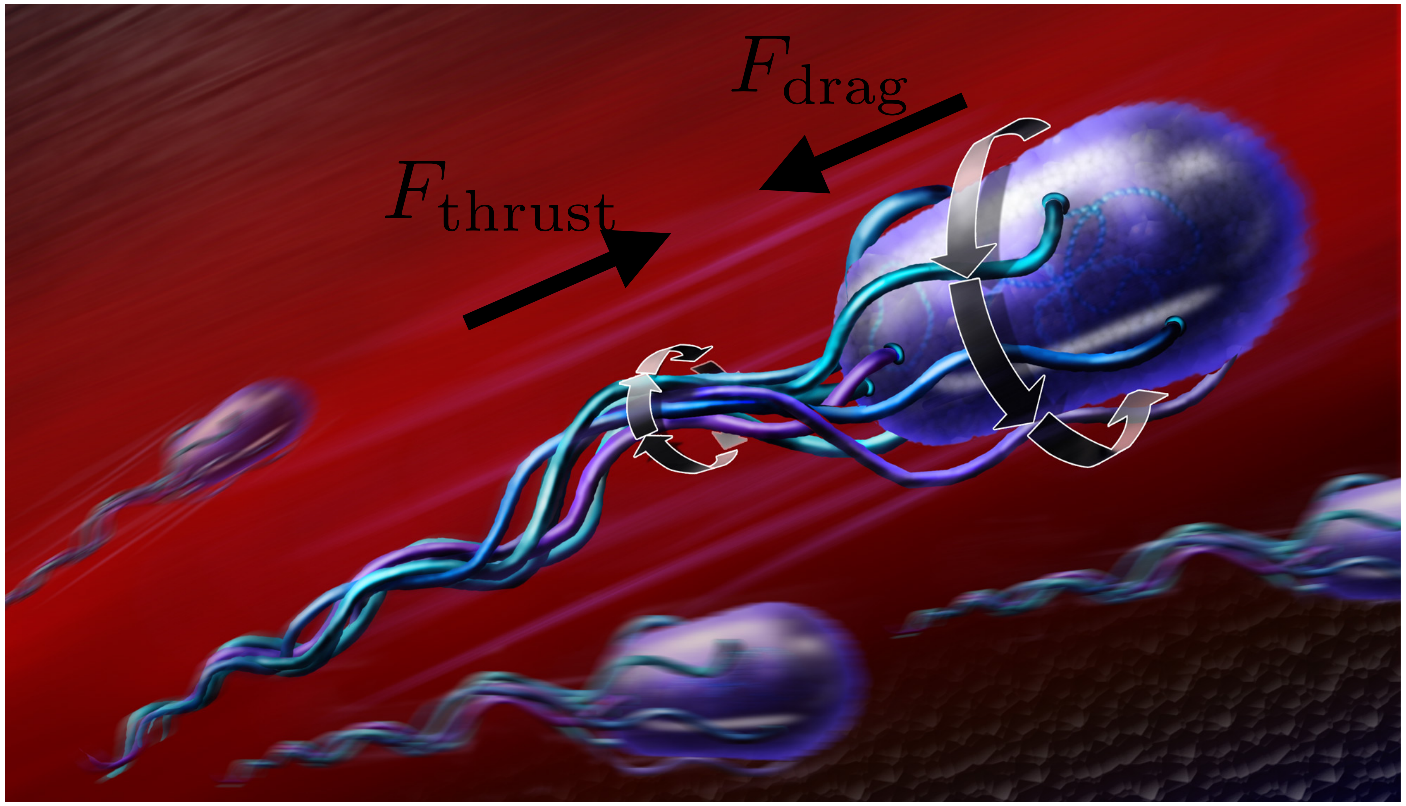
$$N = N_{\text{drag}} \approx 8\pi\eta R^3 \omega_b$$

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

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

$$m\ddot{x} = -6\pi\eta R\dot{x}$$

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

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

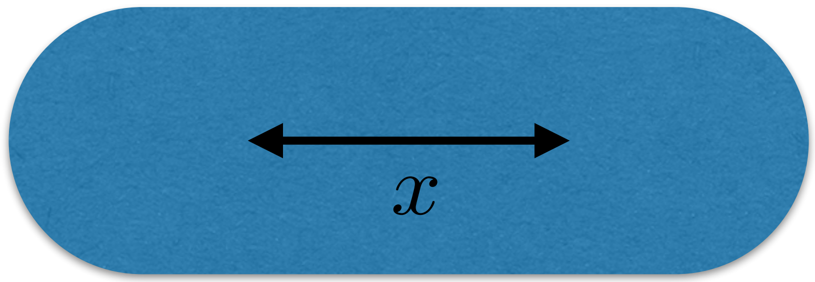
$$x_0 = v_s\tau \sim 0.1\text{Å}$$

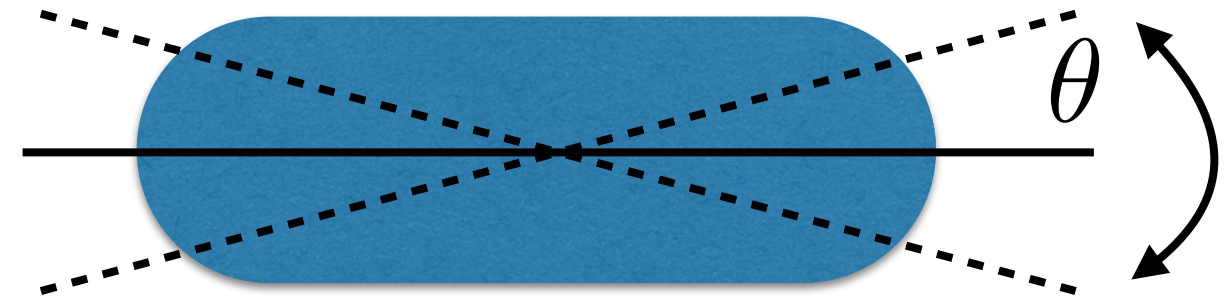
E. coli stops almost instantly!

