Lecture 9: Directed motion in the cell

Goal: Introduce directed motion, driven by non-equilibrium, energy consuming processes.

- Overview of classes of motors
- Ratchet estimates

PBOC Chapter 16.1, 16.3.3

Diffusion in the cell

Active vs. passive transport

Active	Passive
directed motion	passive random walk
something does work	Brownian motion = diffusion (thermal)
energy is consumed	$\langle x^2 \rangle \propto Dt$

Directed motion in the cell

What forms of energy are used?

ATP

GTP

concentration gradient

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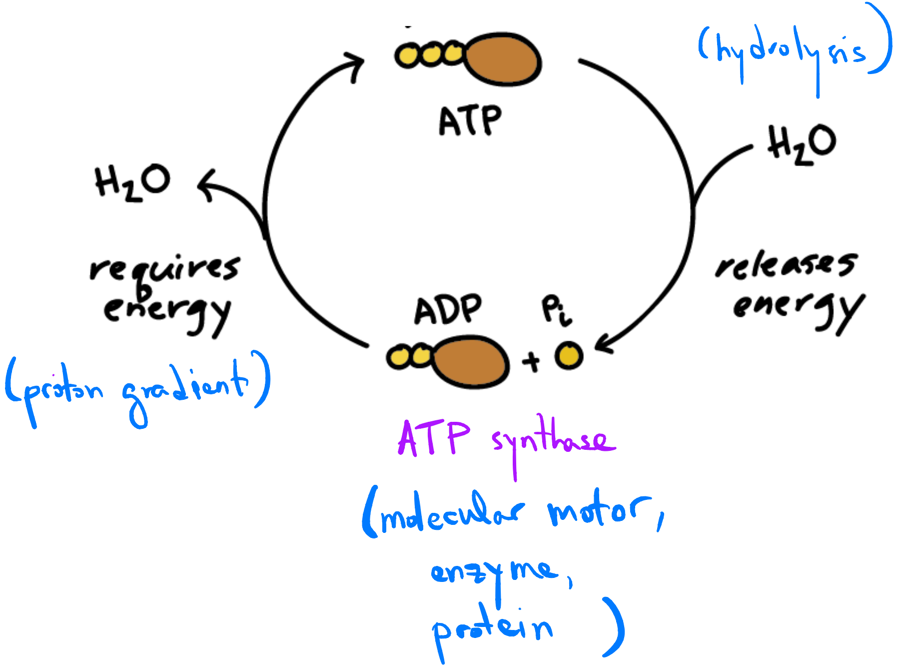
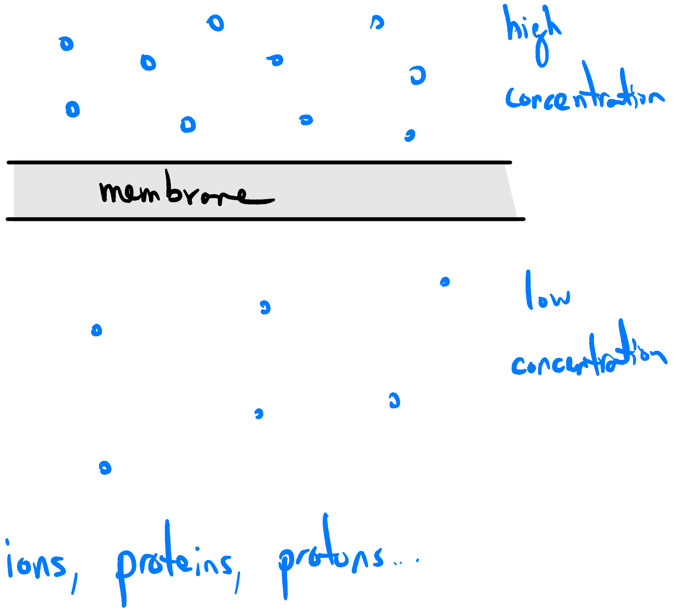
heat engines : thermal gradient

Directed motion in the cell

What forms of energy are used?





Directed motion in the cell

Mechanisms

i) Translational motors
ii) Rotary motors
iii) Polymerization ratchets
iv) Translocation ratchets

