Course content

Topics (lectures)**:**

1. **Introduction to the cell** (1-3)
2. **Biological membranes** (4-5)
3. **Proteins** (6-7)
4. **Dynamics** (8-9)
5. **Genomes** (10-12)

Course structure:

1. **Introduction to systems and concepts**
2. **Description of observations and measurements**
3. **Estimates of relevant numbers / development of quantitative models**
4. **Analysis of research articles**

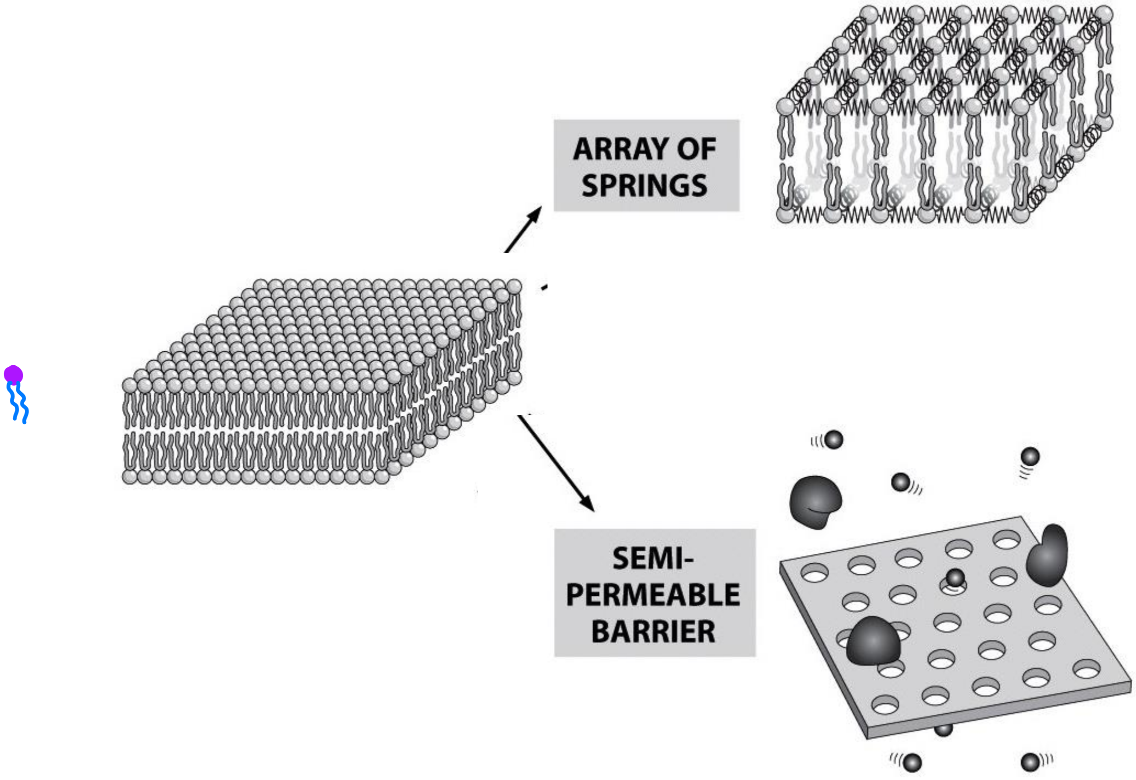
Lecture 4: Biological membranes

Goal: Calculate energy cost for bending membranes away from their equilibrium configurations

- The nature of biological membranes (descriptive)
- On the springiness of membranes (model)
- Structure, energetics, and function of vesicles (example)

PBOC Chapter 11.1, 11.2

Biological membranes

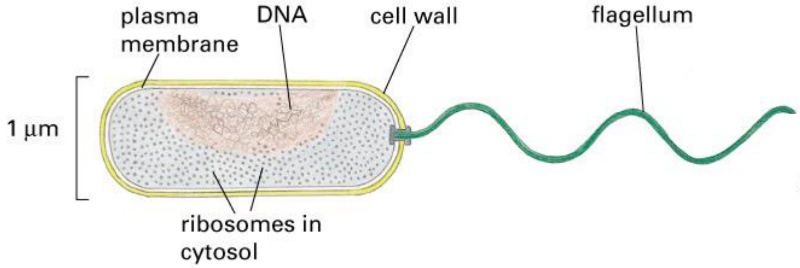


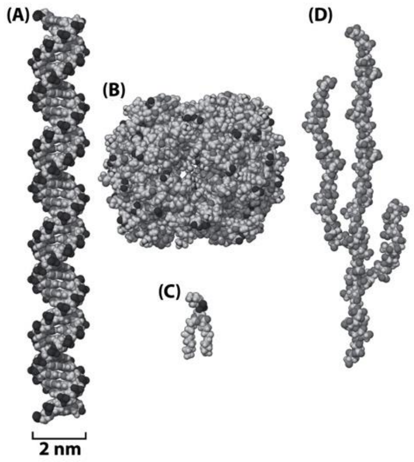
Lecture 4, 5

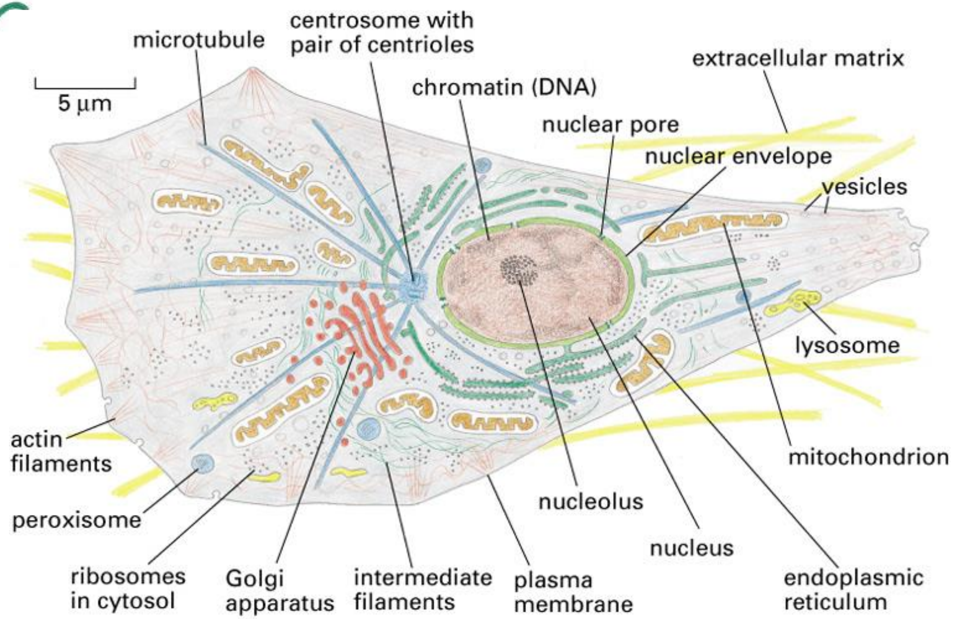
Lecture 7

Basic facts about cells

Previously: *Prokaryotes and Eukaryotes*







Basic facts about cells

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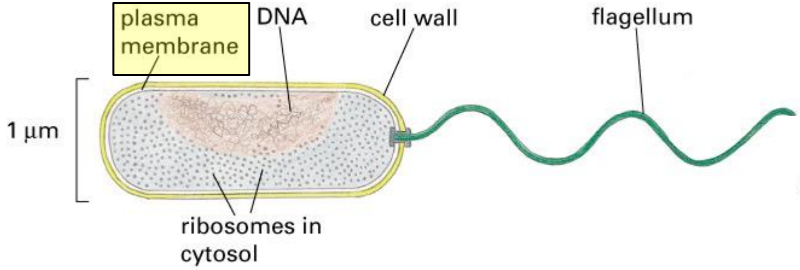
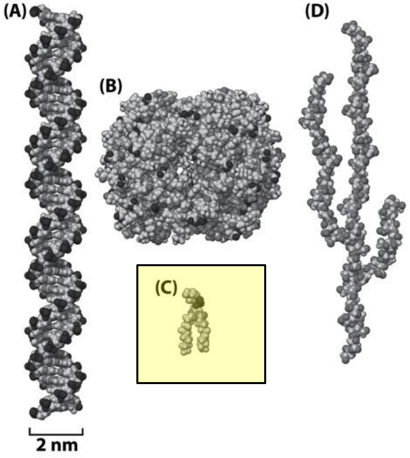
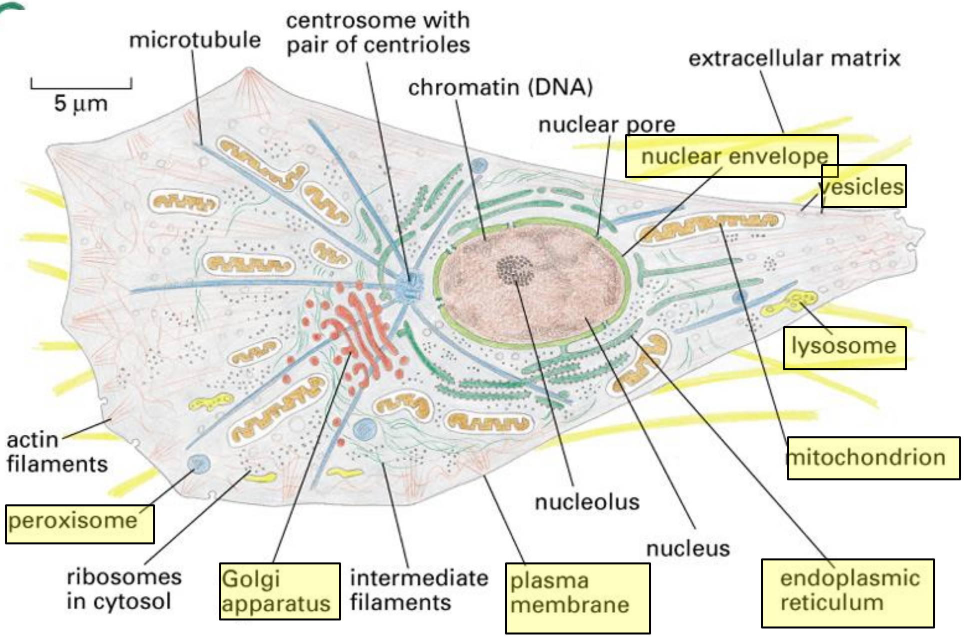






What properties should membranes have?

