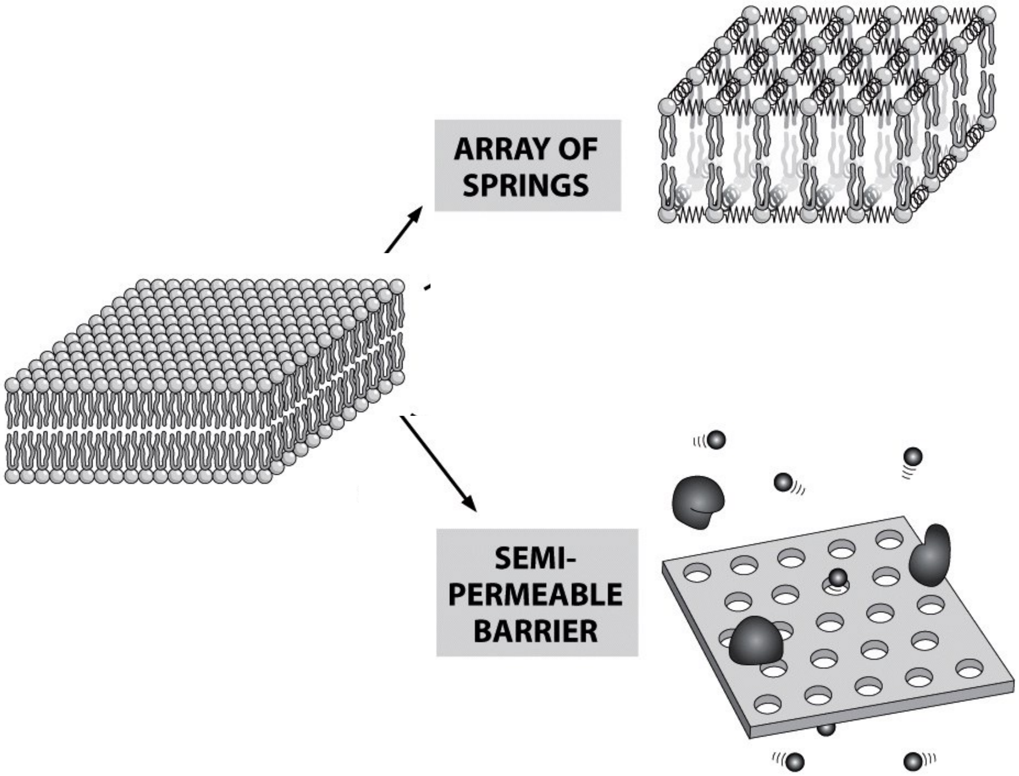
Lecture 5: Biological membranes

Goal: Estimates and models of membrane shapes

- Membrane pulling
- Shapes of organelles
- Shapes of cells

PBOC Chapter 11.3, 11.4

Biological membranes



Lecture 4, 5

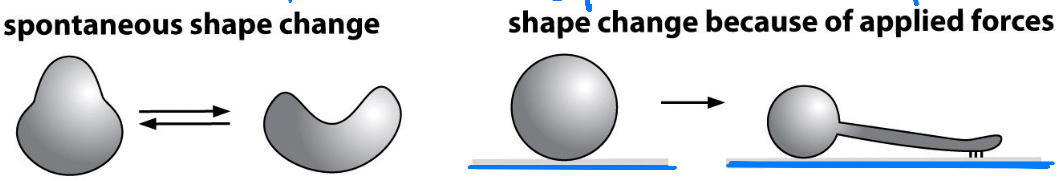
Lecture 7

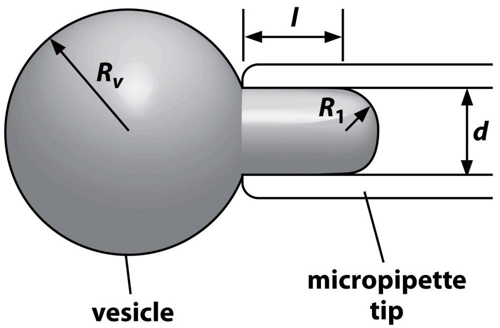
The springiness of biological membranes

Previously:

Membrane shape changes

How? Physical, energy-based description





Can deduce elastic (stretch) modulus from experiment

Assumptions:

mechanical equilibrium

membrane tension is constant

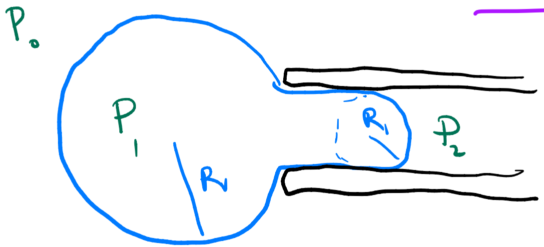
change in area comes from stretching

Model: Calculate energy cost

The springiness of biological membranes

$\boxed{\text{PBoC 11.3}}$

Springiness of membranes

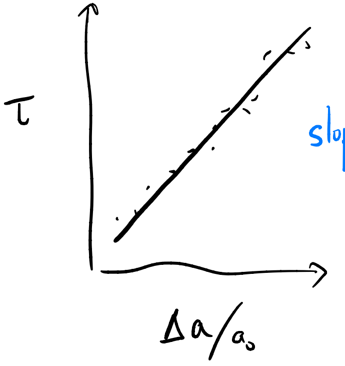


LaPlace pressure:

$$\tau = \frac{\overbrace{P_2 - P_0}^{\text{experimentally imposed}}}{2}\underbrace{\left(\frac{1}{R_1} - \frac{1}{R_v}\right)^{-1}}_{\text{measured}}$$

$$\tau = K_A \frac{\Delta a}{\underbrace{a_0}_{\text{measured}}}$$

$F = -kx$ analogue



slope K_A

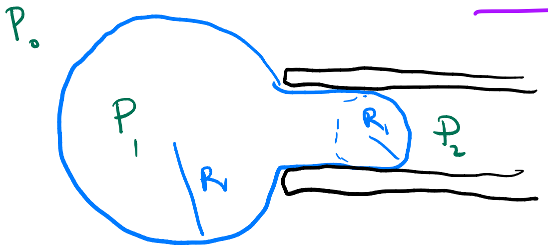
stretch modulus (area) $K_A = 250\ \text{mN/m}$

The springiness of biological membranes

PBoC 11.3

Springiness of membranes

LaPlace pressure:



$$\tau = \frac{\overbrace{P_2 - P_o}^{\text{experimentally imposed}}}{2}\Big(\underbrace{\frac{1}{R_1} - \frac{1}{R_v}}_{\text{measured}}\Big)^{-1}$$