Directed motion in the cell

Translational motors

used for walking along actin or microtubules

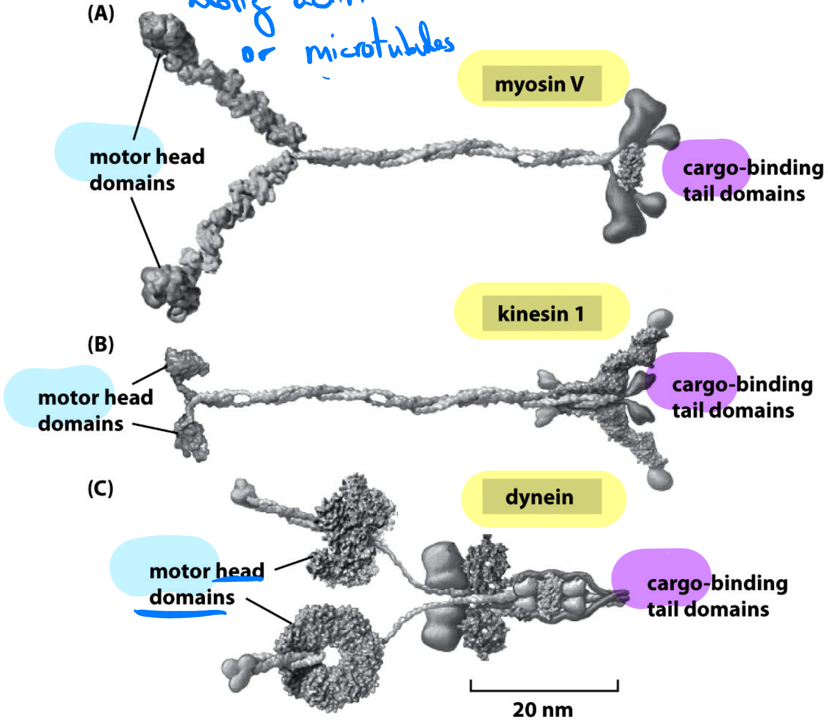


Figure 16.2 Physical Biology of the Cell (© Garland Science 2009)

- Transport vesicles or organelles along cytoskeleton (actin, microtubules)
- Muscle contraction

Force exerted: $F = \frac{E}{\Delta x} = \frac{20\ k_BT}{8\ nm}$ (ATP; kinesin)

$\approx 10\ pN$

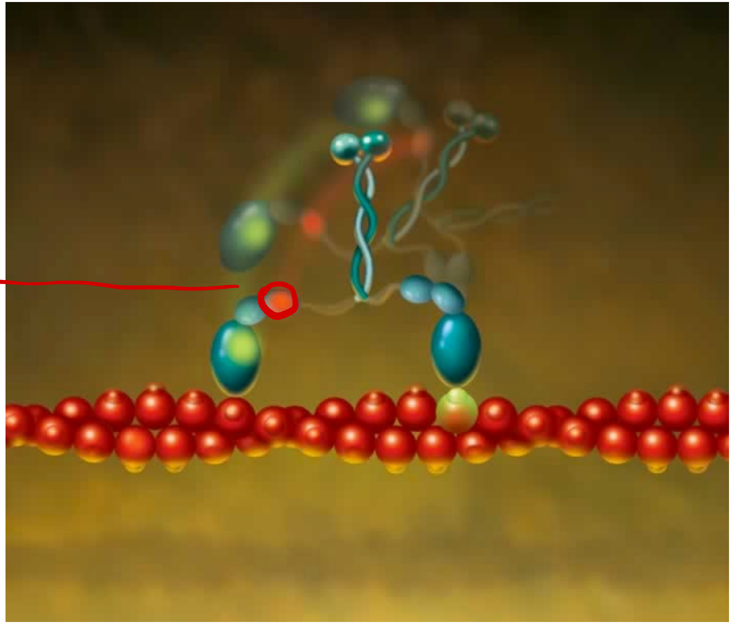
assuming all energy is converted to force

in reality $\sim 60\%$

Directed motion in the cell

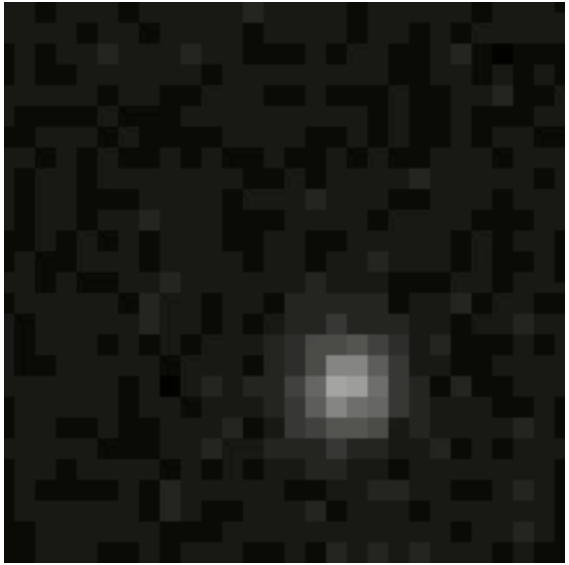
Translational motors

Experiment:



Directed motion in the cell

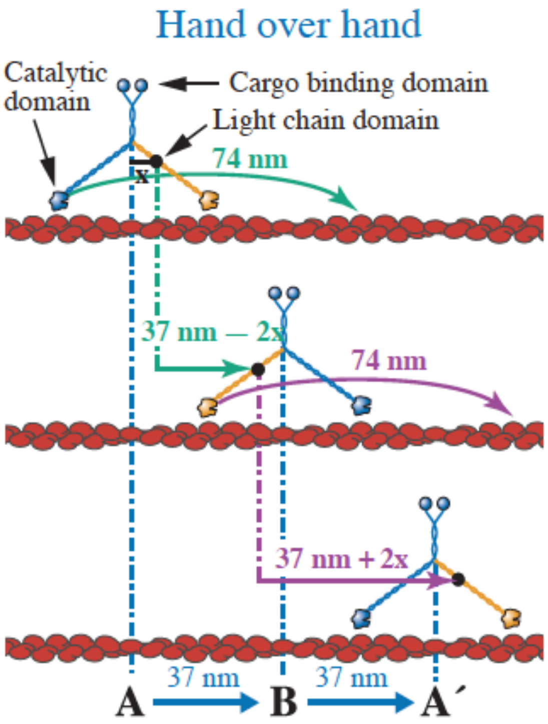
Translational motors

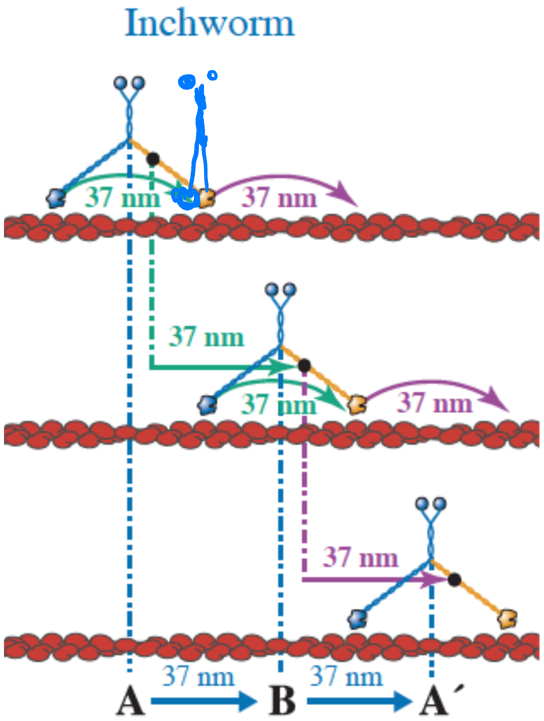


Movement of a single fluorescent dye attached to myosin V for the lower right trace shown in Fig. 3. Each pixel is 86 nm. Discrete steps are clearly visible. The intensity is in gray-scale.

Directed motion in the cell

Translational motors

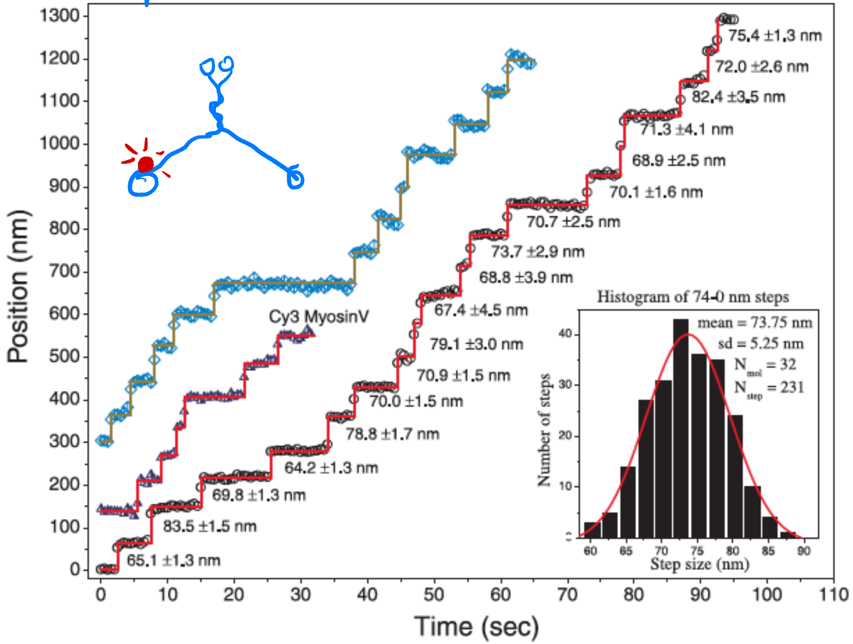




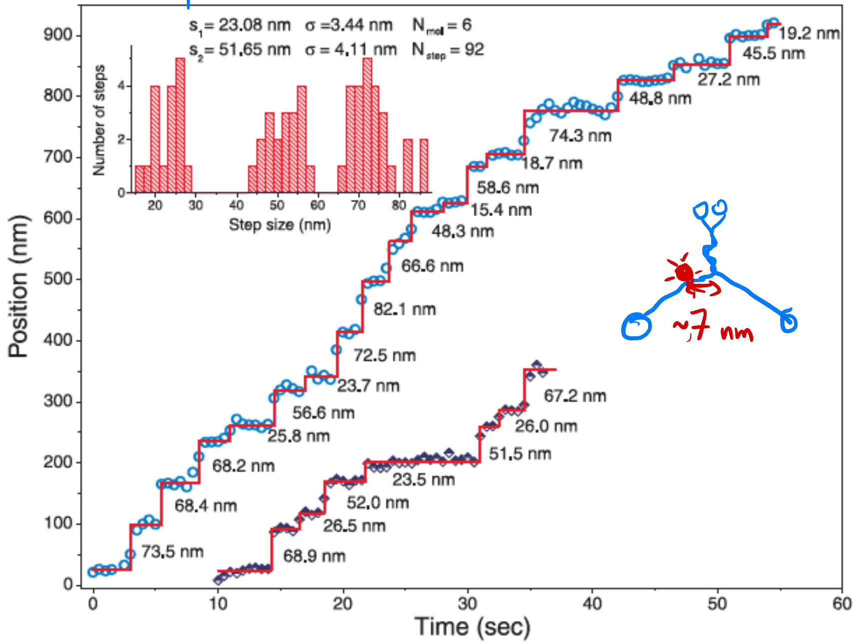
Directed motion in the cell

Translational motors

Dye attached to end of molecule.