signature of low Reynolds numbers

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

Translational and rotational diffusion of E. coli





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

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

Einstein - Stokes relation

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

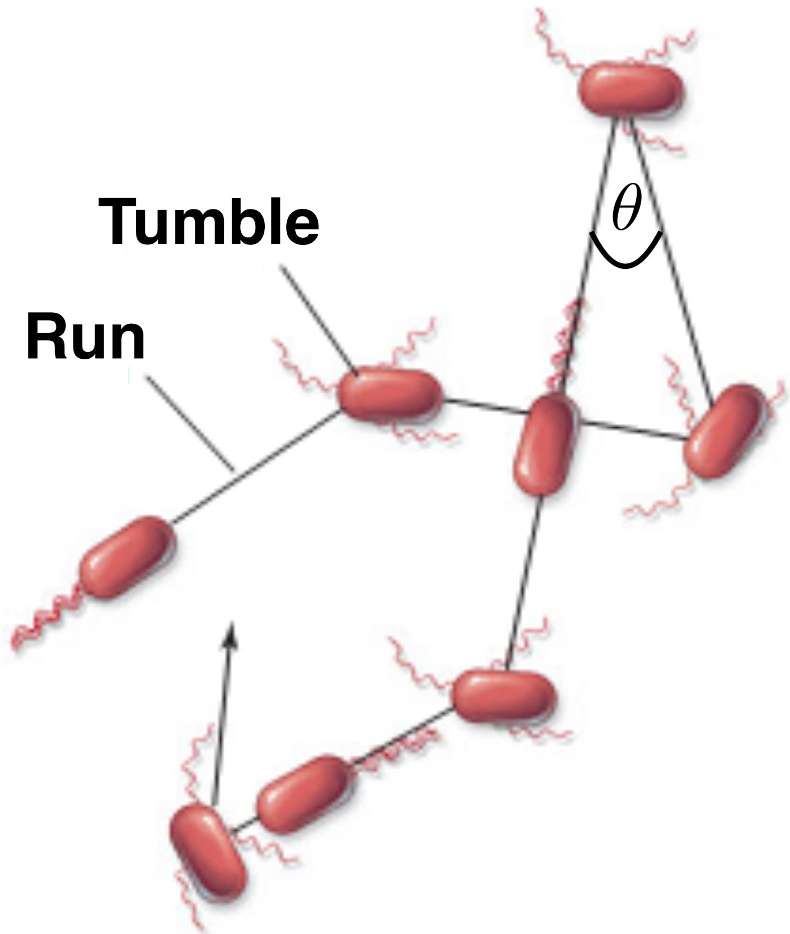
Einstein - Stokes relation

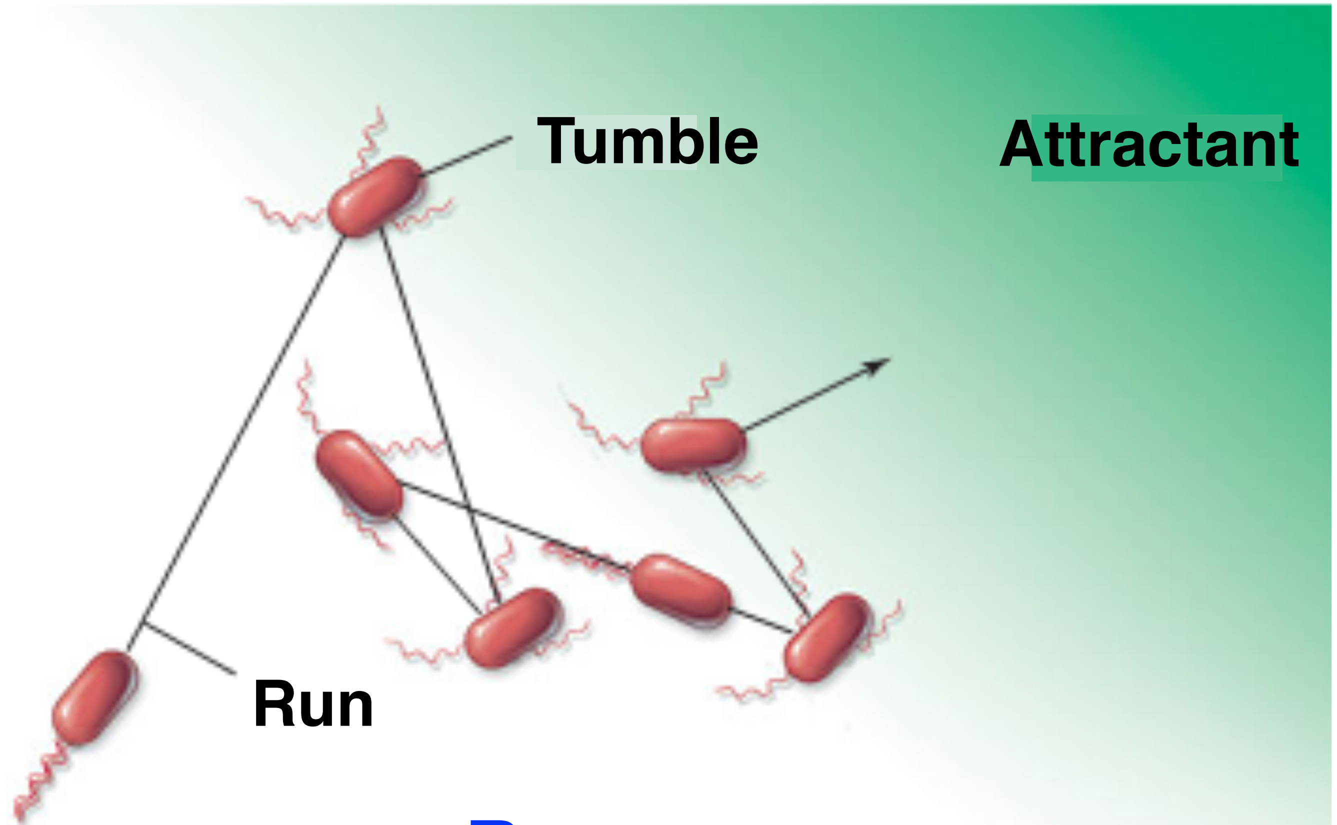
$$D_R \approx \frac{k_B T}{8\pi\eta R^3} \sim 0.2\,\mathrm{rad}^2/\mathrm{s}$$

After ~10s the orientation of E. coli changes by 90⁰ due to the Brownian motion!