Selective barrier

Pass information, molecules, ions (in → out & out → in)

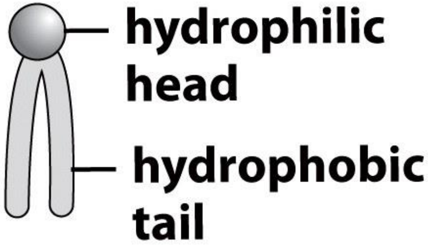
Maintain concentrations of (molecules, ions) inside cell

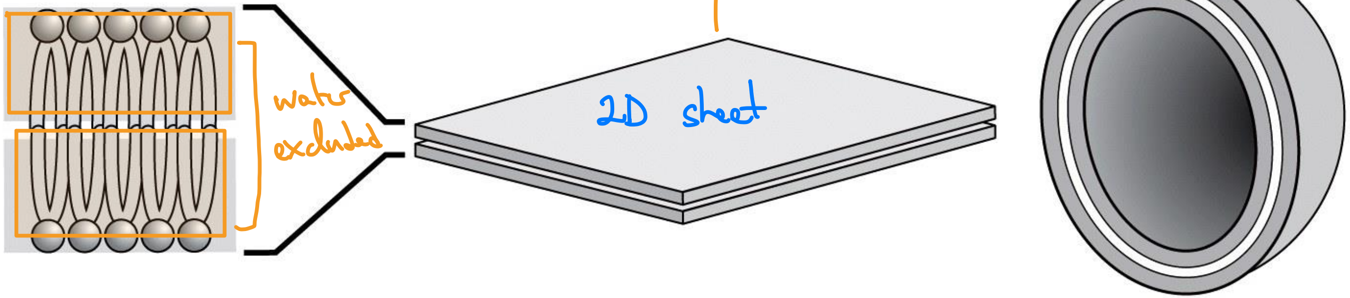
Flexible, able to grow with the cell, change shape

The nature of biological membranes

Lipid molecules

polar, H-bonding





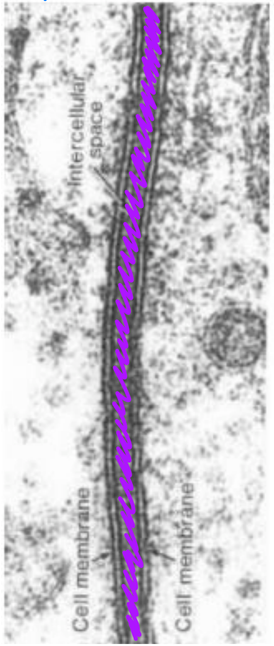
How do we know lipids form bilayers?

The nature of biological membranes

Lipid bilayers

1958

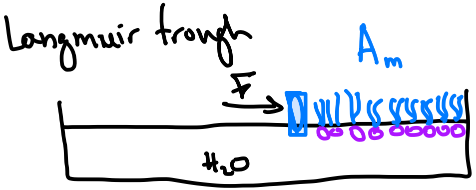
cell 1 cell 2



1924

Gorter & Grendel

Estimate surface area



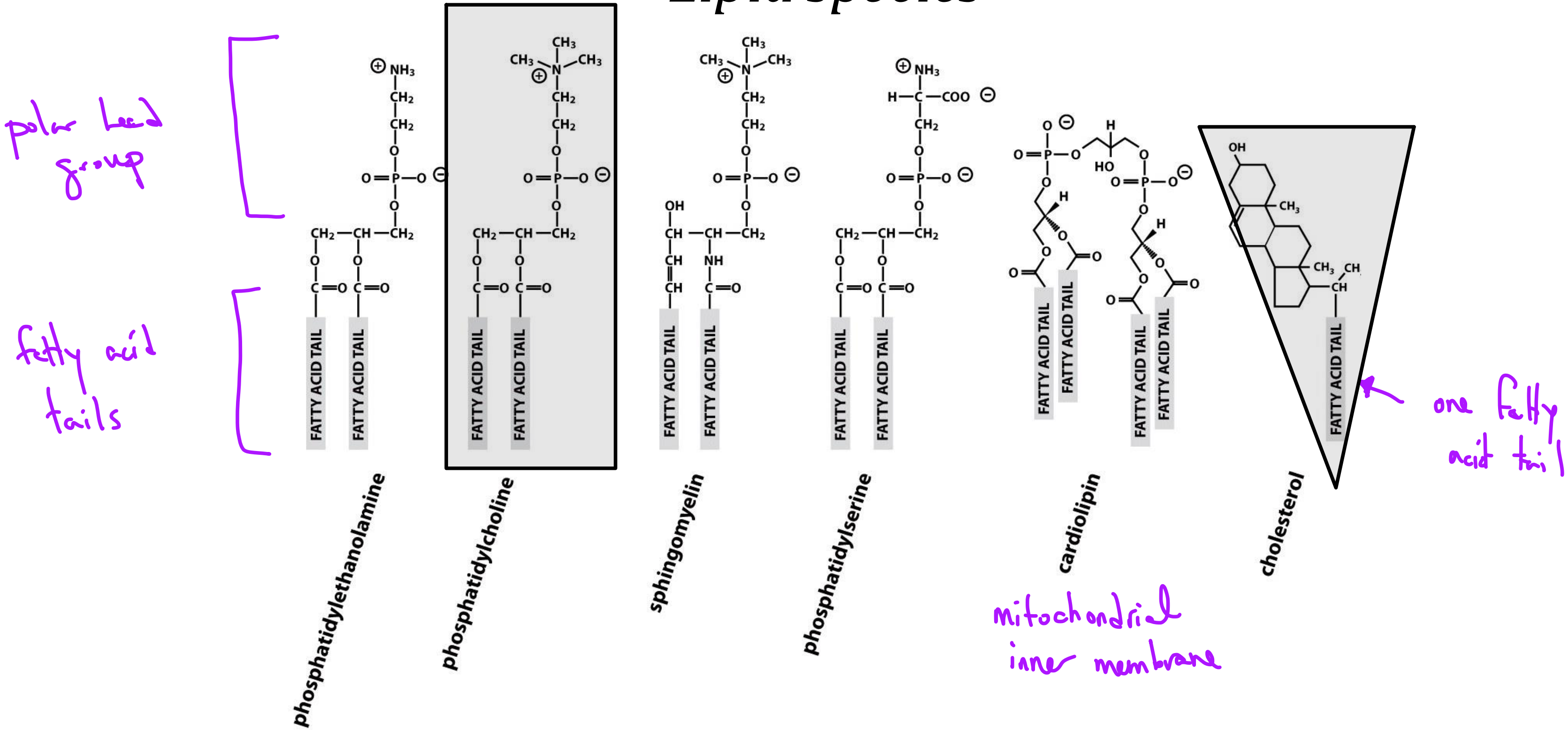
A_s A_m A_s/A_m

TABLE I.

Animal.	Amount of blood used for the analysis.	No. of chromocytes per c.mm.	Surface of one chromocyte.	Total surface of the chromocytes (a).	Surface occupied by all the lipoids of the chromocytes (b).	Factor a:b.
	gm.		sq. µ	sq. m.	sq. m.	
Dog A	40	8,000,000	98	31.3	62	2
	10	6,890,000	90	6.2	12.2	2
Sheep 1	10	9,900,000	29.8	2.95	6.2	2.1
	9	9,900,000	29.8	2.65	5.8	2.2
Rabbit A	10	5,900,000	92.5	5.46	9.9	1.8
	10	5,900,000	92.5	5.46	8.8	1.6
	0.5	5,900,000	92.5	0.27	0.54	2
" B	1	6,600,000	74.4	0.49	0.96	2
	10	6,600,000	74.4	4.9	9.8	2
	10	6,600,000	74.4	4.9	9.8	2
Guinea Pig A	1	5,850,000	89.8	0.52	1.02	2
	1	5,850,000	89.8	0.52	0.97	1.9
Goat 1	1	16,500,000	20.1	0.33	0.66	2
	1	16,500,000	20.1	0.33	0.69	2.1
	10	19,300,000	17.8	3.34	6.1	1.8
	10	19,300,000	17.8	3.34	6.8	2
	1	19,300,000	17.8	0.33	0.63	1.9
Man.	1	4,740,000	99.4	0.47	0.92	2
	1	4,740,000	99.4	0.47	0.89	1.9