Dye attached between end and CM.

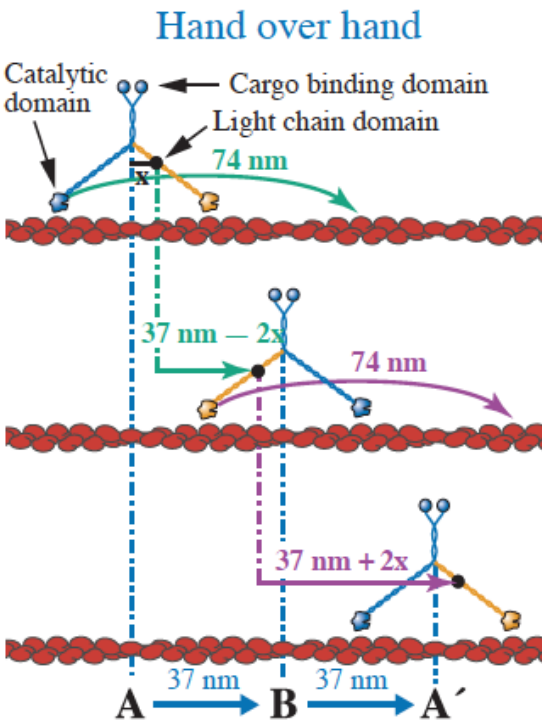


$37 - 2x \simeq 23$

$37 + 2x \simeq 52$

$x \simeq 7$ nm

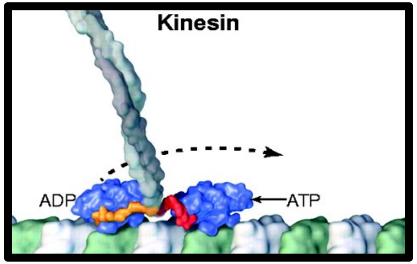
Directed motion in the cell



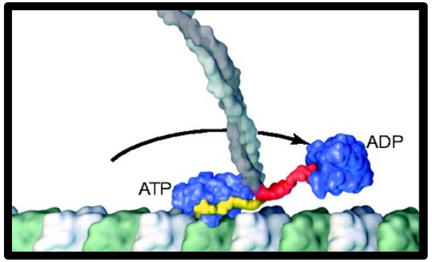
Myosin V Walks Hand-Over-Hand: Single Fluorophore Imaging with 1.5-nm Localization

Ahmet Yildiz,[1] Joseph N. Forkey,[3] Sean A. McKinney,[1,2] Taekjip Ha,[1,2] Yale E. Goldman,[3] Paul R. Selvin[1,2*]

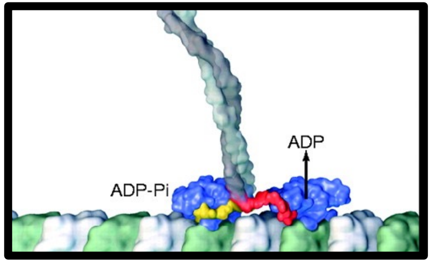
Directed motion in the cell



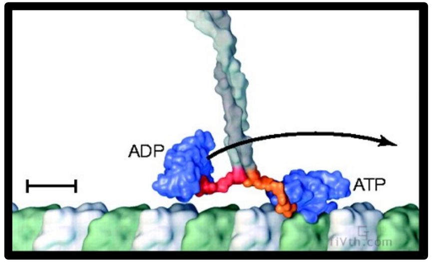
1. Both catalytic cores, “heads” (blue) are bound to tubulin (green/white). Mechanical element is the neck linker (red/orange)



2. ATP binding to the leading head allows the neck linker to dock (yellow). This throws the trailing head forward.



3. After a random diffusional search, the new leading head docks onto the tubulin binding site. This completes the 80 Å displacement step.



4. ADP dissociates, then ATP binds to the leading head and the neck linker begins to zipper onto the core (orange). The trailing head, which has released its Pi and detached its neck linker (red) from the core, is in the process of being thrown forward.

molecular animation

Directed motion in the cell

Rotational motors

Use chemical gradient across membrane to generate torque.

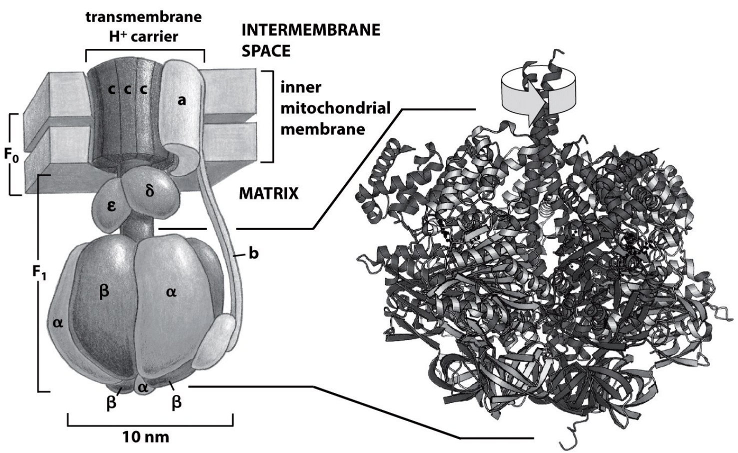


Figure 16.13b Physical Biology of the Cell (© Garland Science 2009)