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

E. coli chemotaxis





Run

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

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

all motors turning counter clockwise

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

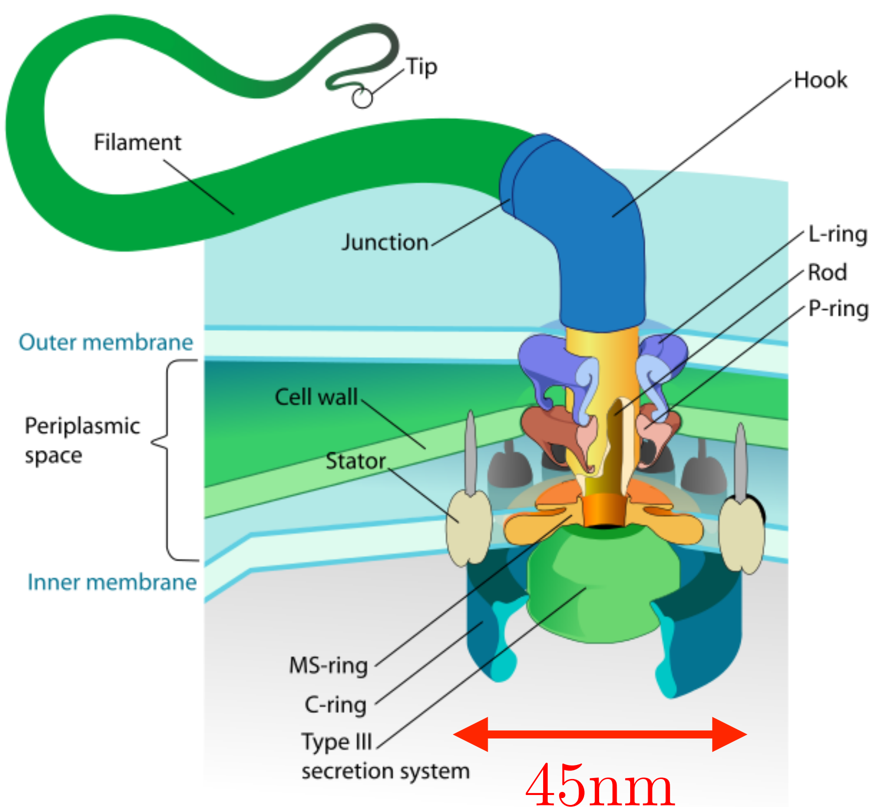
Tumble

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

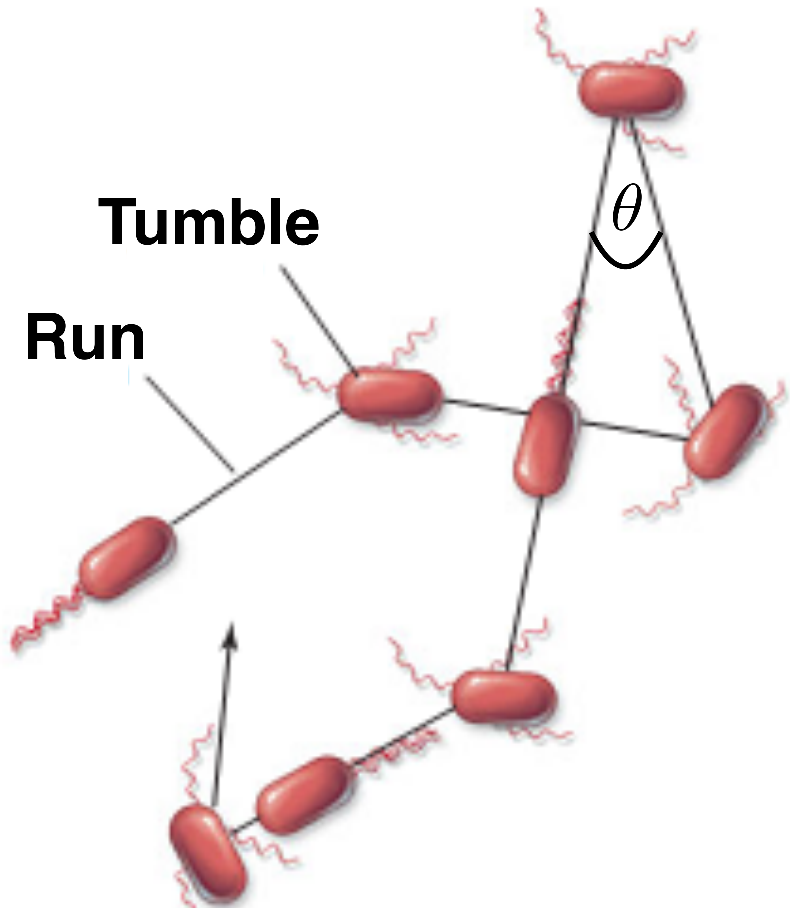
typical duration: $t_t \sim 0.1\text{s}$