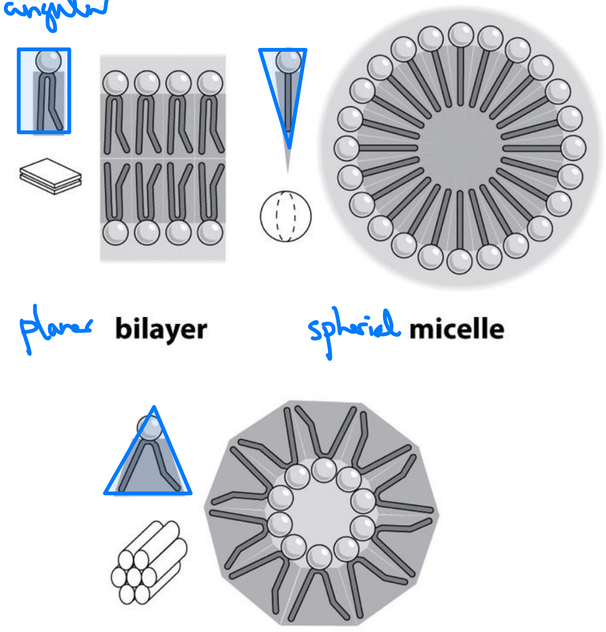
The nature of biological membranes

Lipid species

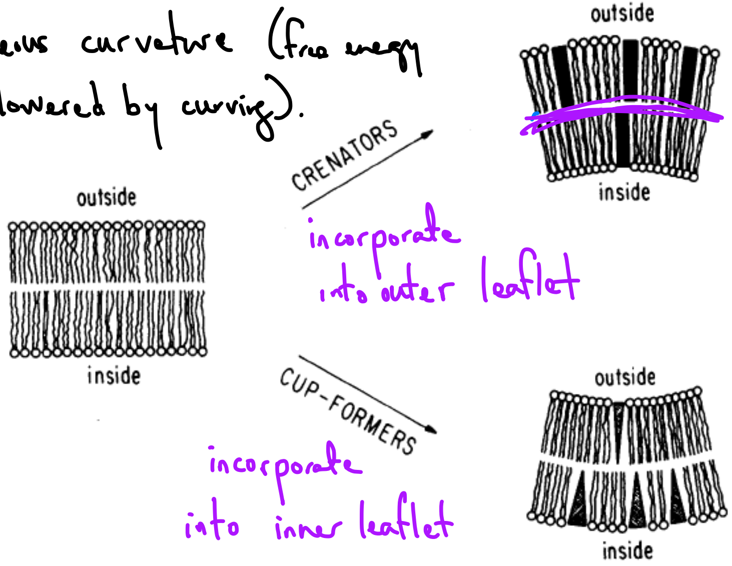


The nature of biological membranes

Lipid shape and self-assembly



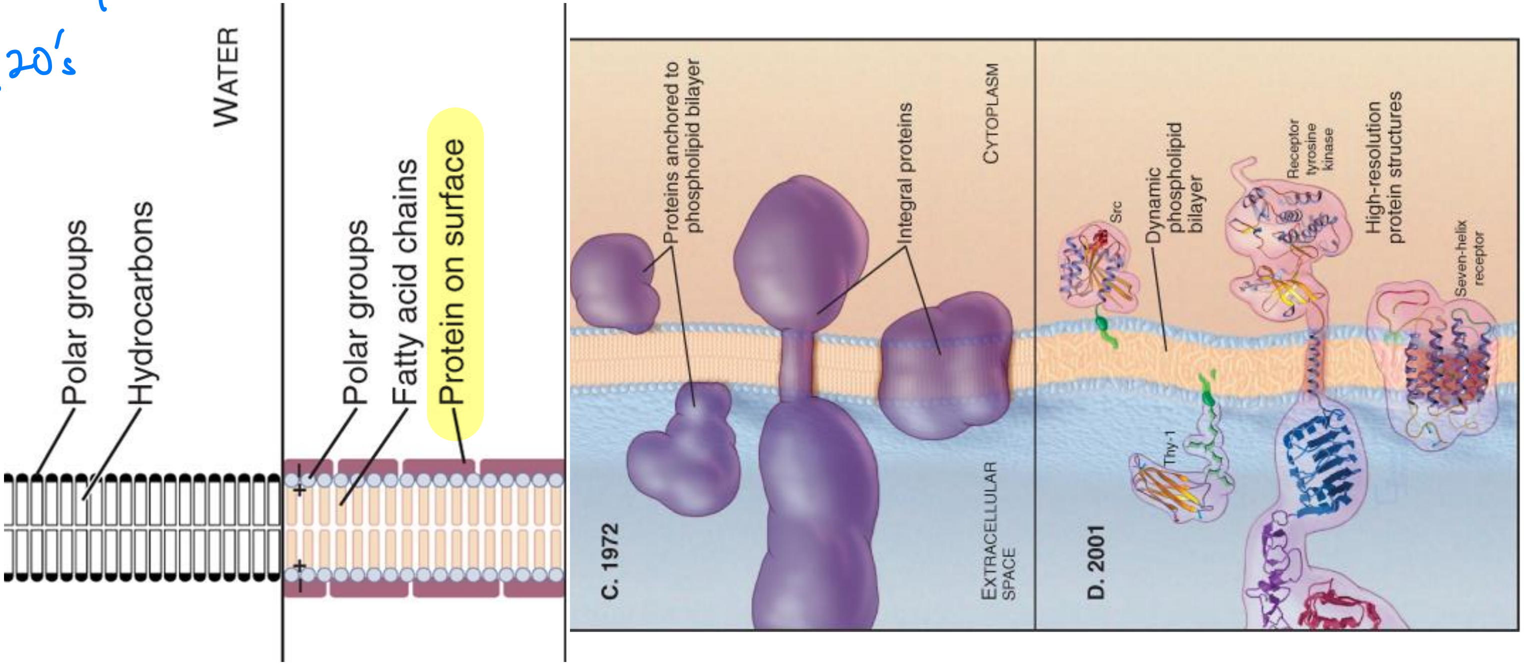
bilayers can have a non-zero spontaneous curvature (free energy may be lowered by curving).



The nature of biological membranes

Structure of biological membranes

Gorter & Grendel
1920's

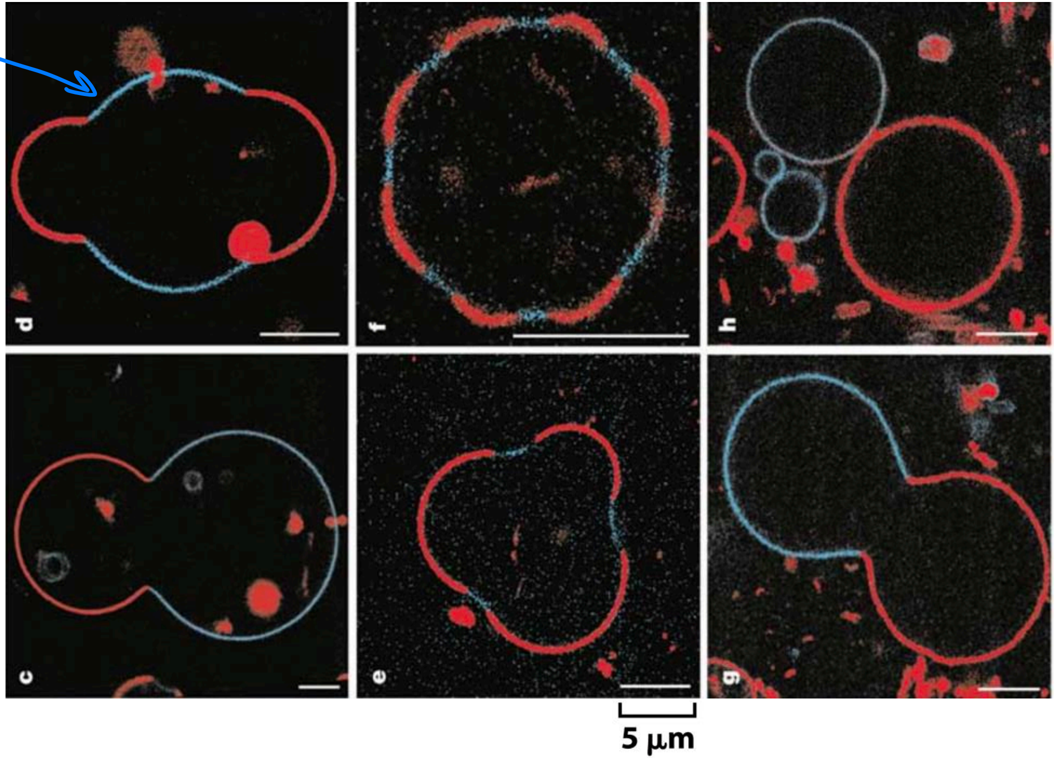


The nature of biological membranes

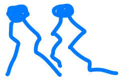
Lipid phase separation and membrane curvature

L_D liquid-disordered

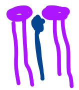
L_o liquid-ordered



L_D :

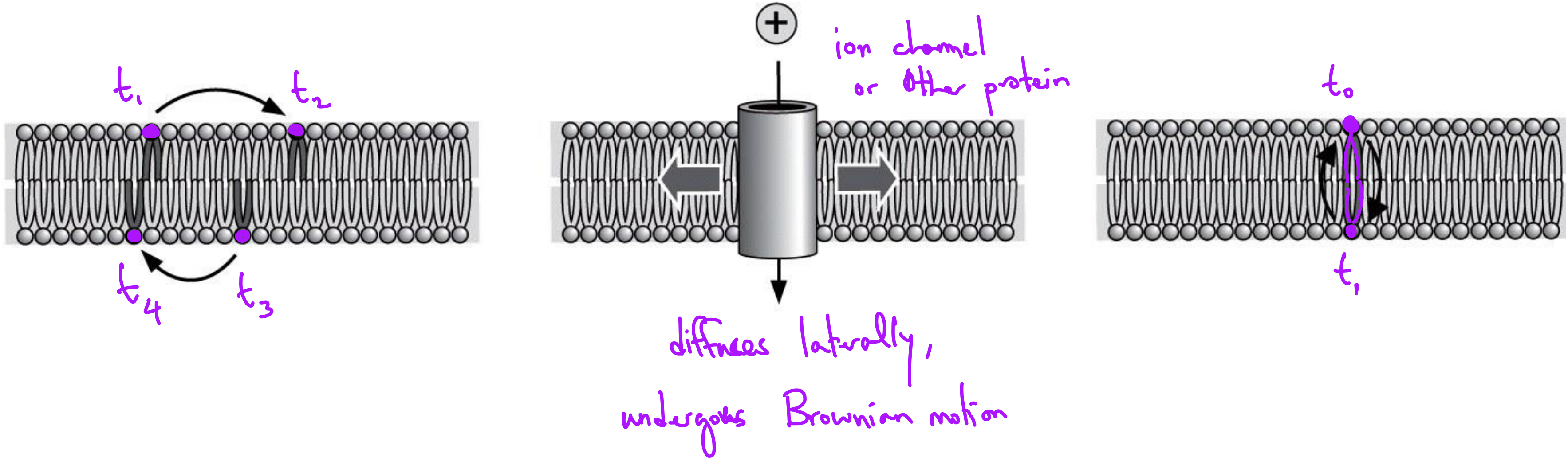


L_o :