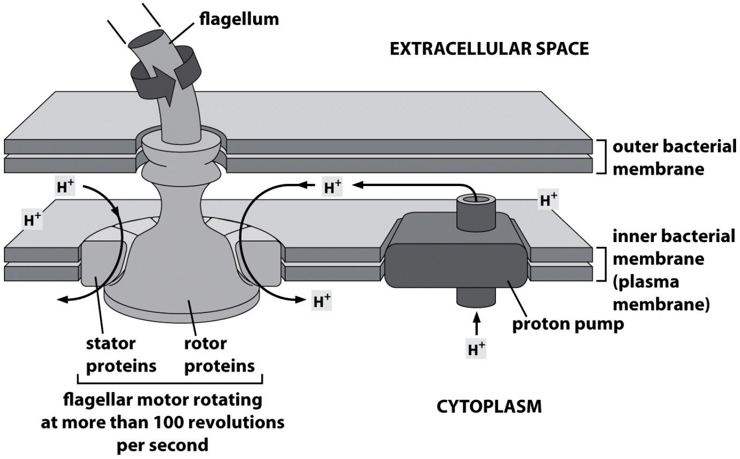
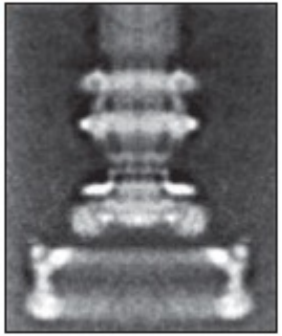


Figure 16.13a Physical Biology of the Cell (© Garland Science 2009)