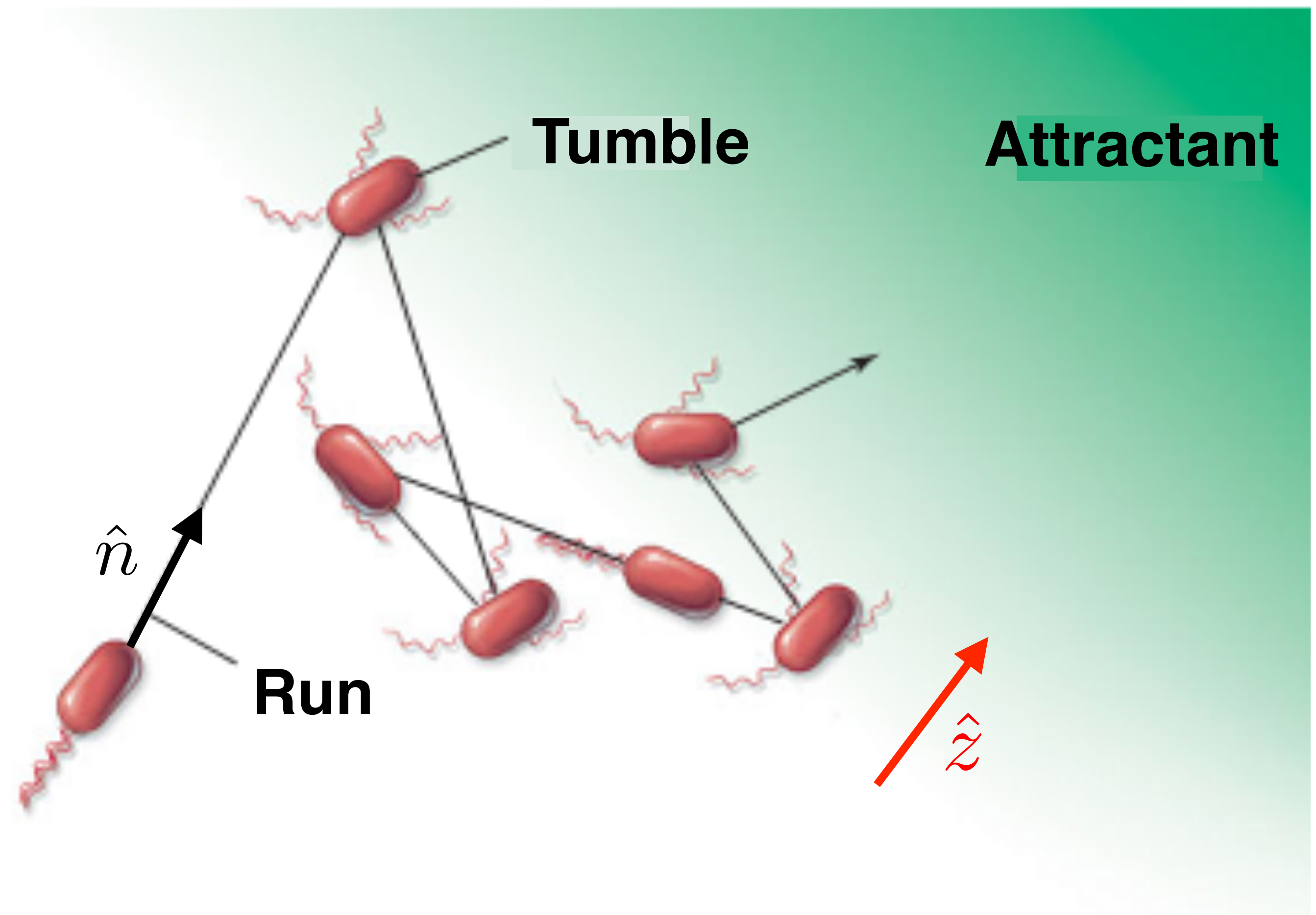
one or more motors turning clockwise

Rotary motor



E. coli chemotaxis





Homogeneous environment

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

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

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

drift velocity

$$v_d = 0$$

effective diffusion

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

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

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

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

$$\langle \Delta z \rangle = \langle v_z(\hat{n}) t_r(\hat{n}) \rangle = \langle v_s(\hat{n} \cdot \hat{z}) t_r(\hat{n}) \rangle$$