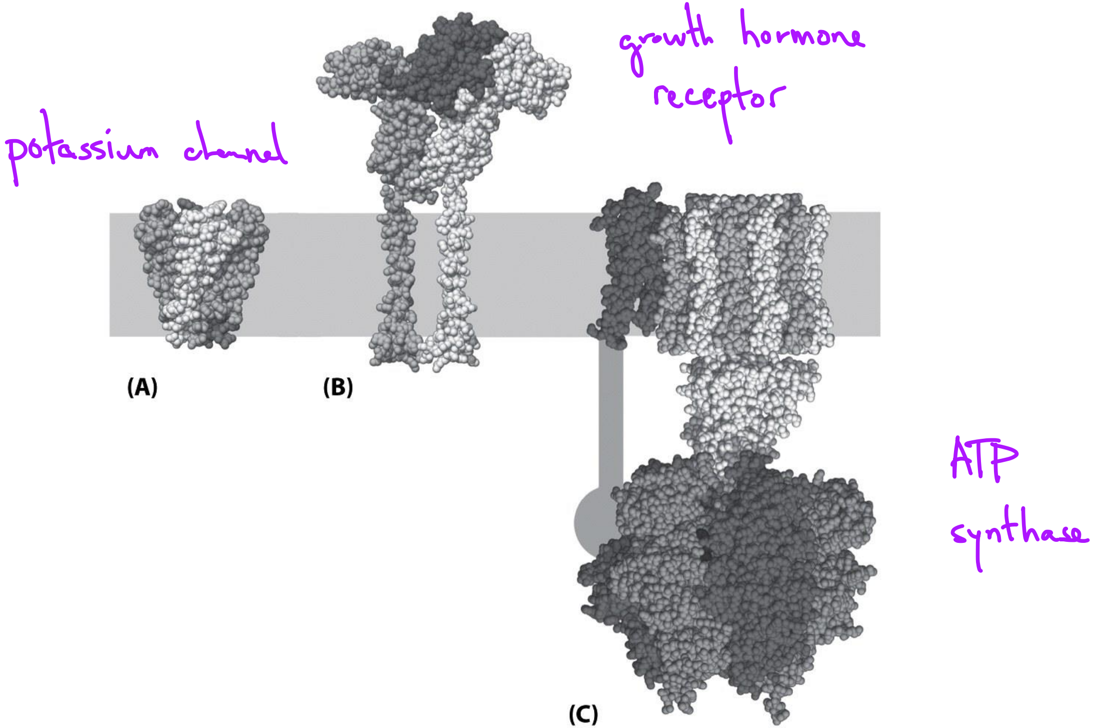
The nature of biological membranes

Biological membranes are fluidlike in-plane



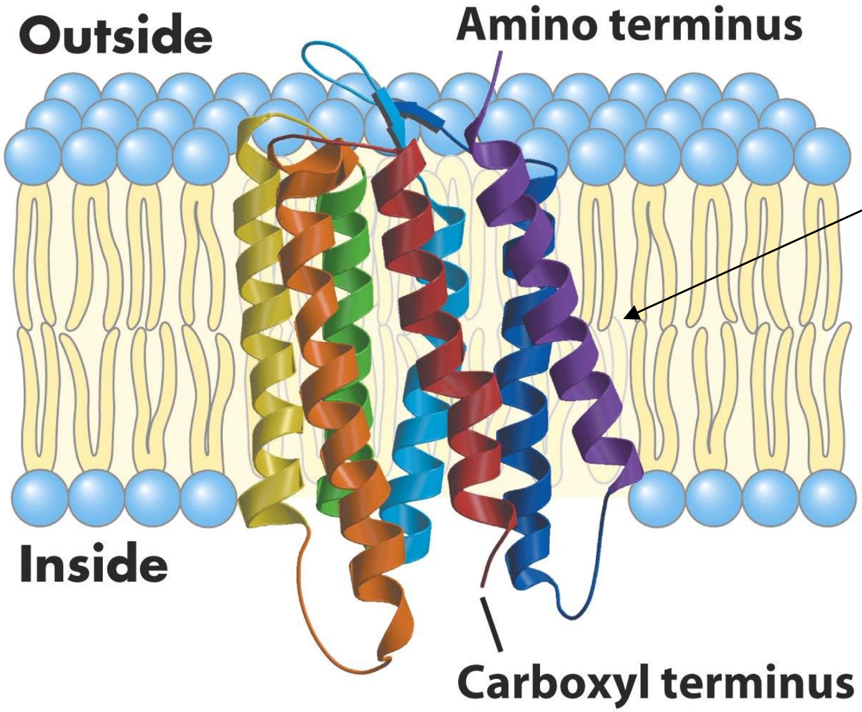
The nature of biological membranes

Transmembrane proteins

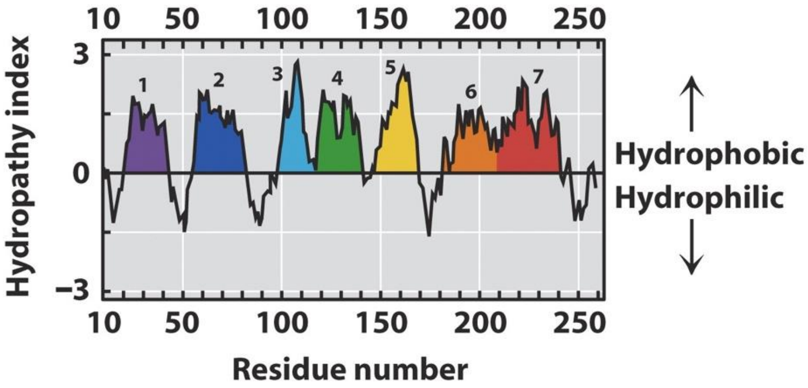


The nature of biological membranes

Transmembrane proteins

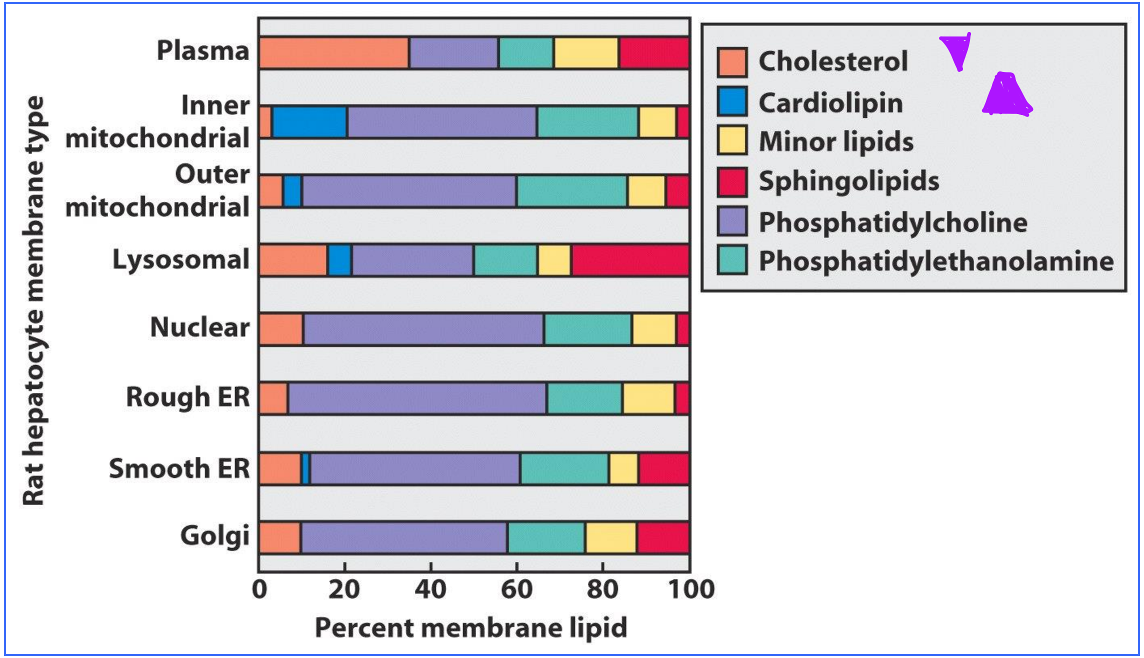


7 helices connected by hydrophilic loops



The nature of biological membranes

Lipid composition of organelles

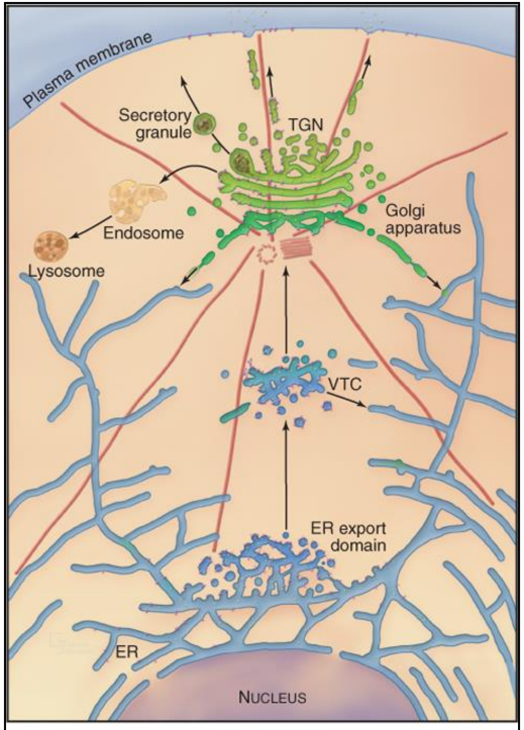


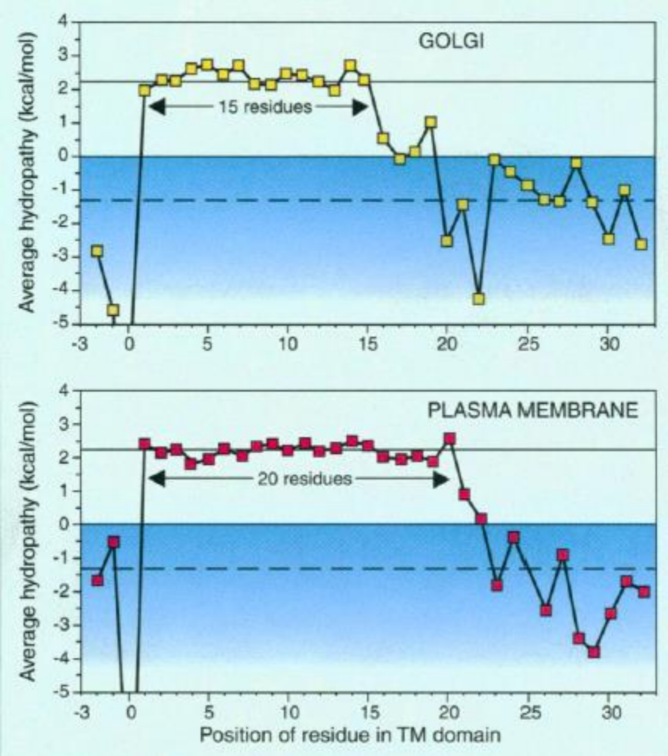
The nature of biological membranes

Transmembrane proteins

"hydrophobic matching"