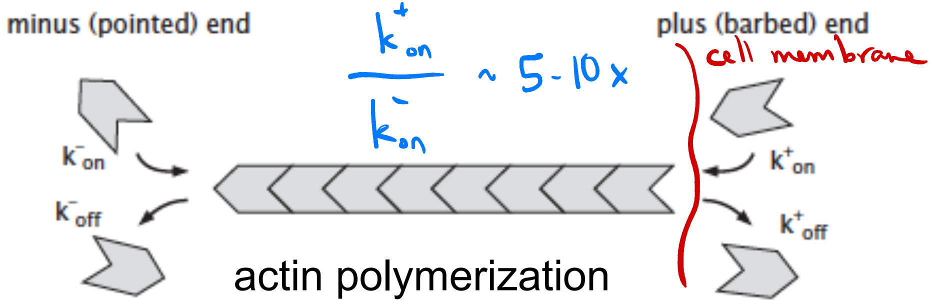
ATP synthase

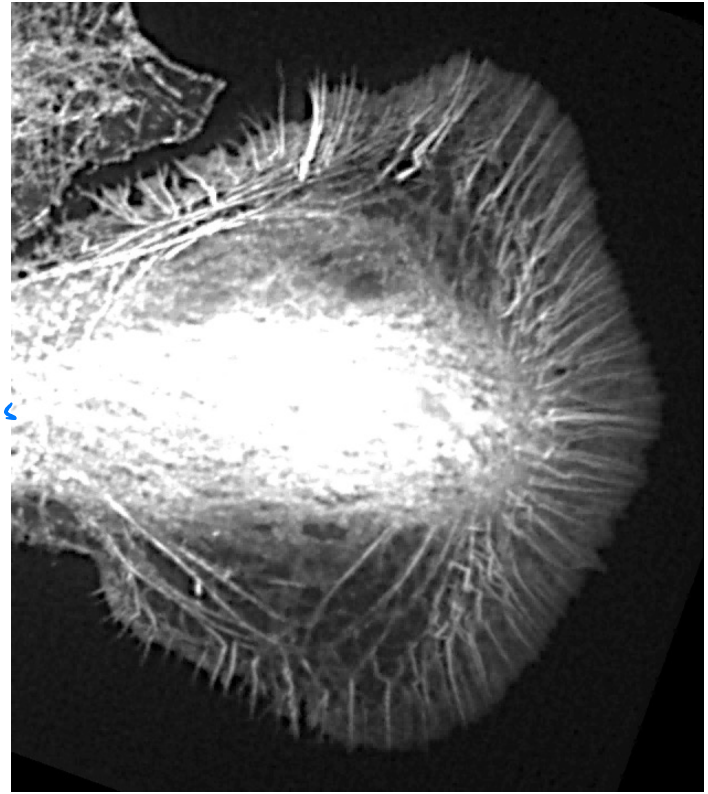
bacterial flagellum

https://www.youtube.com/watch?v=cwDRZGj2nnY

Directed motion in the cell

Polymerization motors / ratchet

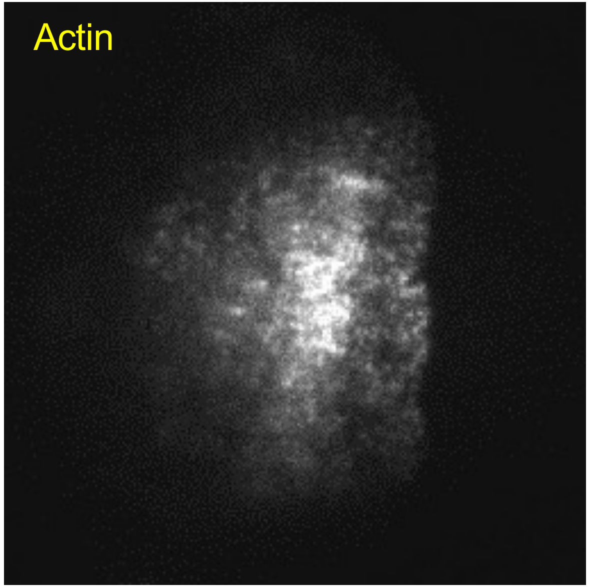


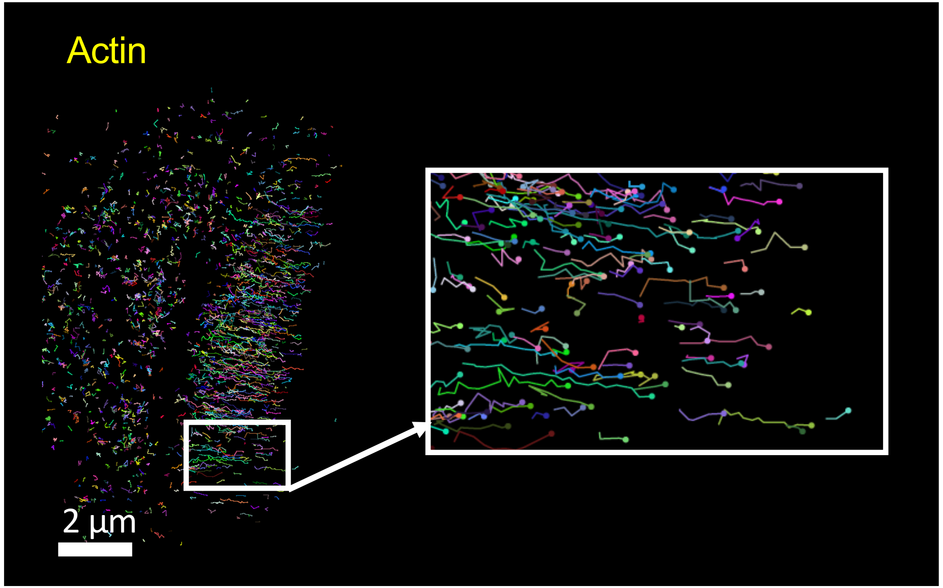


- polarized biopolymers. different rate constants for binding / unbinding to different ends.
- generates motion by stochastic fluctuation + polymerization, "Ratchet"
- actin flows away from cell edge

Directed motion in the cell

Polymerization motors / ratchet



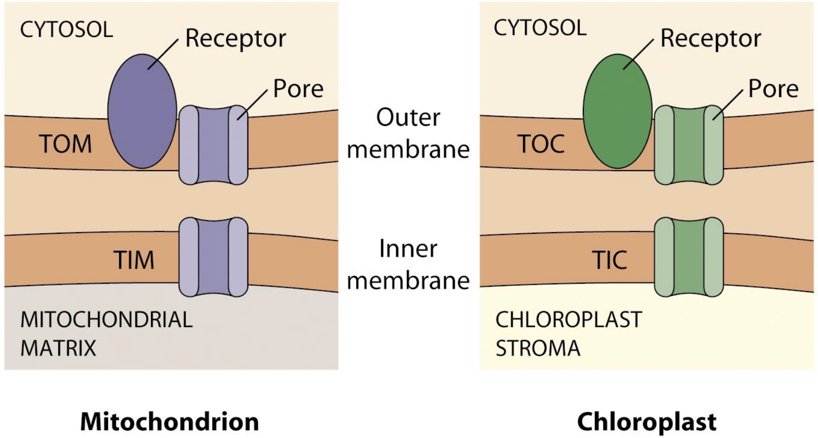


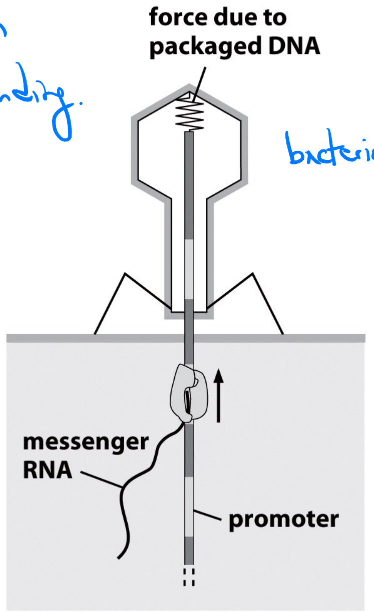
Directed motion in the cell

Translocation motors / ratchet

Move macromolecules across membranes (nucleic acids, proteins)

generates motion by differential binding. "Ratchet"