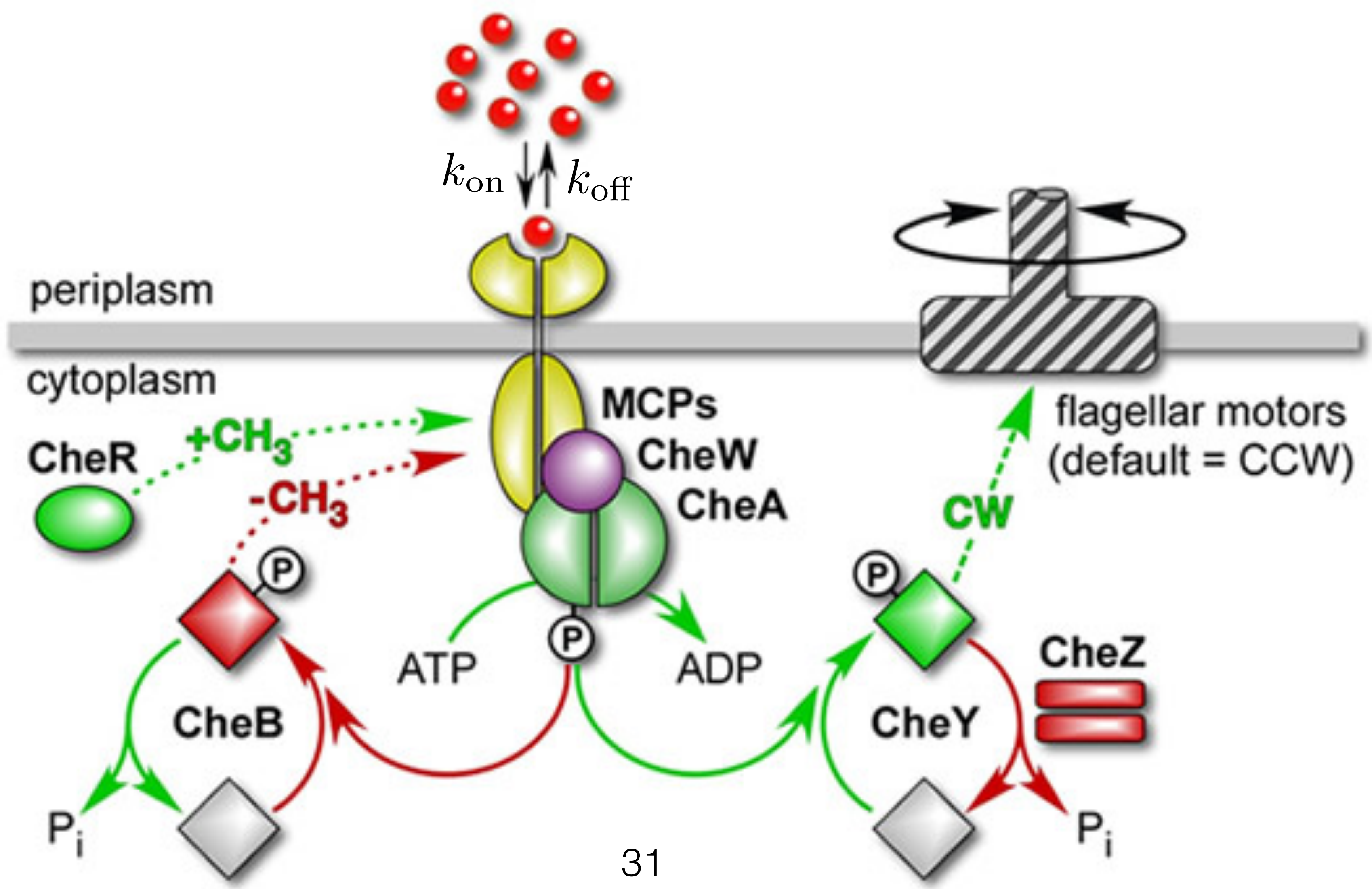
Sensing of environment

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

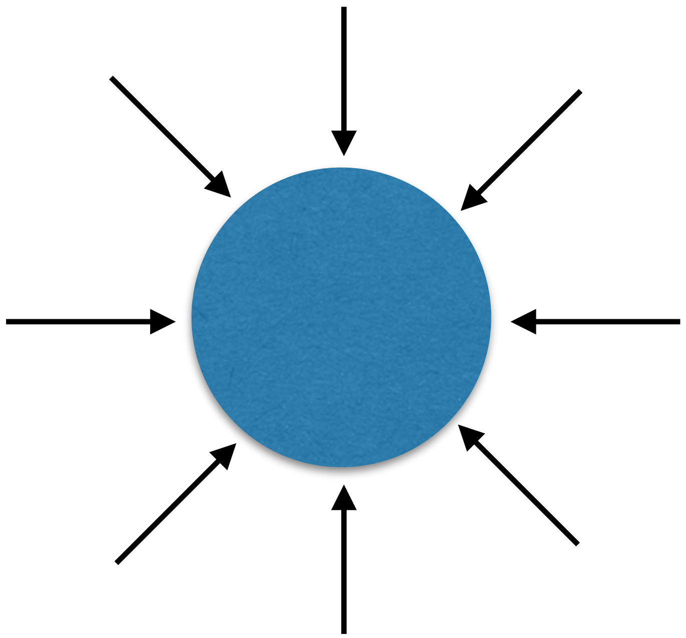
Average fraction of bound receptors p_B is related to concentration c of molecules.

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

Chemical signaling 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

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

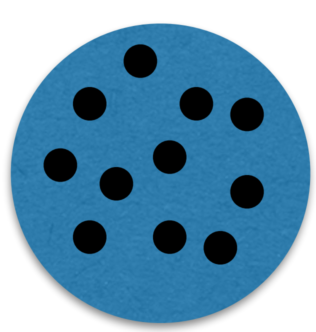
flux density of molecules

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

rate of absorbing molecules

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

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



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

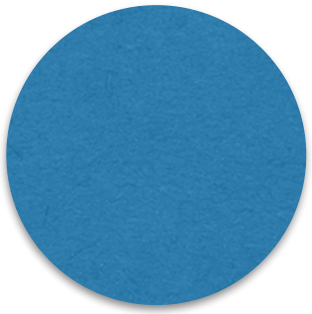
$$N = \pi R/s \sim 3000$$

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

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

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

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!