matching between lipid bilayer thickness and protein transmembrane length





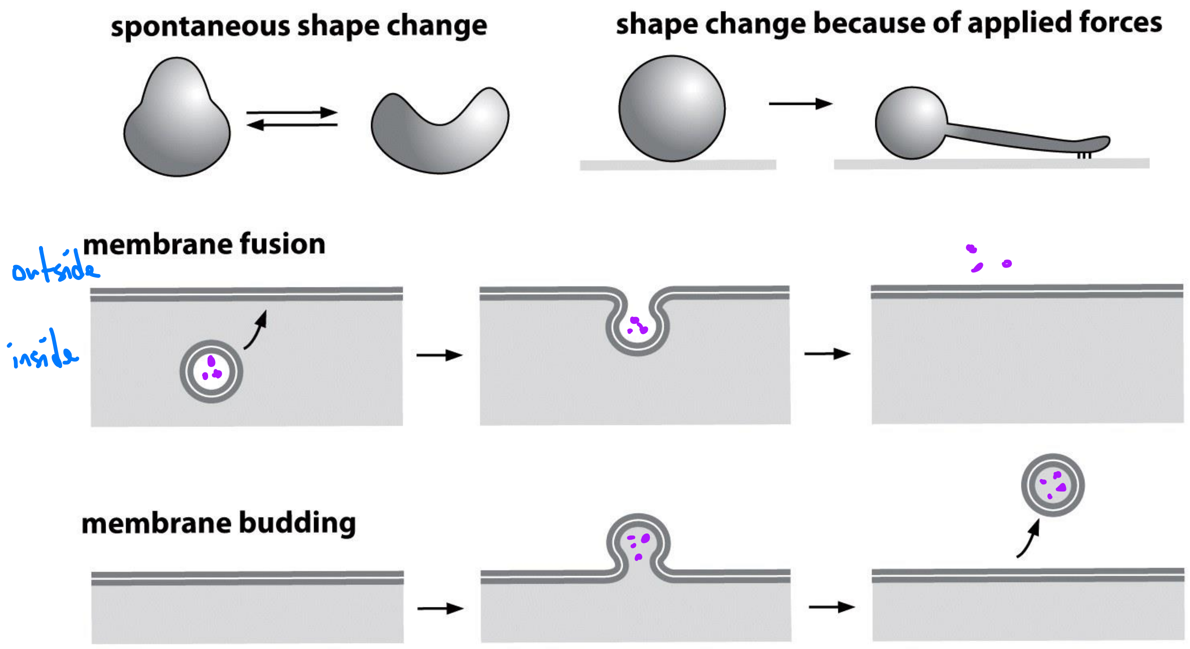
Lecture 4: Biological membranes

Summary

- Membranes are made of lipids & proteins
- Membranes can self-assemble through hydrophobic interactions
- Proteins in membranes can form channels to allow for selective transport
- Lipids & proteins both contribute to minimum energy shape of a membrane, and to the cost to deform it.

The springiness of biological membranes

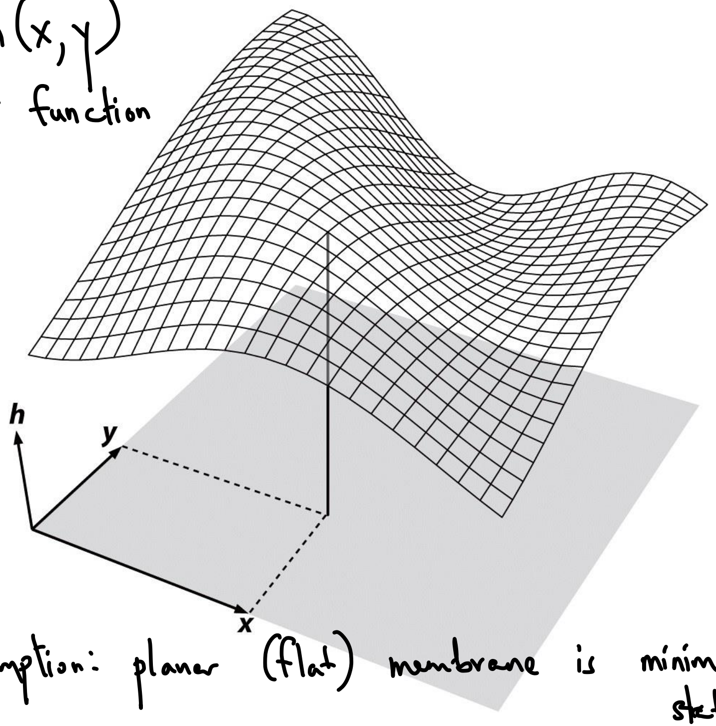
Membrane shape changes



The springiness of biological membranes

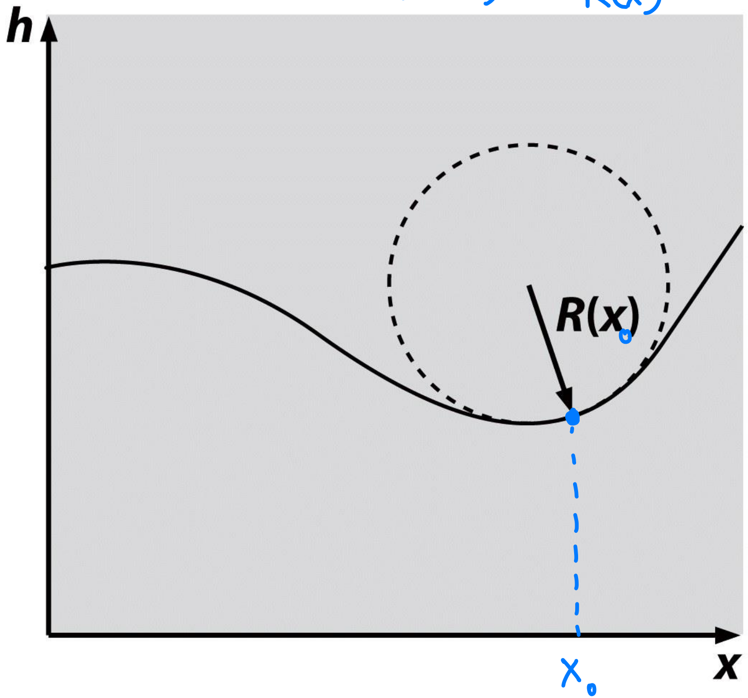
Membrane shape

$h(x,y)$
height function



Assumption: planar (flat) membrane is minimum energy state

curvature $\kappa(x) = \frac{1}{R(x)}$

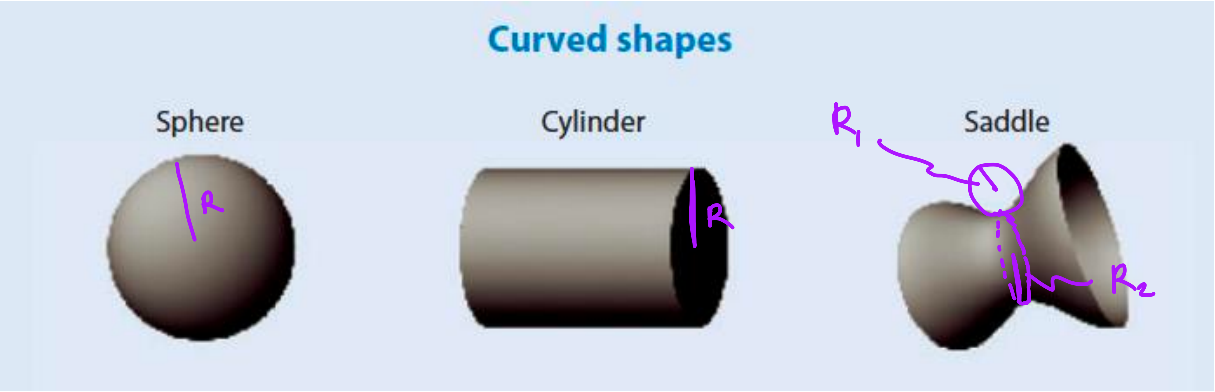


The springiness of biological membranes

Membrane shape: Curvature

shapes

Plane



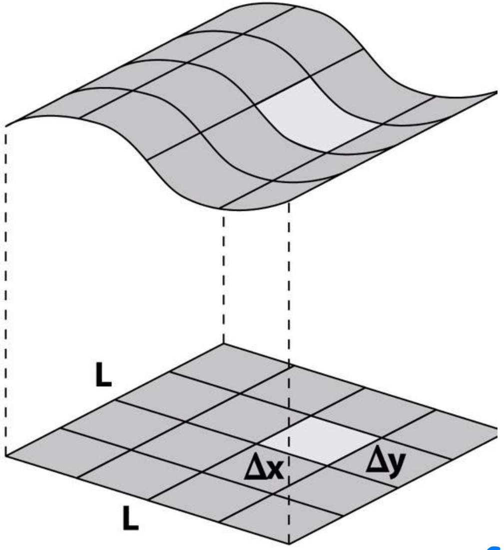
principal curvatures

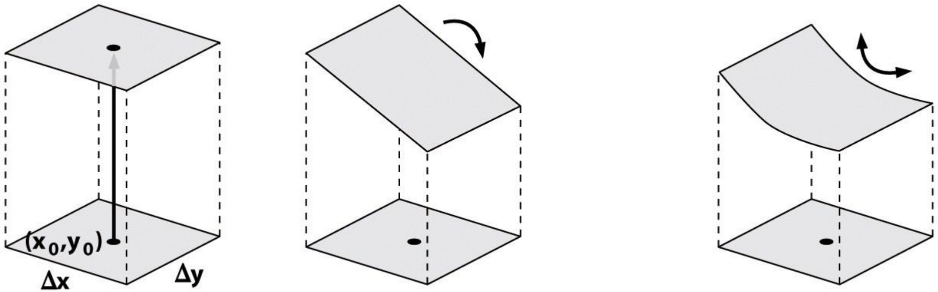
	Plane	Sphere	Cylinder	Saddle
k_1	0	$\frac{1}{R}$	0	$\frac{1}{R_1}$
k_2	0	$\frac{1}{R}$	$\frac{1}{R}$	$\frac{1}{R_2}$