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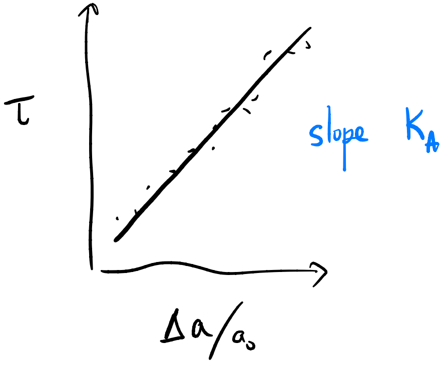
$F = kx$ analogue



area stretch modulus $K_A = 250 \ mN/m$

How to compare? Rubber 10-100 MPa Bone 14 GPa Titanium 116 GPa

$Pa = \frac{N}{m^2}$

membrane thickness? ~ 5 nm

$$250 \times 10^{-3} \frac{N}{m} \Big/ 5 \times 10^{-9} m = 50 \times 10^{6} N/m^2$$

$$= 50 \text{ MPa}$$

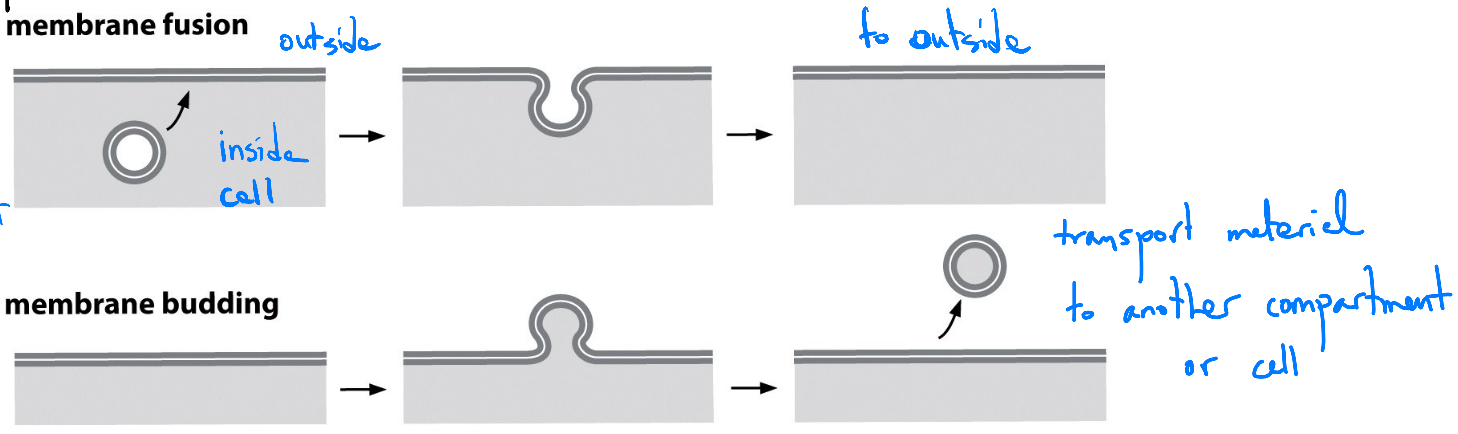
Structure, energetics, and function of membranes

Vesicles in cells

dynamic processes:

Definition: roughly spherical membrane compartment (bilayer).

Size: 20 nm - 5 μm



purposes of vesicles

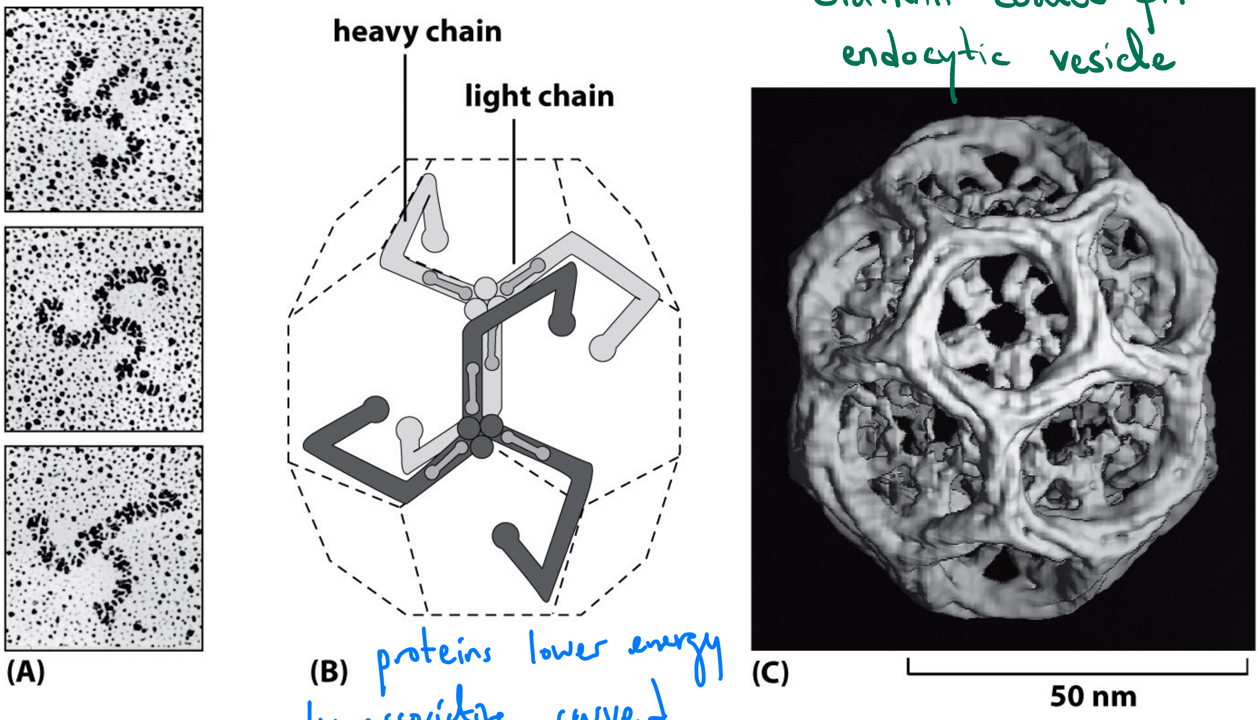
- exocytosis: deliver material outside
- intra/inter-cellular transport: move material within/between cells
- endocytosis: bring material inside (clathrin)