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

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

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

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

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

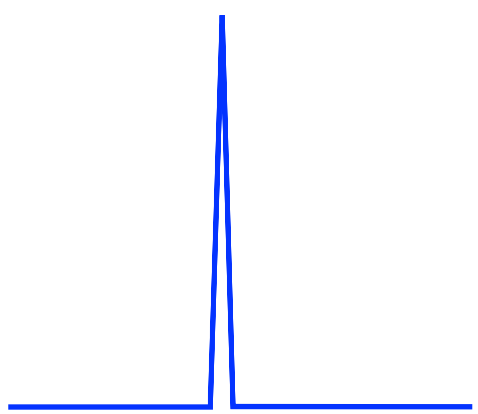
Molar concentration

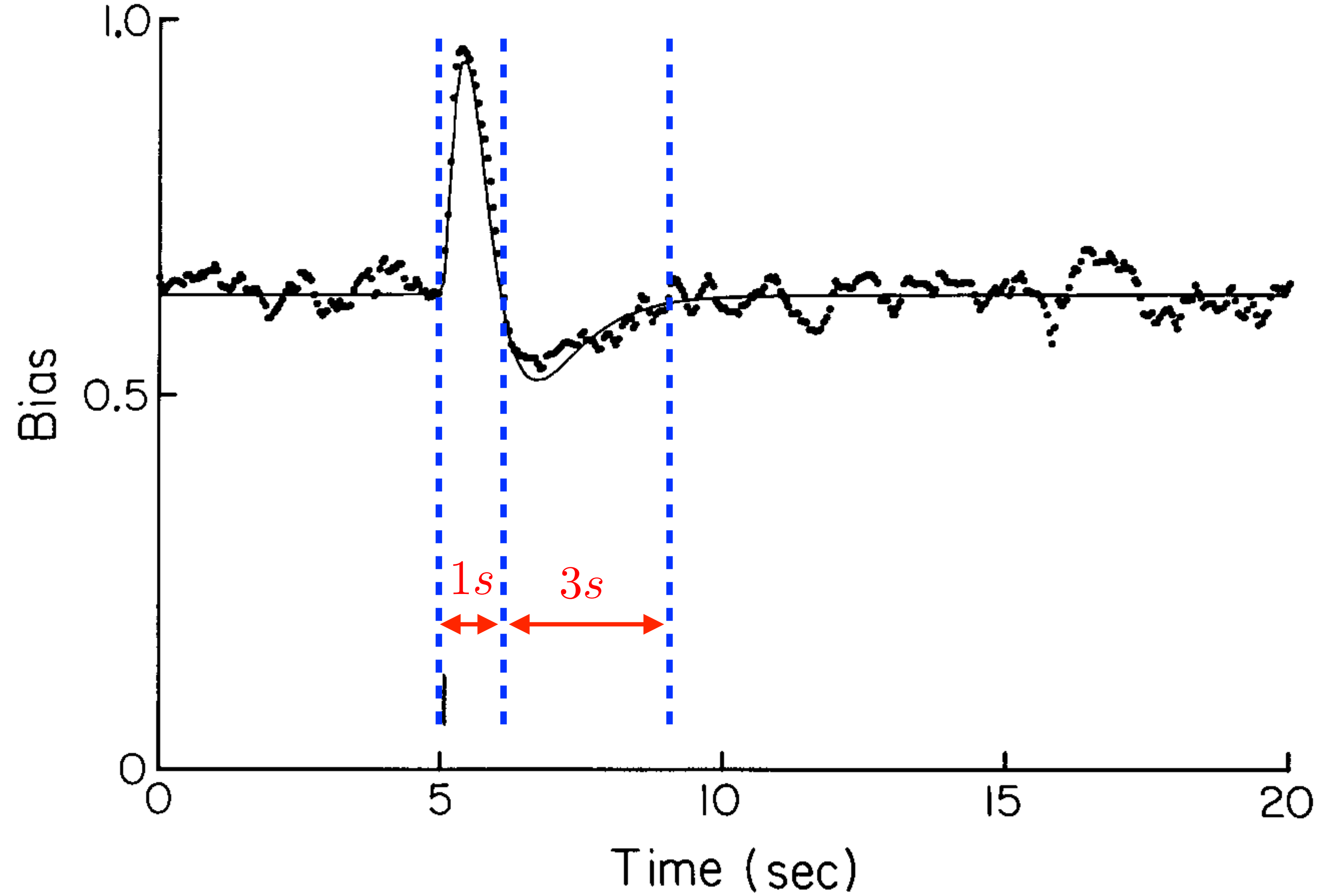
$$1M = 6 \times 10^{26}\text{m}^{-3}$$

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





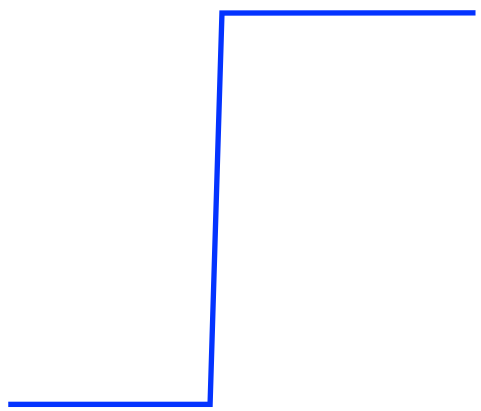
E. coli integrates measured concentration observed during the last second and compare this with measured concentration during the previous 3 seconds. If difference is positive then increase the probability of runs, otherwise increase the probability of tumbles.