The springiness of biological membranes

Membrane shape: Taylor expansion

$h(x,y)$





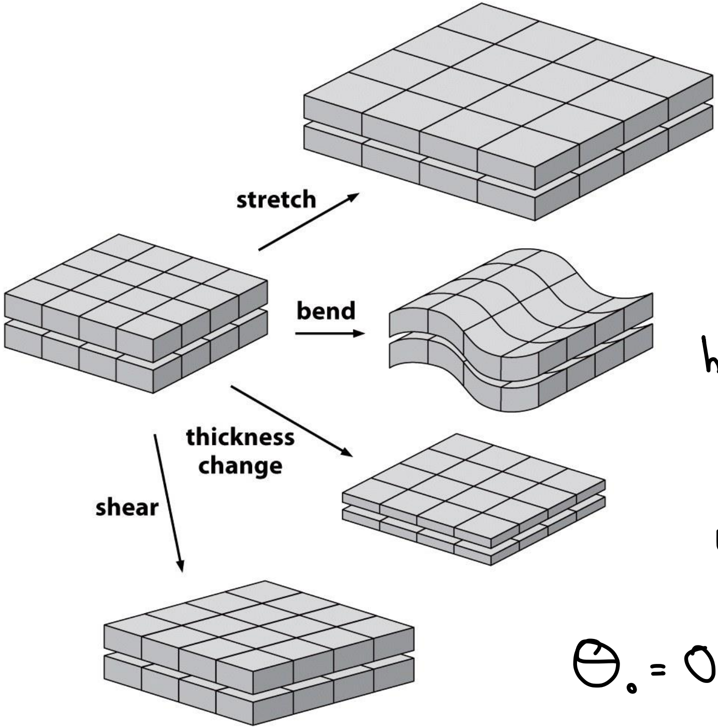
$$h(x,y) = \underbrace{h(x_0,y_0)}_{\text{translate}} + \underbrace{\frac{\partial h}{\partial x}\Delta x + \frac{\partial h}{\partial y}\Delta y}_{\text{rotate}} + \underbrace{\tfrac{1}{2}\underbrace{\frac{\partial^2 h}{\partial x^2}}_{K_{11}}\Delta x^2 + \underbrace{\frac{\partial^2 h}{\partial x \partial y}}_{K_{12}=K_{21}}\Delta x\Delta y + \tfrac{1}{2}\underbrace{\frac{\partial^2 h}{\partial y^2}}_{K_{22}}\Delta y^2}_{\text{bend}}$$

curvature matrix : $\begin{pmatrix} K_{11} & K_{12} \\ K_{21} & K_{22} \end{pmatrix}$

Principal curvatures are <u>eigenvalues</u>

The springiness of biological membranes

Membrane elasticity



change area

$a_0 \to a_0 + \Delta a$

change height

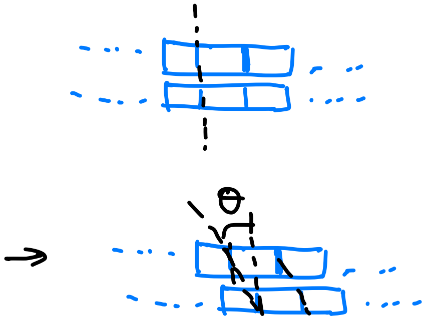
$h = \text{const} \to h(x,y)$

change thickness

$w_0 \to w(x,y)$ or $w_0 + \Delta w$

$\Theta_0 = 0 \to |\Theta| > 0$

Shear:

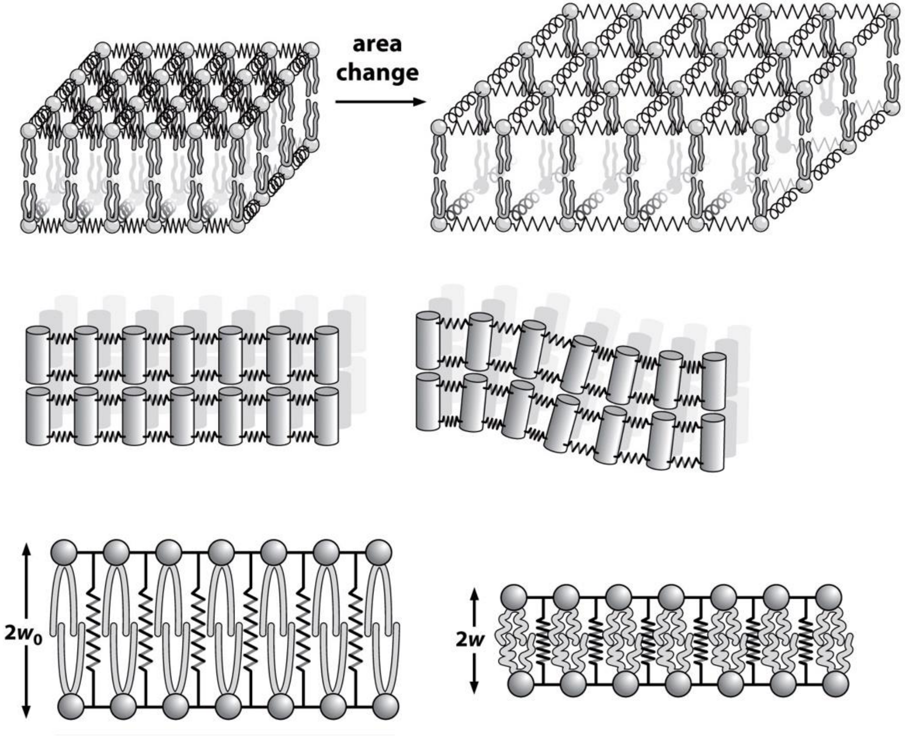


shear angle

The springiness of biological membranes

Membrane elasticity

analogs of Hooke: $\frac{1}{2}k(\Delta x)^2$



$$G_{stretch} = \frac{K_A}{2}\int_{area}\left(\frac{\Delta a}{a_0}\right)^2 dA$$

K_A units energy/area

$$G_{bend} = \frac{K_b}{2}\int_{area}\left(\kappa_1 + \kappa_2\right)^2 dA$$

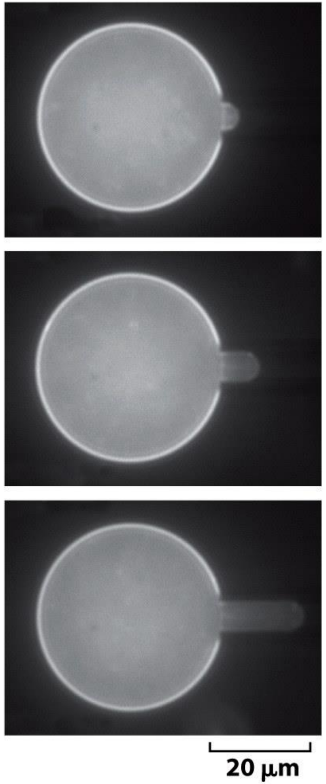
K_b units energy

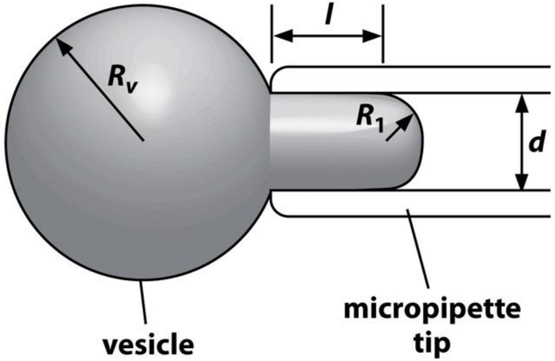
$$G_{thickness} = \frac{K_T}{2}\int_{area}\left(\frac{w - w_0}{w_0}\right)^2 dA$$

K_T units energy/area

The springiness of biological membranes

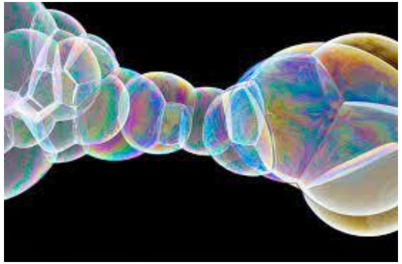
Shape deformation model





Section 11.3.1

The springiness of biological membranes



Springiness of membranes

Laplace pressure

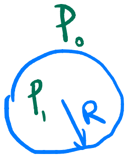
$$P_1 - P_0 = \Delta P = \frac{2\tau}{R}$$

τ is surface tension (energy/area)

The springiness of biological membranes

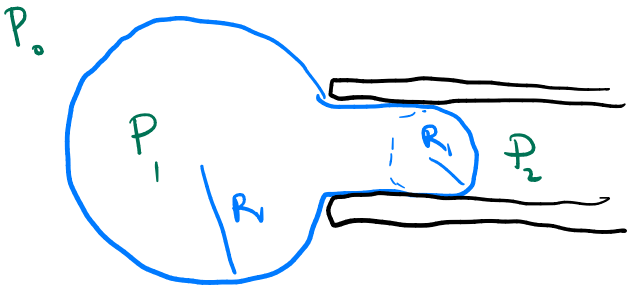
Springiness of membranes

Laplace pressure
(soap bubbles)
Mechanical equilibrium



$$P_1 - P_0 = \Delta P = \frac{2\tau}{R}$$

τ surface tension (energy/area)



$$\tau = \frac{P_2 - P_0}{2}\left(\frac{1}{R_1} - \frac{1}{R_v}\right)^{-1}$$

($P_2 - P_0$: experimentally imposed; R_1, R_v: measured)

Assumption: τ is constant for a continuous membrane

$$= K_A \frac{\Delta a}{a_0}$$

(a_0: measured)