Structure, energetics, and function of membranes

Vesicles in cells: Proteins shape membranes

"clathrin-coated pit"
endocytic vesicle

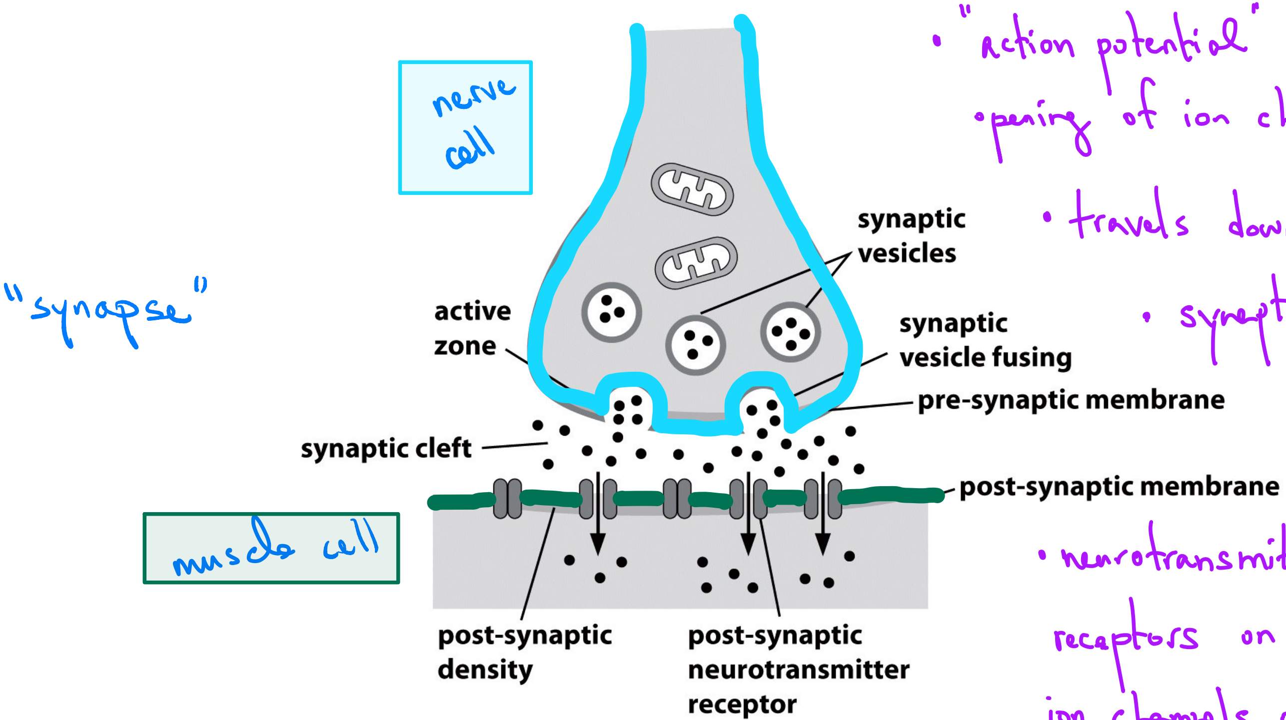
clathrin
protein



proteins lower energy by associating, curved.

Structure, energetics, and function of membranes

Vesicles in cells: synaptic signalling between nerve cells



- "action potential" is generated by opening of ion channels in nerve cell
- travels down to the synapse
- synaptic vesicles fuse, releasing contents into synaptic cleft
- neurotransmitter molecules bind receptors on muscle cell → ion channels open, trigger contraction

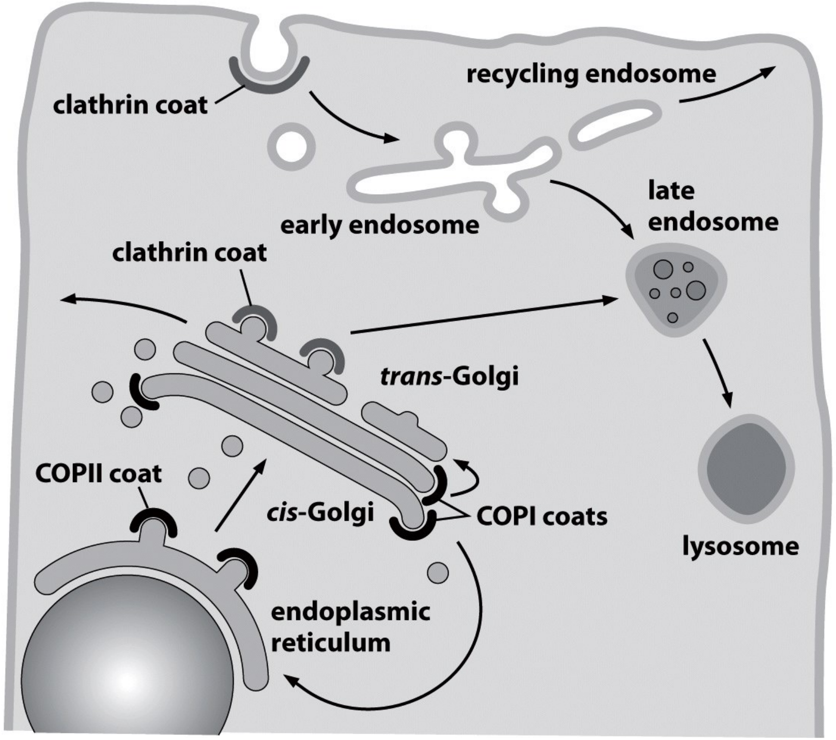
Structure, energetics, and function of membranes

Vesicles in cells: intracellular transport

Secretory pathway,
from protein production
to modification to
targeting to interior
or surface.
"assembly line"

Common shapes:

spheres
tubes



organelles communicate
via vesicles

Structure, energetics, and function of membranes

Vesicles in cells: energy cost

What is the energy to make one vesicle, 10 nm in radius? (Assume spherical, $K_B = 10\ k_BT$)

$\downarrow$

elastic

Structure, energetics, and function of membranes

Vesicles in cells: energy cost

What is the energy to make one vesicle, 10 nm in radius? (Assume spherical, $K_B = 10\,k_BT$)

bending modulus has units of energy

$$G_{bend} = \frac{K_B}{2} \int_{surface} (\kappa_1 + \kappa_2)^2 \, dA$$

$$= \frac{K_B}{2} \int_{surface} \left(\frac{1}{R} + \frac{1}{R}\right)^2 dA = \frac{2K_B}{R^2}(4\pi R^2) = \boxed{8\pi K_B}$$

Surprising! Independent of R

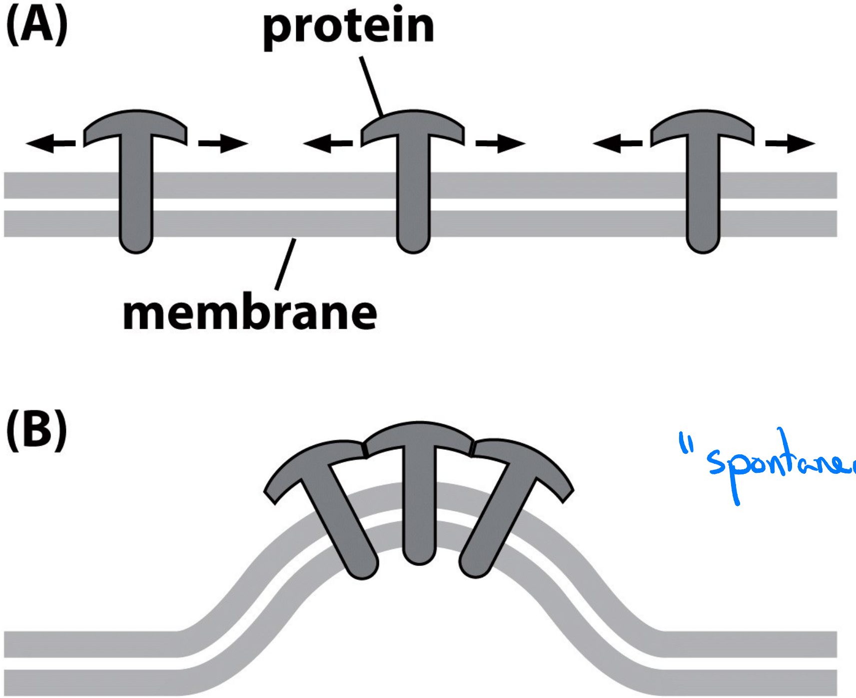
Estimate: $G_b \approx 250\,k_BT \gg k_BT$