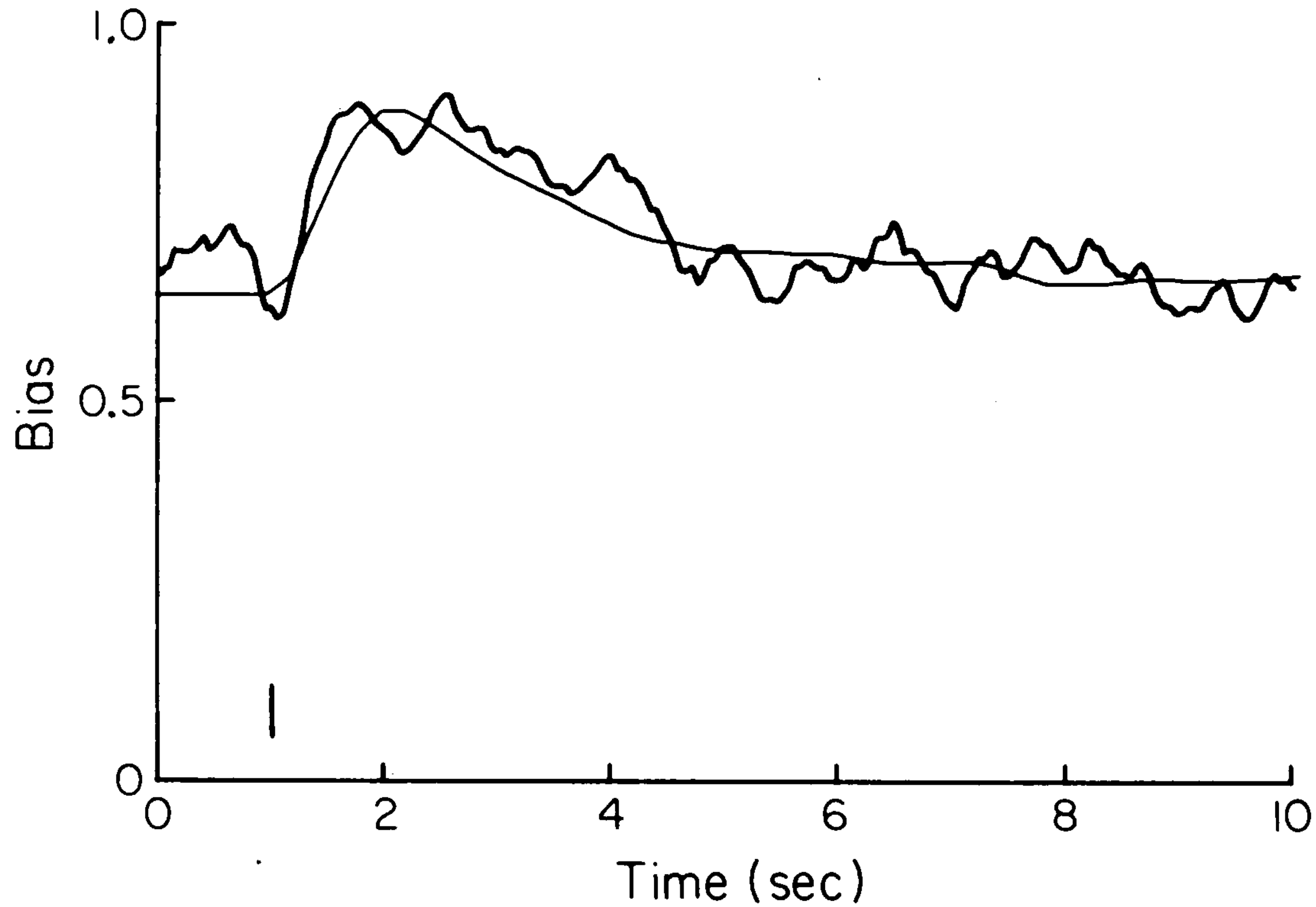
J. E. Segall, S. M. Block, and H. C. Berg, PNAS **83**, 8987–8991 (1986)

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!

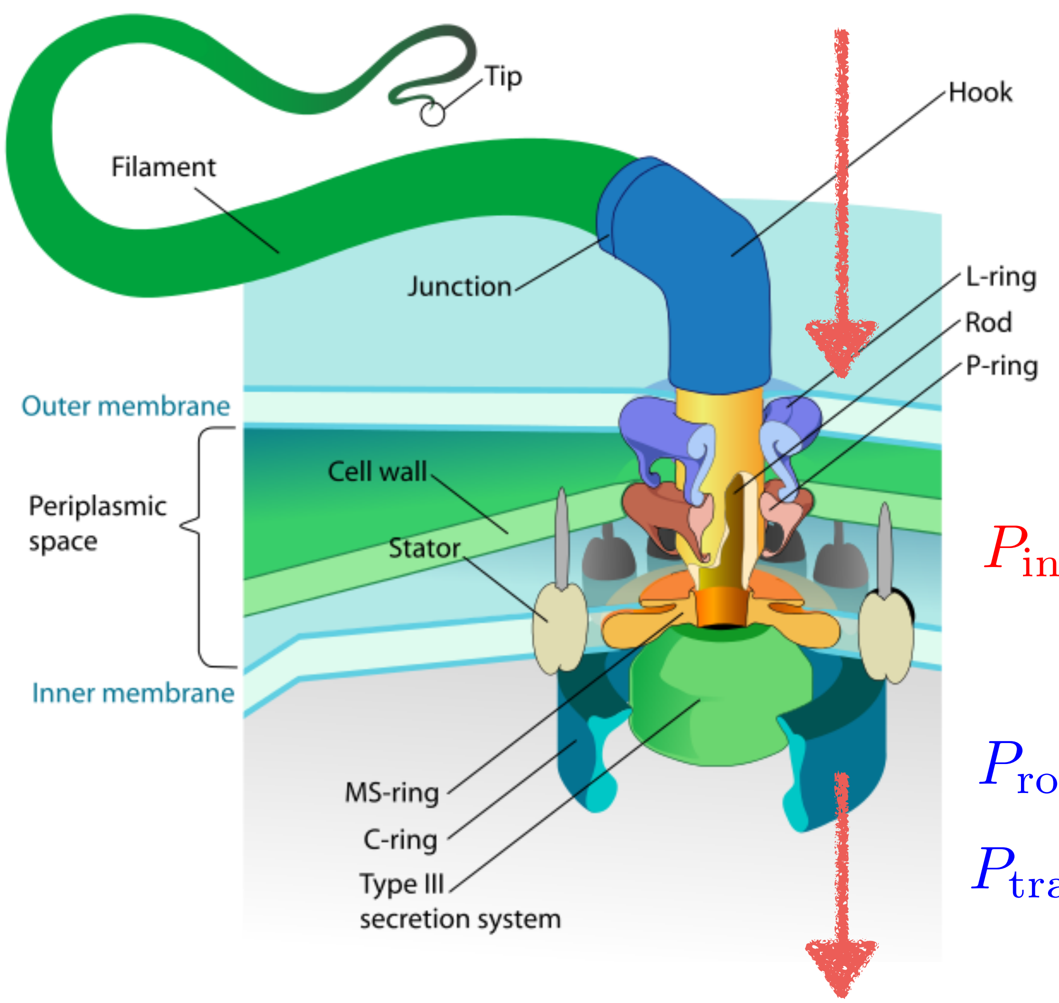
J. E. Segall, S. M. Block, and H. C. Berg,
PNAS **83**, 8987–8991 (1986)

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

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

Change in pH

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

Total protonmotive force

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

Need 1200 protons per one body revolution

Input power

$$P_{\text{in}} = n \times e\Delta p \times f = 1200 \times 0.17\text{eV} \times 10\text{Hz} \approx 3.2 \times 10^5 \text{pN nm/s}$$