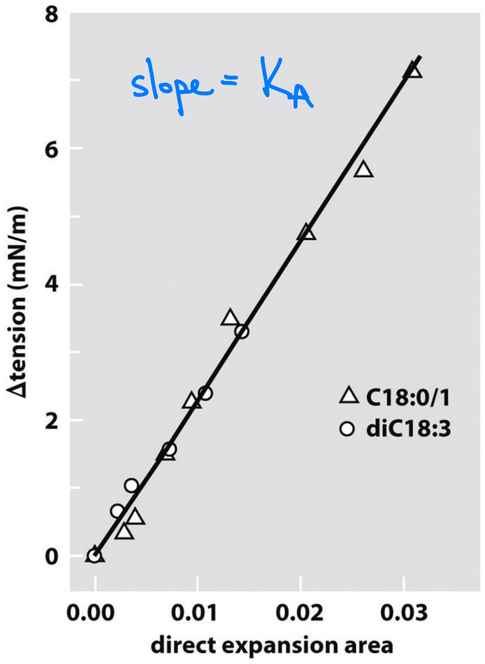
Assumption: Change in area comes from stretching, not from de-wrinkling

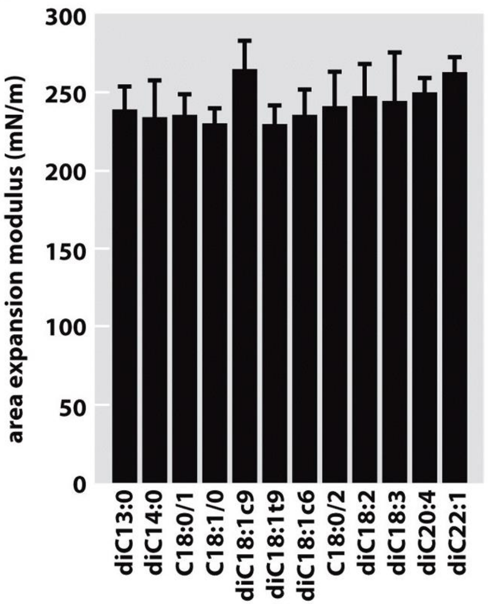
⇒ estimate stretch constant

The springiness of biological membranes

Springiness of membranes

linear force-extension relationship





Lecture 4: Biological membranes

Summary

- Membranes can undergo shape changes in response to applied forces
- Deformation modes: area, curvature, thickness

  Linear force-displacement relation ⇒ energy can be calculated
- Energies of deformation plus LaPlace pressure allows us to estimate elastic constant of membrane

Lecture 5: Biological membranes

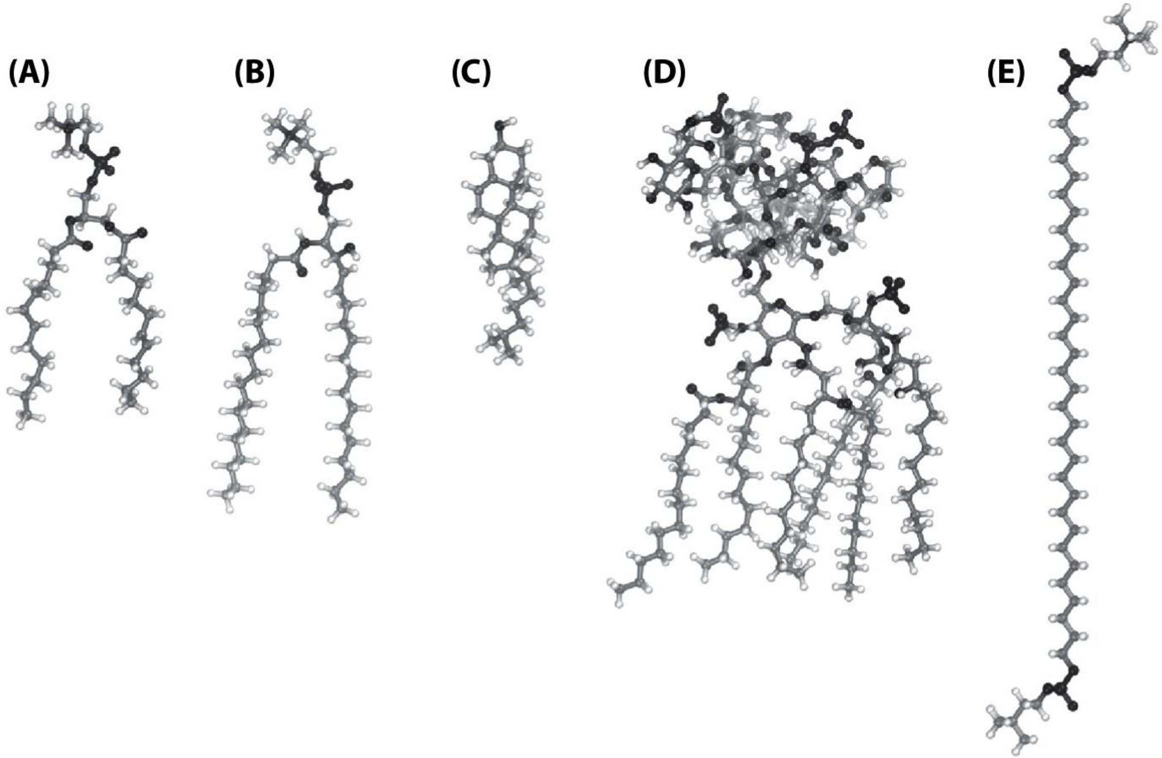
Goal: Estimates and models of membrane shapes