energy comes from protein-protein interactions, spontaneous curvature of lipids

Structure, energetics, and function of membranes

Vesicles in cells: Proteins shape membranes

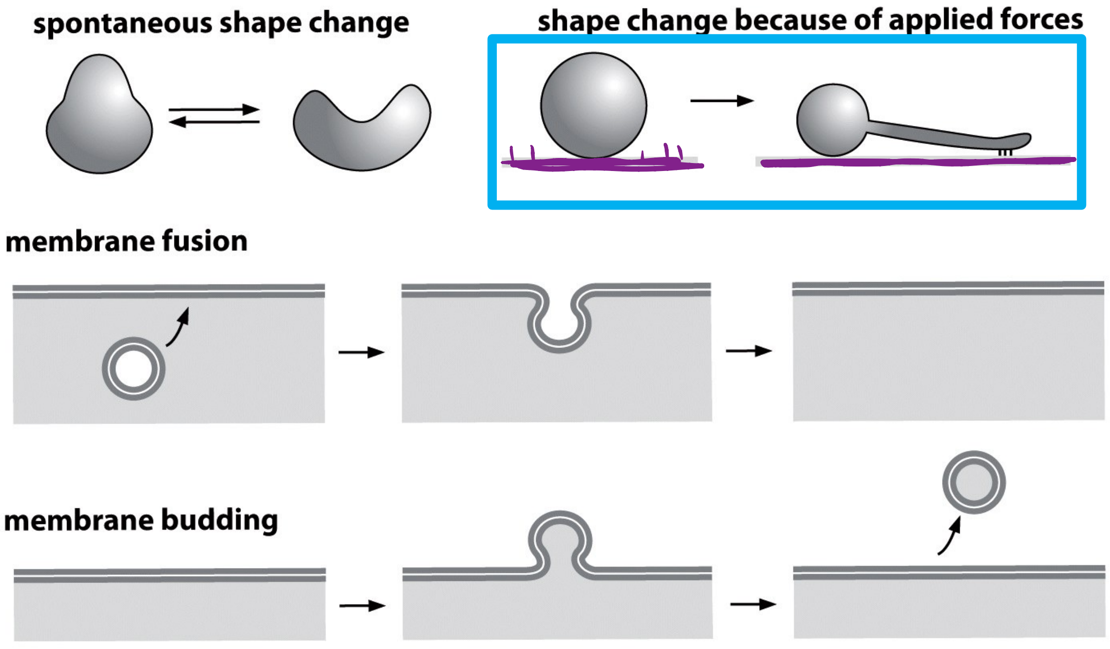
clathrin
:
COP1
COP II



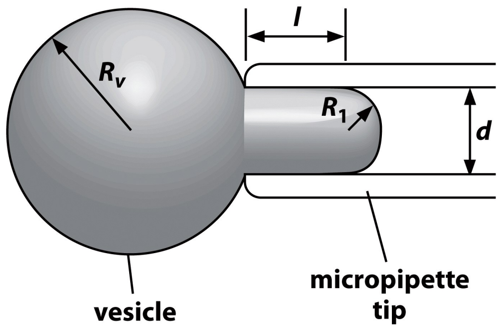
"spontaneous curvature"

Structure, energetics, and function of membranes

Membrane shape changes



molecular motors : exert forces

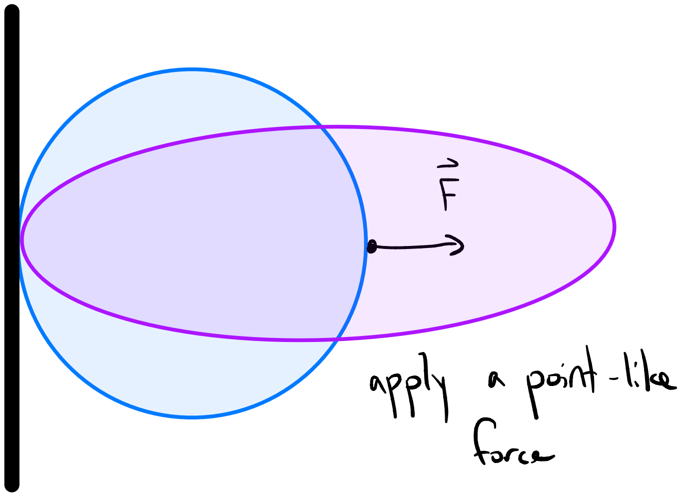


Structure, energetics, and function of membranes

Membrane pulling model

Spherical vesicle. What will happen if you use optical tweezers to pull on a bead attached to the membrane?

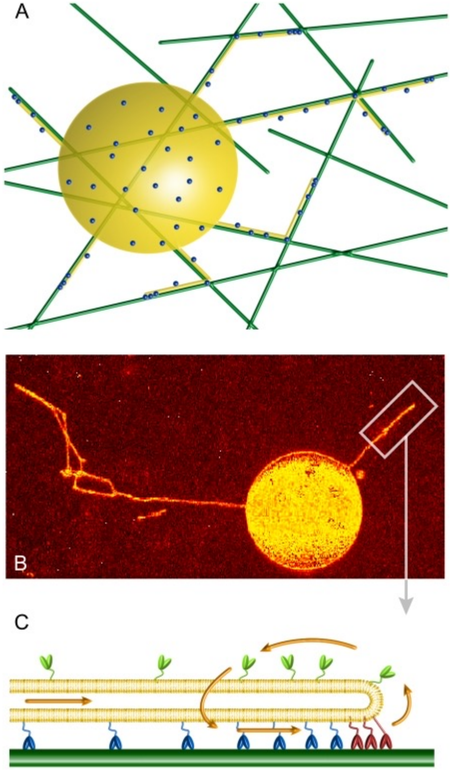
https://www.youtube.com/watch?v=8PZfglBI77A