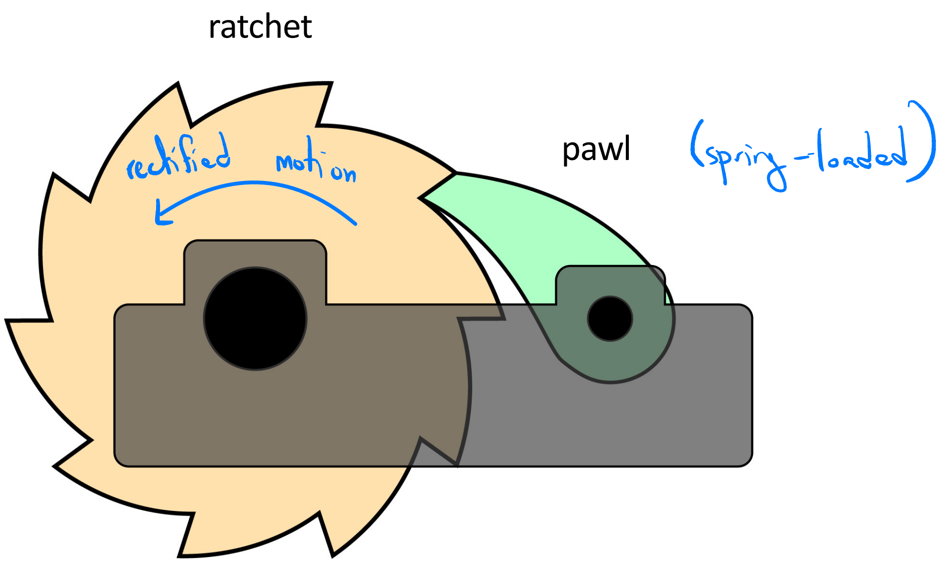
bacteriophage

bacterium

Figure 16.17b Physical Biology of the Cell (© Garland Science 2009)

Transport in cellular systems

Ratchets enforce unidirectionality



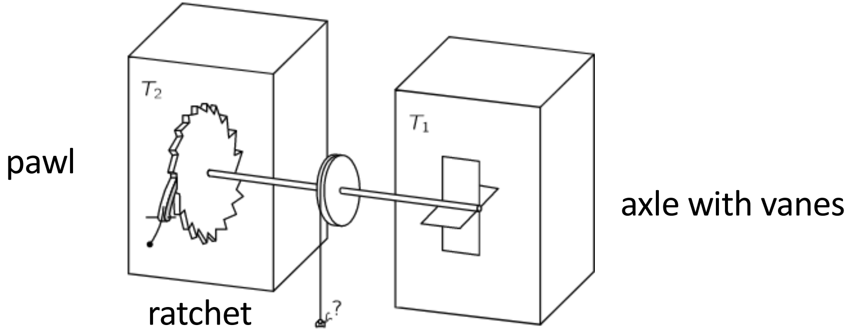
a device in which a toothed rack or wheel is engaged by a pawl to permit motion in one direction only

Transport in cellular systems

Brownian ratchet: Perpetual motion

Recall: Carnot, work cannot be extracted from a system in the absence of a temperature gradient.

Feynman proposed a thought experiment.



Suppose $T_1 = T_2$

- molecular collisions turn paddle
- pawl allows ratchet to turn only in one direction

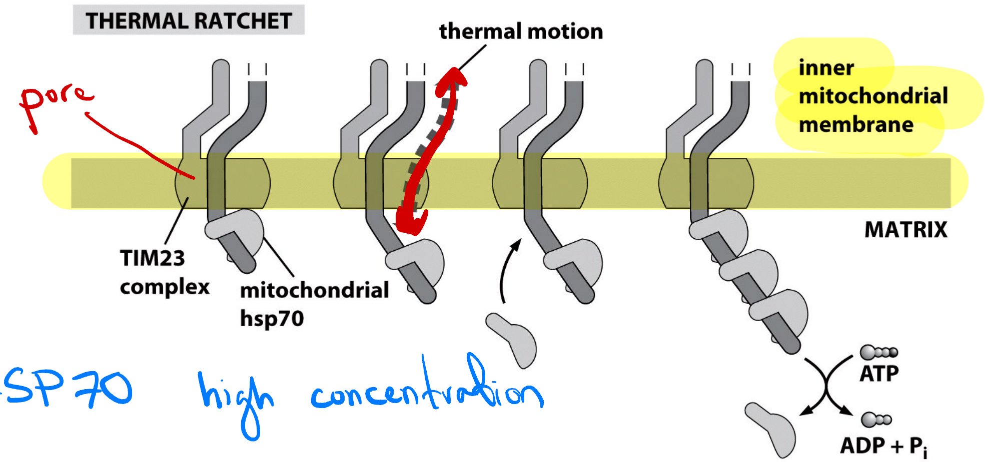
What is missing?

pawl is also subject to thermal fluctuations directly. Need $T_1 > T_2$

Transport in cellular systems

Directed motion: Translocation

HSP70 low concentration



HSP70 high concentration

Figure 16.16a Physical Biology of the Cell (© Garland Science 2009)