Power loss due to Stokes drag

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

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

Motor efficiency

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

pH value of solutions

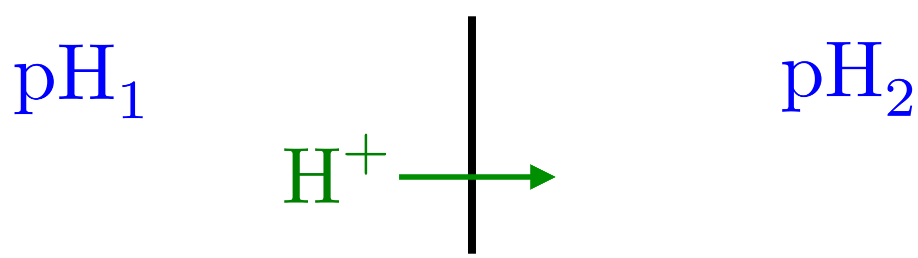
$$\frac{[\mathrm{H}^+][\mathrm{OH}^-]}{c_0^2} = \frac{[\mathrm{H_2O}]K_{\mathrm{eq}}(T,p)}{c_0^2} \approx 10^{-14}$$

$$c_0 = 1\mathrm{M}$$

at room temperature

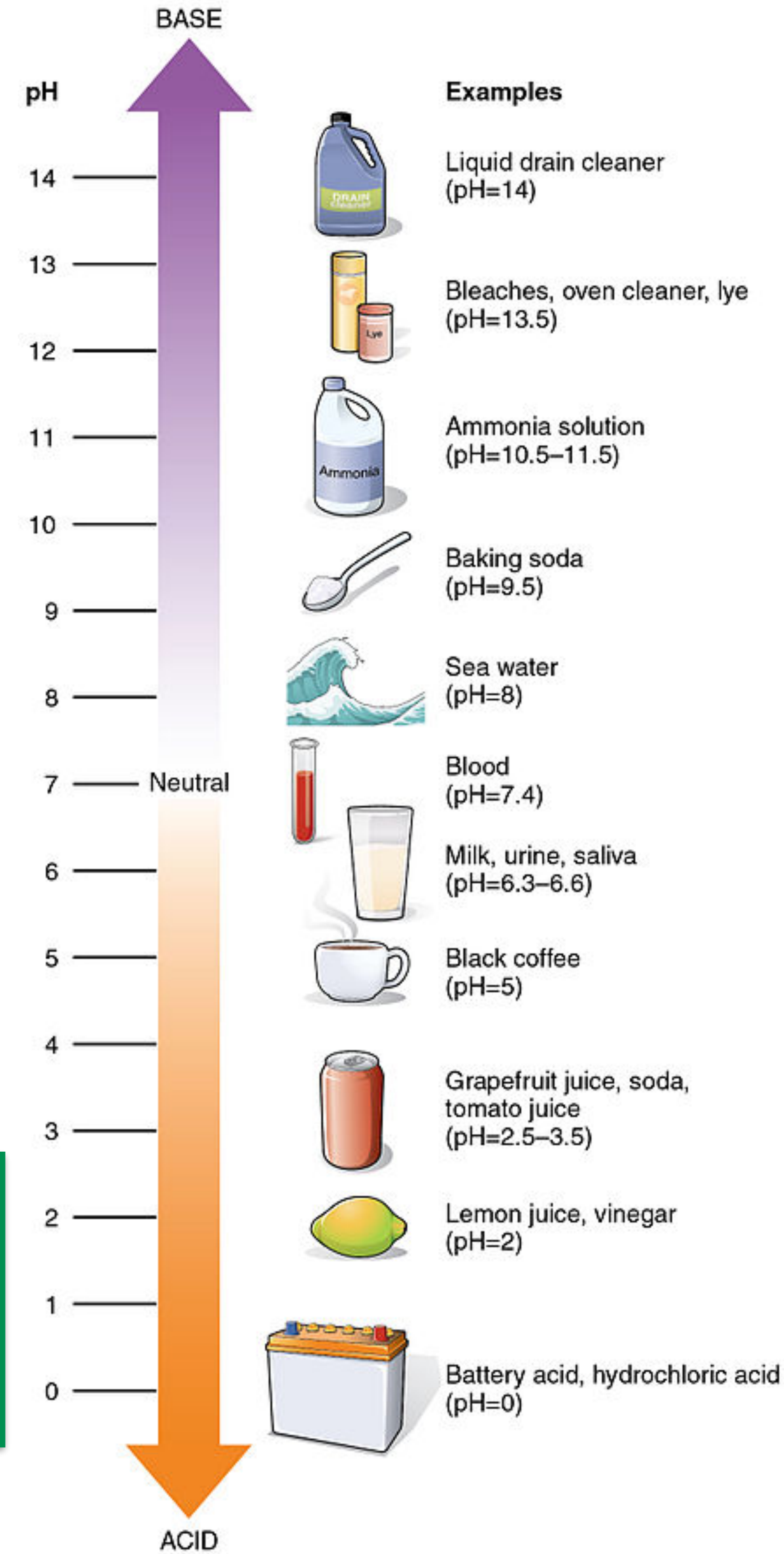
$$\mathrm{pH} = -\log_{10}\left([\mathrm{H}^+]/c_0\right)$$
$$\mathrm{pOH} = -\log_{10}\left([\mathrm{OH}^-]/c_0\right) \approx 14 - \mathrm{pH}$$

How much free energy is changed when H^+ goes to environment with different pH?



$$\mu_2 - \mu_1 = k_B T \ln\left([\mathrm{H}^+]_2/[\mathrm{H}^+]_1\right)$$
$$E = \frac{\mu_2 - \mu_1}{e_0} \approx -\frac{2.3026\, k_B T}{e_0}(\mathrm{pH}_2 - \mathrm{pH}_1)$$

Nernst electric potential *E*



Further reading