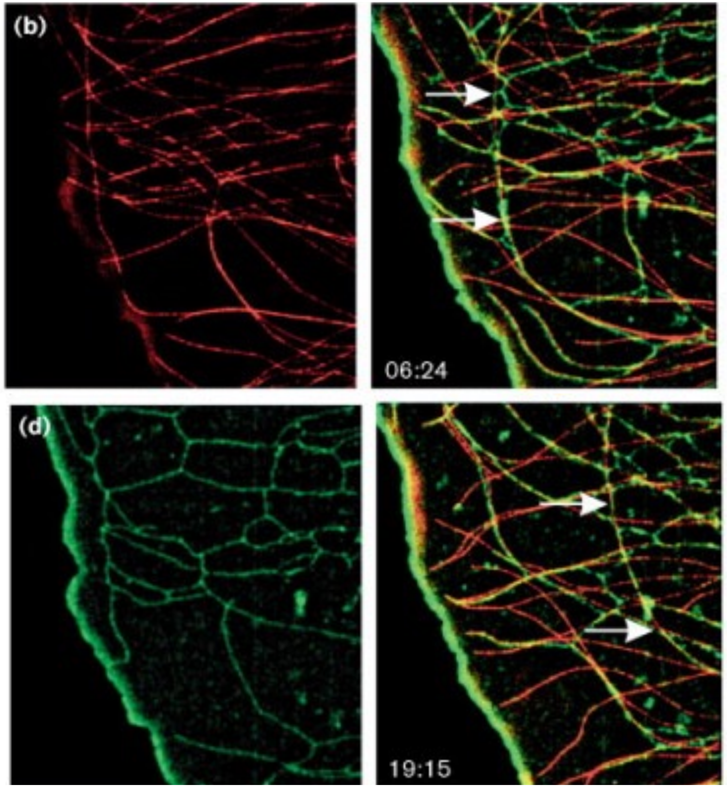


What shape do you expect the membrane to take?

Structure, energetics, and function of membranes

Motors pull membranes





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Structure, energetics, and function of membranes

Membrane pulling model

Spherical vesicle. What will happen if you use optical tweezers to pull on a bead attached to the membrane?

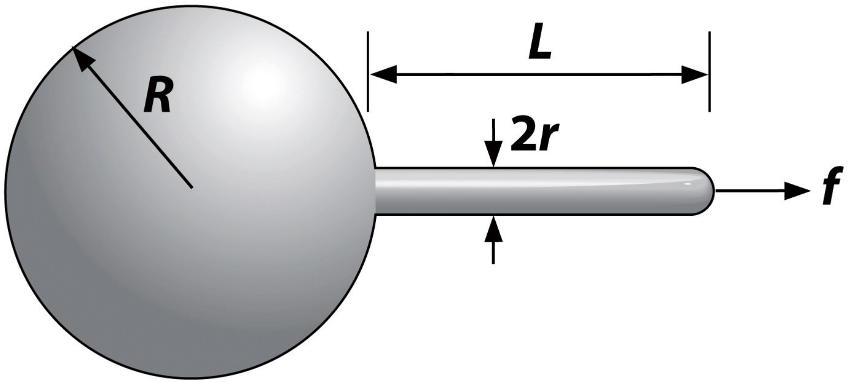
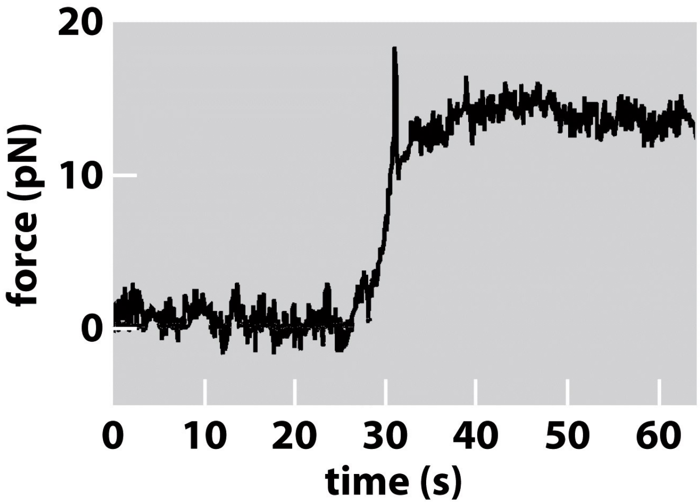


Figure 11.26 Physical Biology of the Cell (© Garland Science 2009)



What is the equilibrium shape? Minimize free energy. PBOC 11.3.2

- bending
- stretching
- work done against pressure difference
- work done by applied force

1. Bending

		vesicle	tube	cap
principal curvatures	κ_1	$1/R$	$1/r$	$1/r$
	κ_2	$1/R$	0	$1/r$
	$\int dA$	$4\pi R^2$	$2\pi r L$	$2\pi r^2$
	G_{bend}	$8\pi K_b$	$\dfrac{\pi K_b L}{R}$	$4\pi K_b$

What is the equilibrium shape? Minimize free energy. PBOC 11.3.2

- bending
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1. bending

	vesicle	tube	cap
κ_1	$1/R$	$1/r$	$1/r$
κ_2	$1/R$	0	$1/r$
$\int dA$	$4\pi R^2$	$2\pi r L$	$2\pi r^2$
G_{bend}	$8\pi K_b$	$\dfrac{\pi K_b L}{R}$	$4\pi K_b$

2. stretching

$$G_{stretch} = \frac{K_A}{2}\frac{(\Delta a)^2}{a_0} = \frac{K_A}{2}\frac{(2\pi r L + 4\pi R^2 - 4\pi R_0^2)^2}{4\pi R_0^2}$$

$R, L \gg r$

ignore cap

$$\frac{K_A}{2}\int\left(\frac{\Delta a}{a_0}\right)^2 dA$$

3. work against pressure $(\Delta V = 0)$

$$G_{PV} = -V\Delta P = -\underbrace{\Delta P}_{\text{pressure difference inside \& out}}\left[\frac{4}{3}\pi R^3 + \pi r^2 L\right]$$

4. work by applied force $G_{load} = -fL$ (analogue of $W = F\Delta x$)