- thermal motion
- binding enforces direction
- non-equilibrium aspect

Transport in cellular systems

Directed motion: Translocation

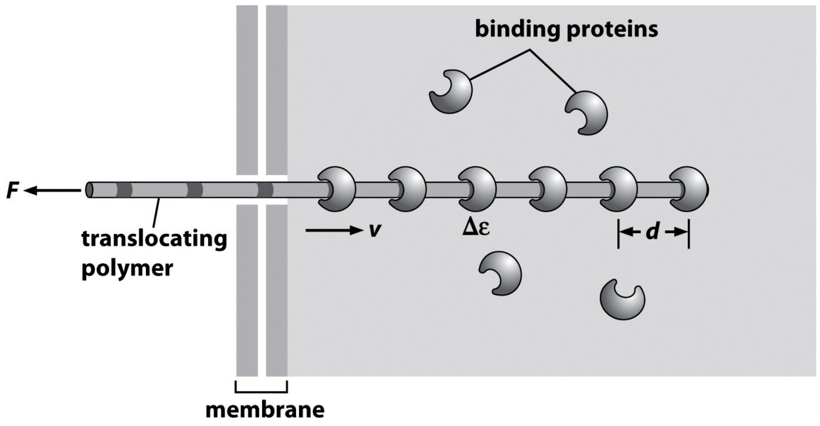


Figure 16.51 Physical Biology of the Cell (© Garland Science 2009)

d distance between binding sites

L polymer length

N number of sites $N = \frac{L}{d}$

Estimate two timescales:

1. Time for polymer to diffuse by its length L τ_1

2. Time for polymer to diffuse by its length L when assisted by binding (translocation ratchet) τ_2

Transport in cellular systems

Directed motion: Translocation

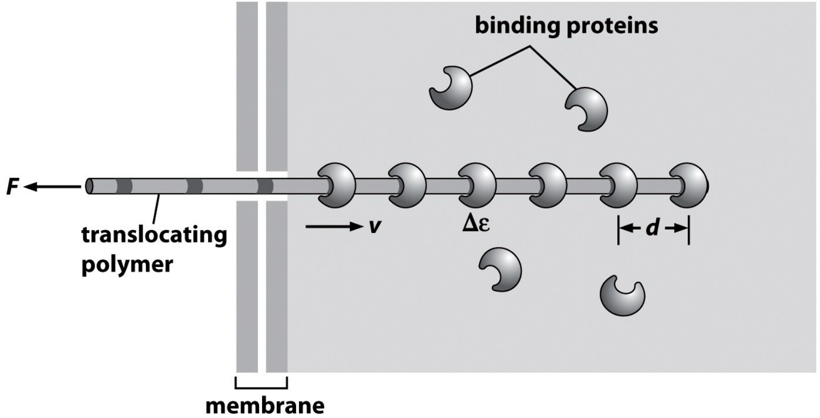


Figure 16.51 Physical Biology of the Cell (© Garland Science 2009)

d distance between binding sites

L polymer length

N number of sites $N = \frac{L}{d}$

$$\tau_1 \propto \frac{\langle x^2 \rangle}{D} = \frac{L^2}{D} = \frac{(Nd)^2}{D}$$

Estimate two timescales:

1. Time for polymer to diffuse by its length L τ_1

2. Time for polymer to diffuse by its length L when assisted by binding (translocation ratchet) τ_2

$$\tau_2 \propto N\tau_0$$ — time to diffuse d

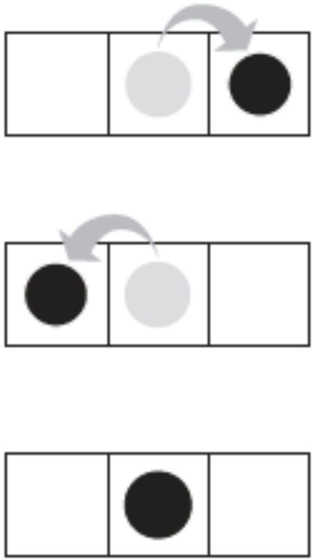
$$= N\frac{d^2}{D} = \frac{\tau_1}{N}$$

More precise model: 16.84 - 16.89

Transport in cellular systems

Directed motion: Translocation

TRAJECTORY	DISPLACEMENT *x*	WEIGHT



Transport in cellular systems

Directed motion: Translocation

TRAJECTORY	DISPLACEMENT *x*	WEIGHT
	d	$k_+ \Delta t$
	$-d$	$k_- \Delta t$
	0	$1-(k_+ + k_-)\Delta t$

Mean displacement

$$\langle \Delta x \rangle = \underbrace{(k_+ - k_-)d}_{\text{drift velocity } v_d}\Delta t$$

Variance

$$\langle \Delta x^2 \rangle = k_+ \Delta t d^2 + k_- \Delta t d^2$$

$$= \underbrace{d^2 (k_+ + k_-)}_{\text{effective diff. coeff. } D_{eff}}\Delta t$$

$$\tau = \frac{L}{v_d} \overset{\text{limit } k_- \to 0}{=} \frac{Nd \cdot d}{D_{eff}} = \frac{Nd^2}{D_{eff}}$$

Lecture 9: Directed motion in the cell

Summary:

- Directed motion uses conversion of chemical energy (ATP) into mechanical energy or concentration gradients into rectified / biased random walks, "ratchet".
- Four main classes of motors: translational
  rotary
  polymerization
  translocation
- Model ratchets as biased random walk
- Estimate differences between diffusion vs. directed motion