Minimize free energy G_{tot} with respect to R, r, L

$$\frac{\partial G_{tot}}{\partial R} = 0 \Rightarrow \text{Laplace relation} \quad \Delta P = \frac{2}{R}\overbrace{K_A\frac{(\Delta a)}{a_0}}^{\tau \text{ tension}}$$

$$\frac{\partial G_{tot}}{\partial r} = 0 \Rightarrow r = \sqrt{\frac{K_b}{2\tau}} \quad \text{(neglecting } \Delta P \text{ term)} \approx \boxed{50 \text{ nm}}$$

$$\frac{\partial G_{tot}}{\partial L} = 0 \Rightarrow f = 2\pi\sqrt{2K_b\tau}$$

Experiment: $f \approx 10$ pN

$$\tau \approx \boxed{0.015 \text{ pN/nm}}$$

motors $\sim$ pN/5 nm $= \boxed{0.2 \text{ pN/nm}}$

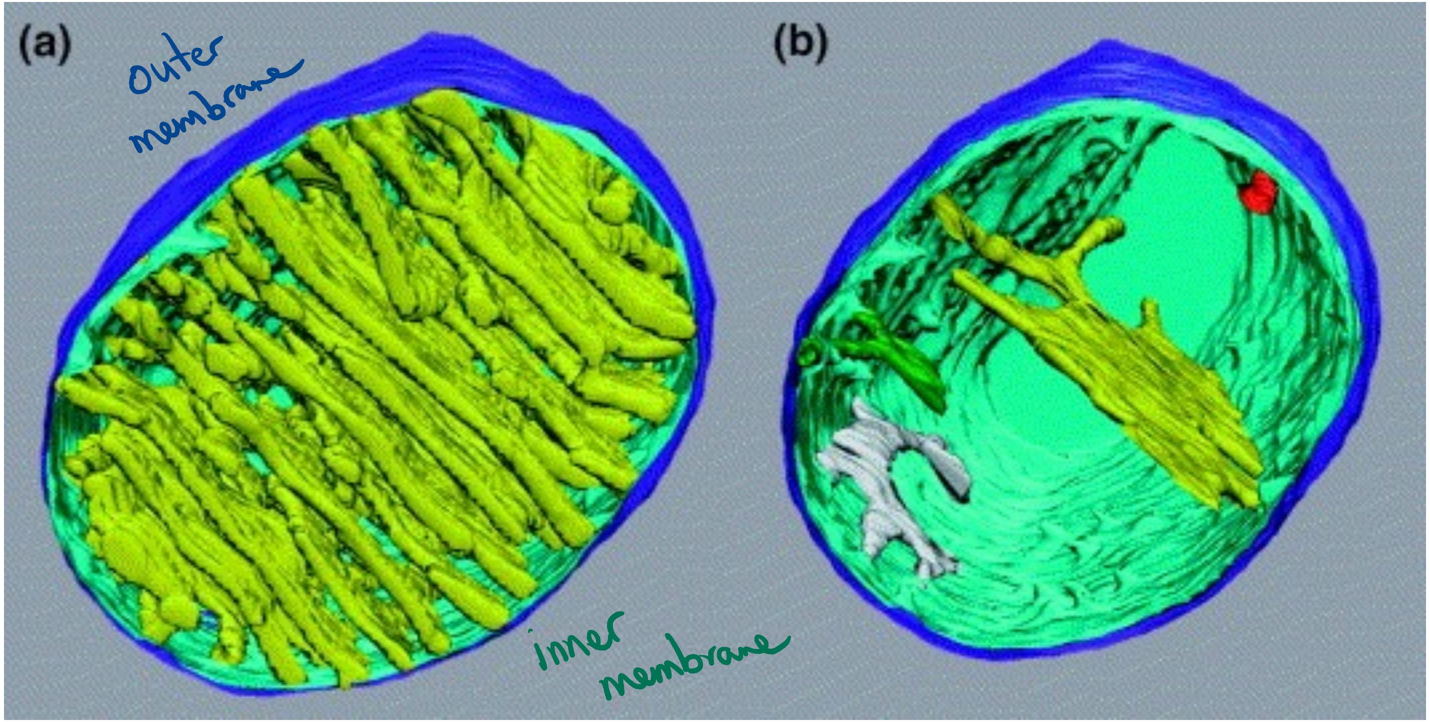
Membranes and shape

Organelle shape: mitochondria

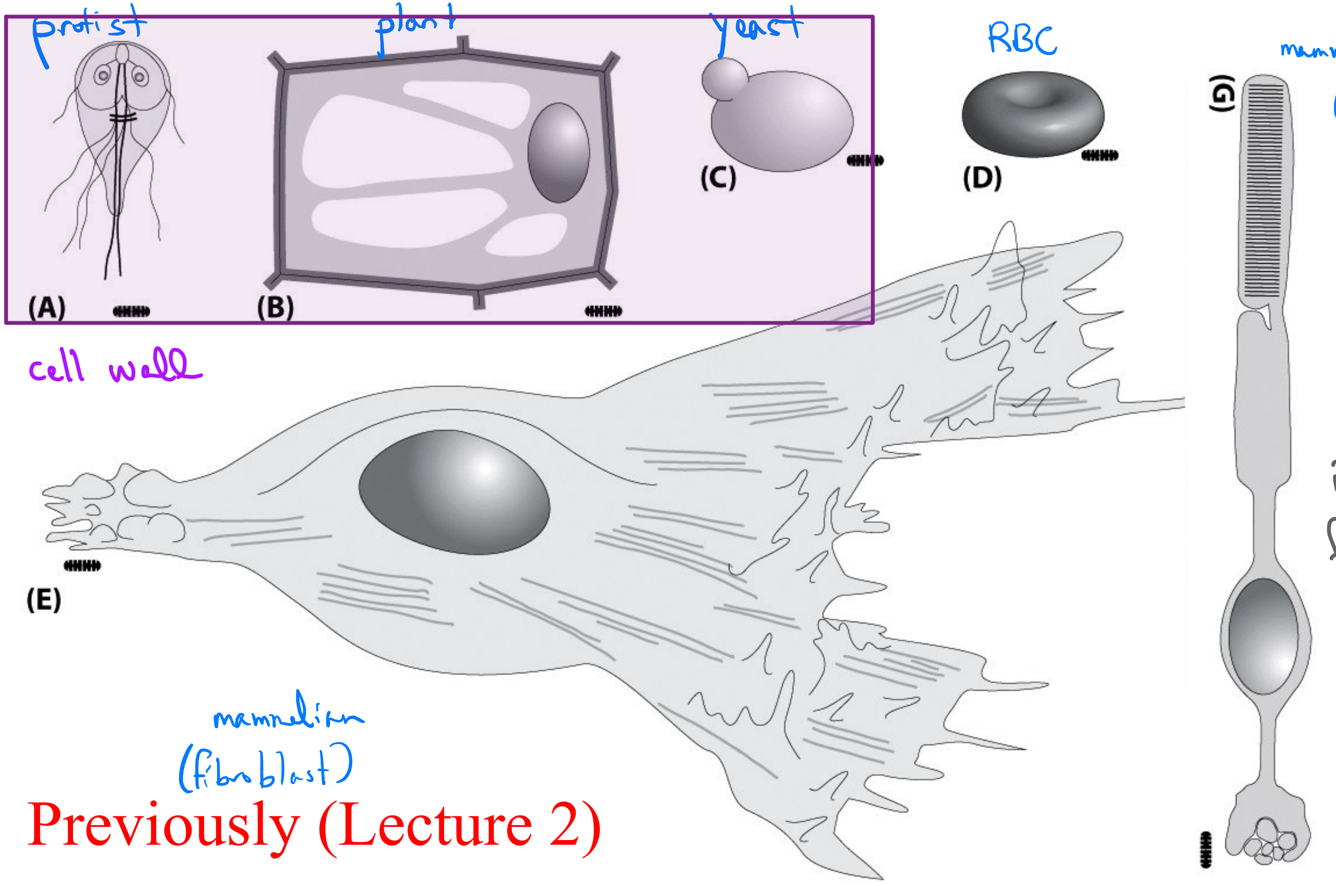
inner membrane area ~ 10 x outer membrane area ~ 0.01 plasma membrane area

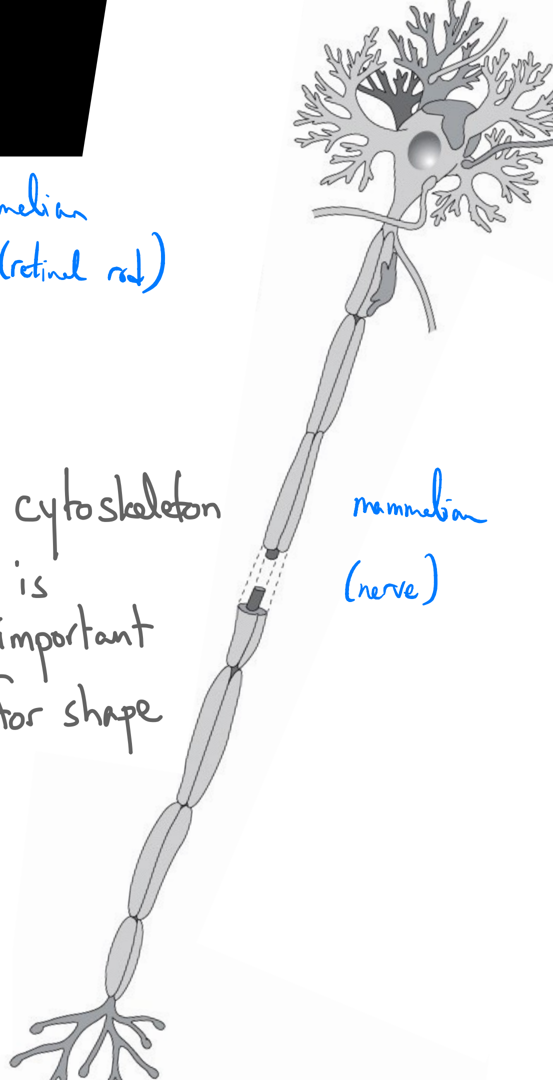
What drives non-spherical shapes?

We don't know! But would like to...



Membranes and shape: Cell shape





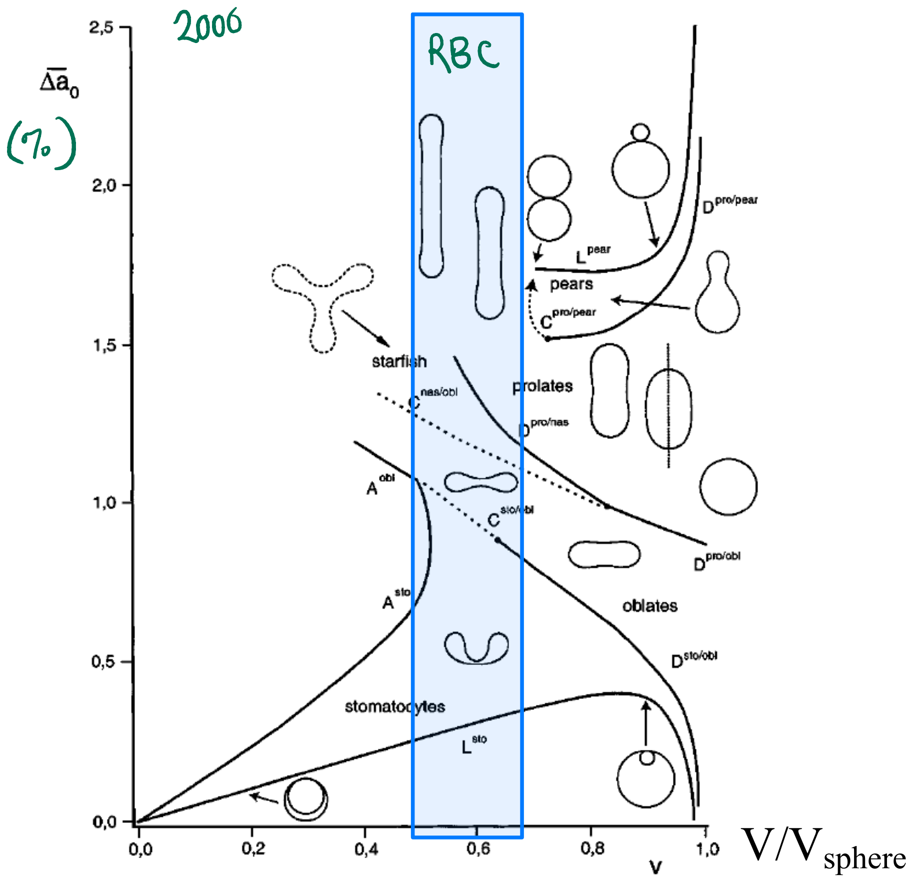
Previously (Lecture 2)

Membranes and shape

Vesicle shapes: stretch and bend

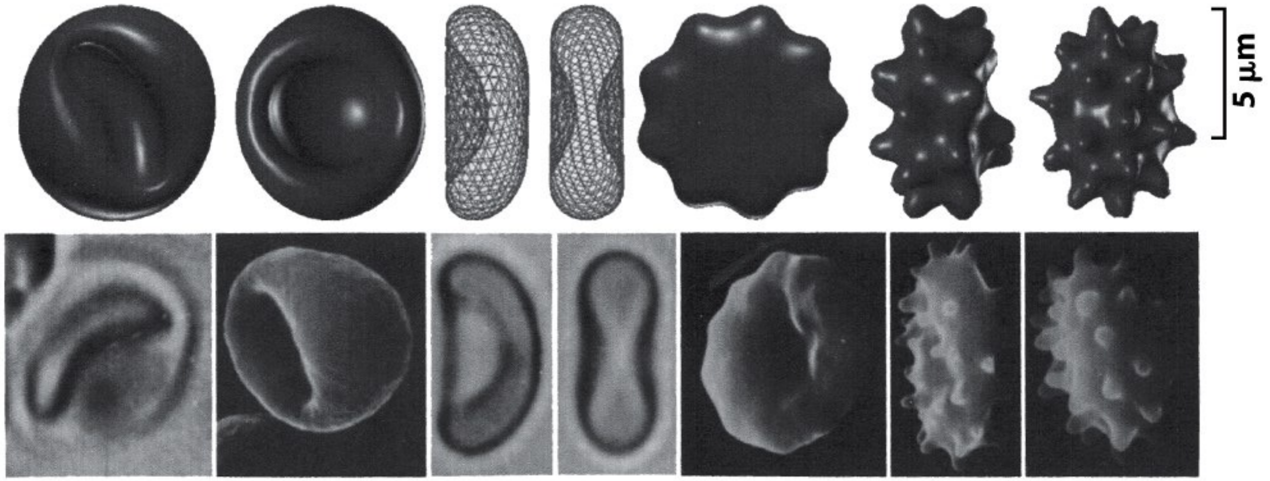
(no shear, fluids don't resist shear)

minimize free energy for different volumes, different leaflet area differences (inner/outer) $\overline{\Delta a}_0$



Membranes and shape

Previously: *Cells as minimizers*



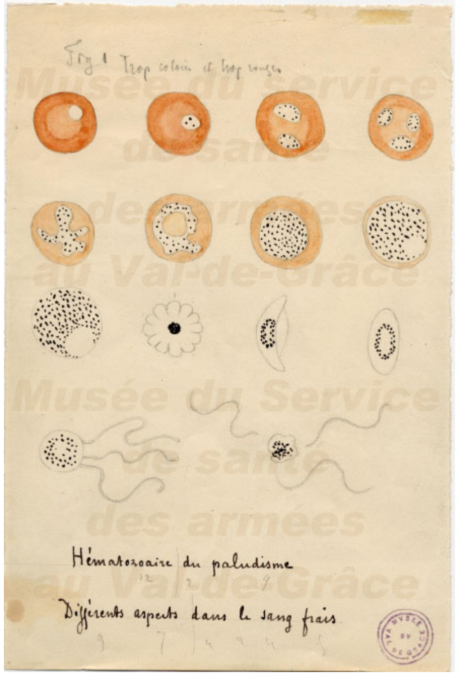
changes in area difference between two leaflets of bilayer

bend + stretch elasticity dominates

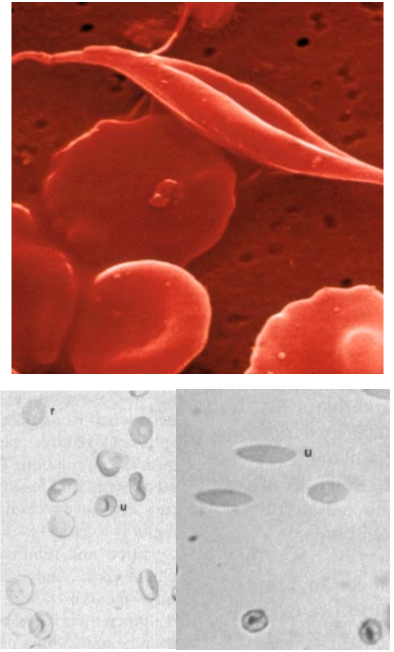
shear elasticity becomes important → cytoskeletal network (spectrin protein)

Membrane and shape

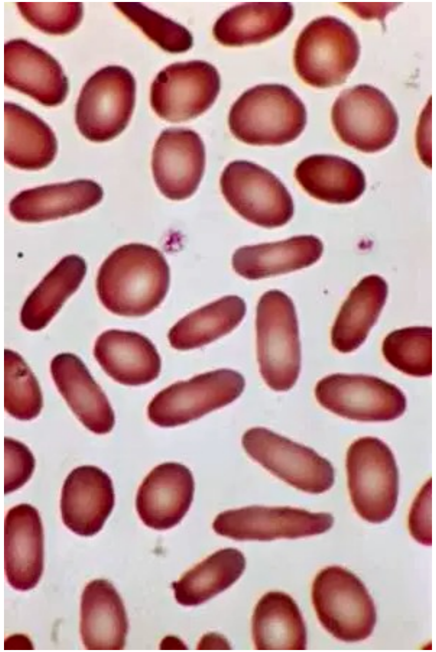
Red blood cell shape and disease



Malaria



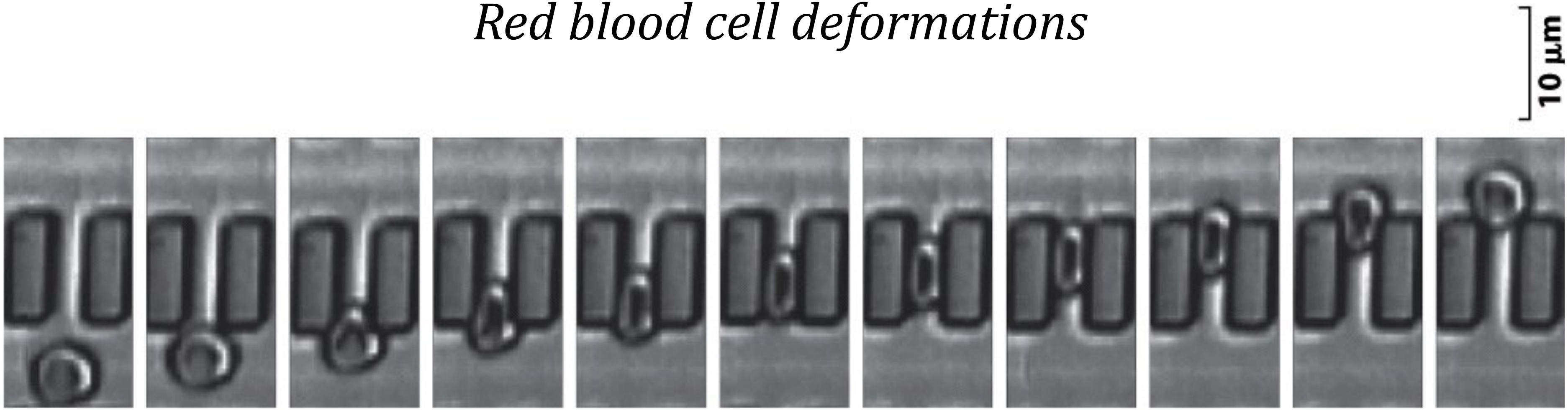
Sickle cell anemia



Hereditary elliptocytosis

Membranes and shape

Red blood cell deformations



How much would the elasticity have to change to prevent RBC from passing through capillary? → disease

Lecture 5: Biological membranes

Summary

- Vesicles transport molecules and can bud and fuse from membranes (plasma mem., organelles)
  - protein coats  or lipids 

    can lower energy to bend membrane (spontaneous curvature)
- Membranes can change shape due to applied forces.
  - In cells, proteins (molecular motors)
  - In vitro, also optical tweezers & micropipettes
  - Mammalian cell shape comes from cytoskeleton (red blood cell example)
  - Plants, yeast, bacteria cell shapes come from cell wall

Lecture 6: Proteins; entropy rules

Goal: Introduce Boltzmann distribution, probability of microstate

- Ligand-receptor binding
- Gene regulation
- Cooperativity

PBOC Chapter 6.1.1, 6.1.2, 6.4
(except 6.4.4)