- Membrane pulling
- Shapes of organelles
- Shapes of cells

PBOC Chapter 11.3, 11.4

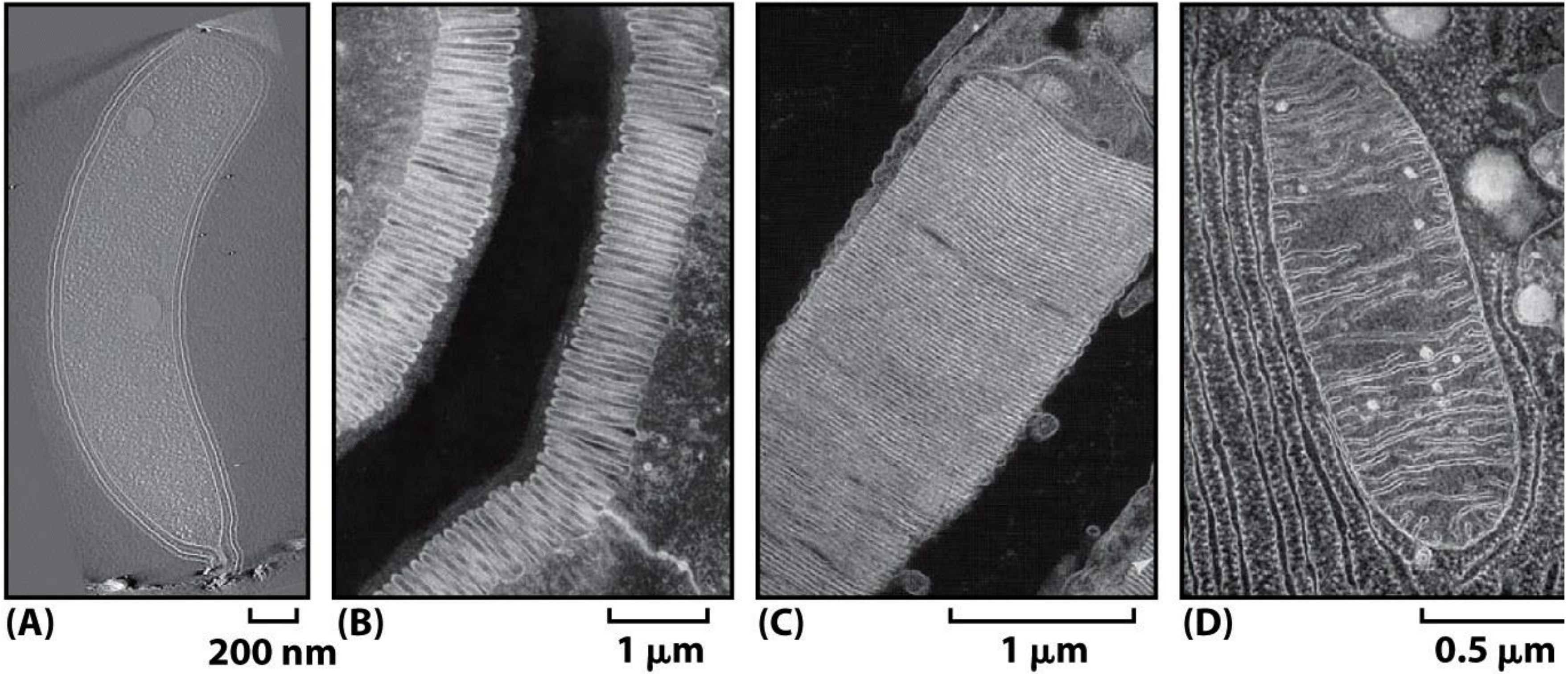
The nature of biological membranes

Cells and membranes



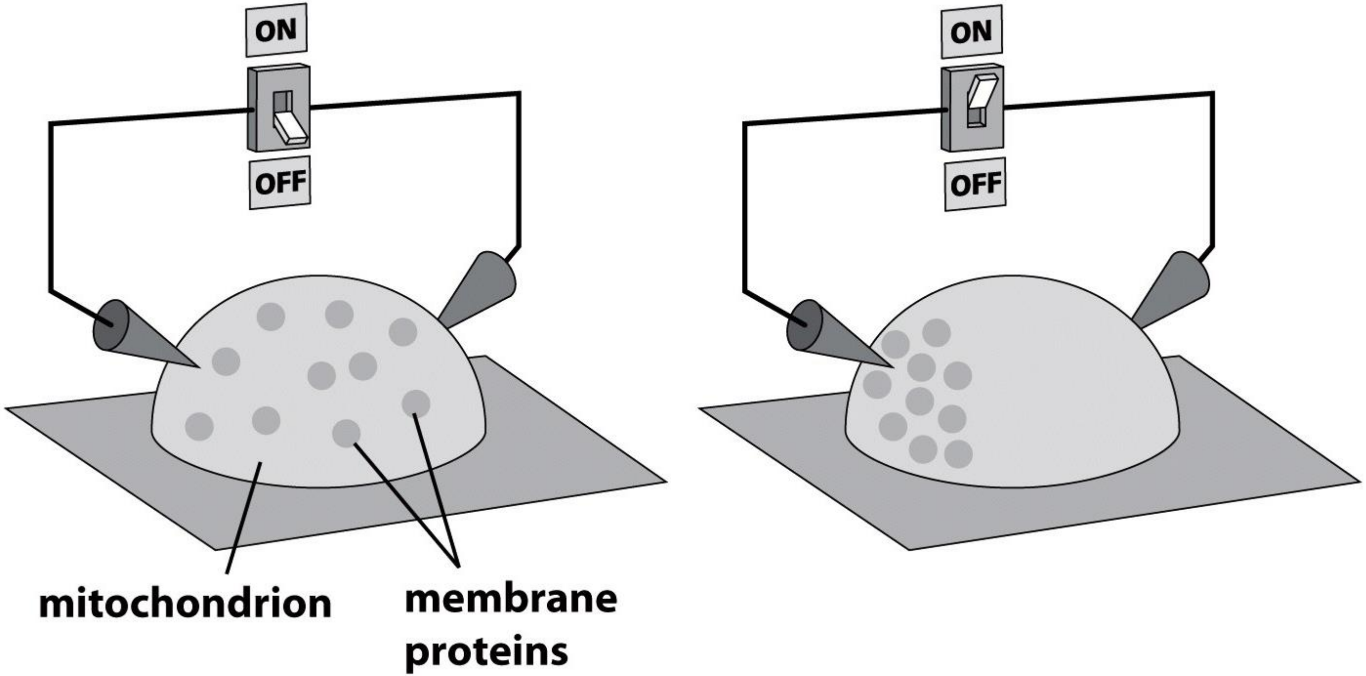
The nature of biological membranes

Cells and membranes



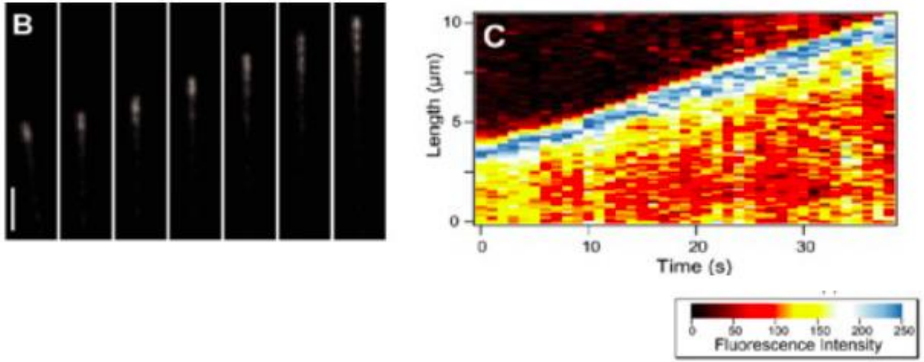
The nature of biological membranes

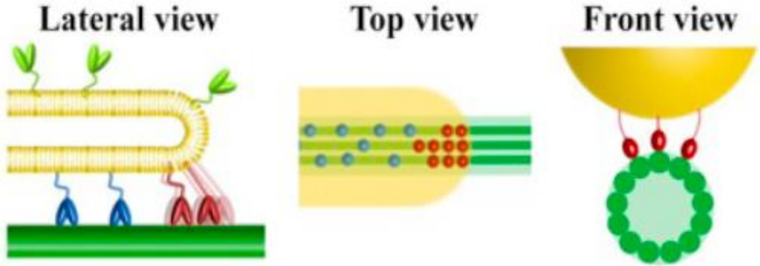
Biological membranes are fluidlike in-plane



The springiness of biological membranes

Motors pull membranes





O. Campàs, C. Leduc et al, Biophys. J. (2008)

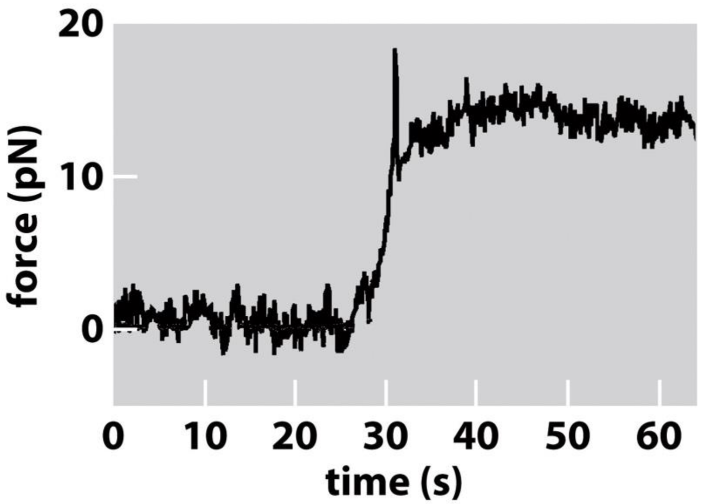
On average, 9 motors are pulling the tube at the same time

The springiness of biological membranes

Shape deformation model

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

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

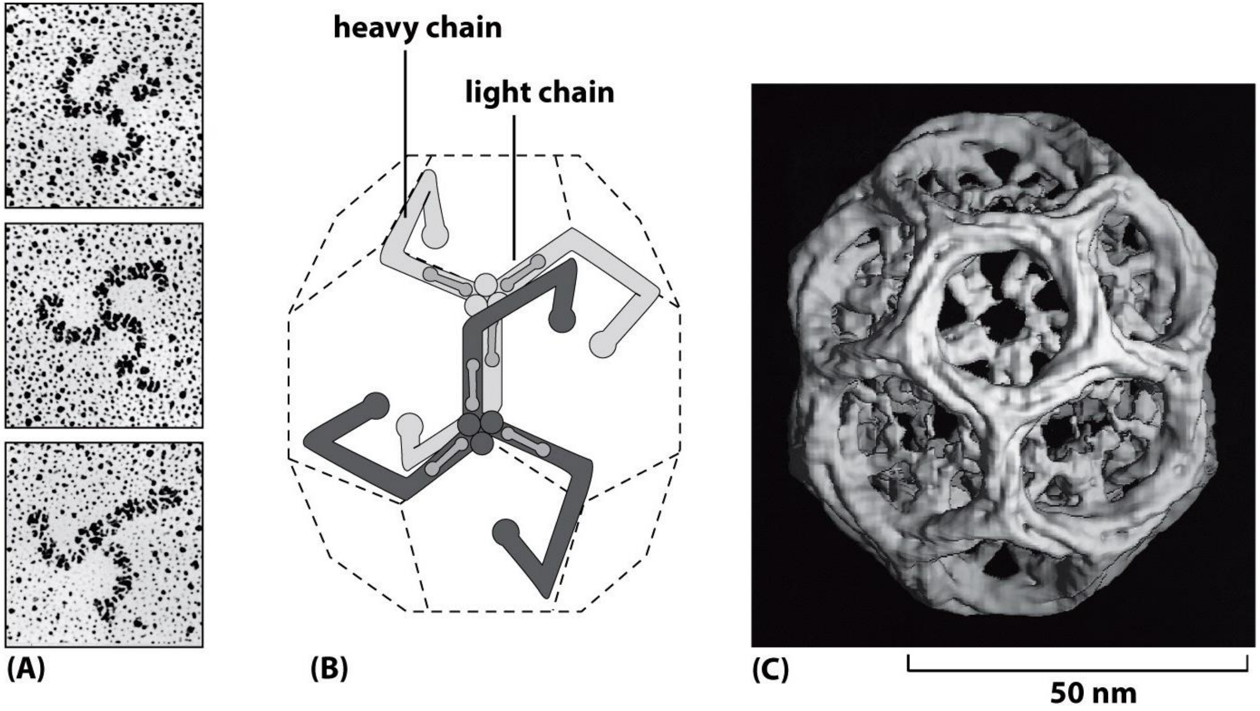


The springiness of biological membranes

Springiness of membranes

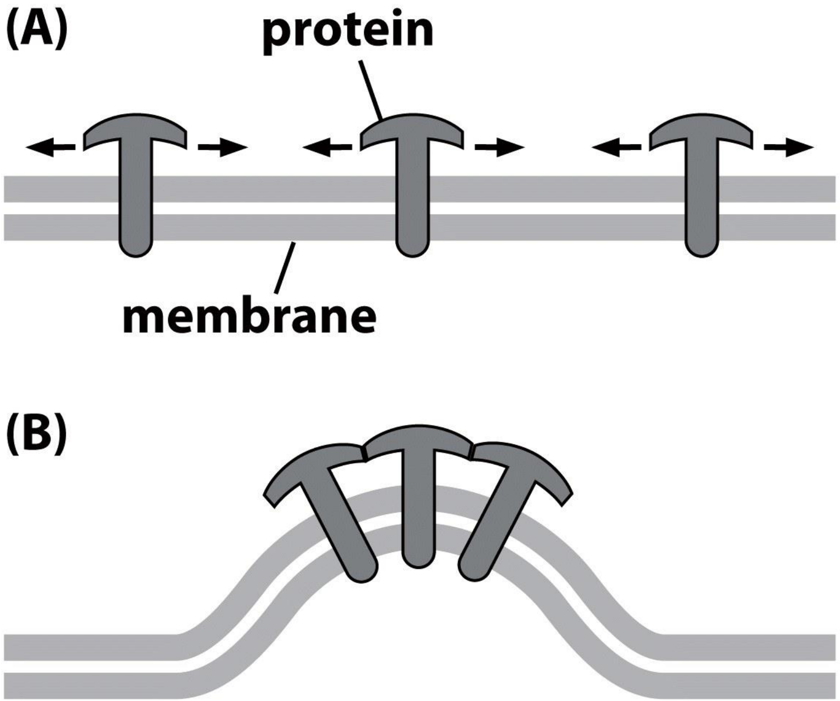
The springiness of biological membranes

Proteins shape membranes



The springiness of biological membranes

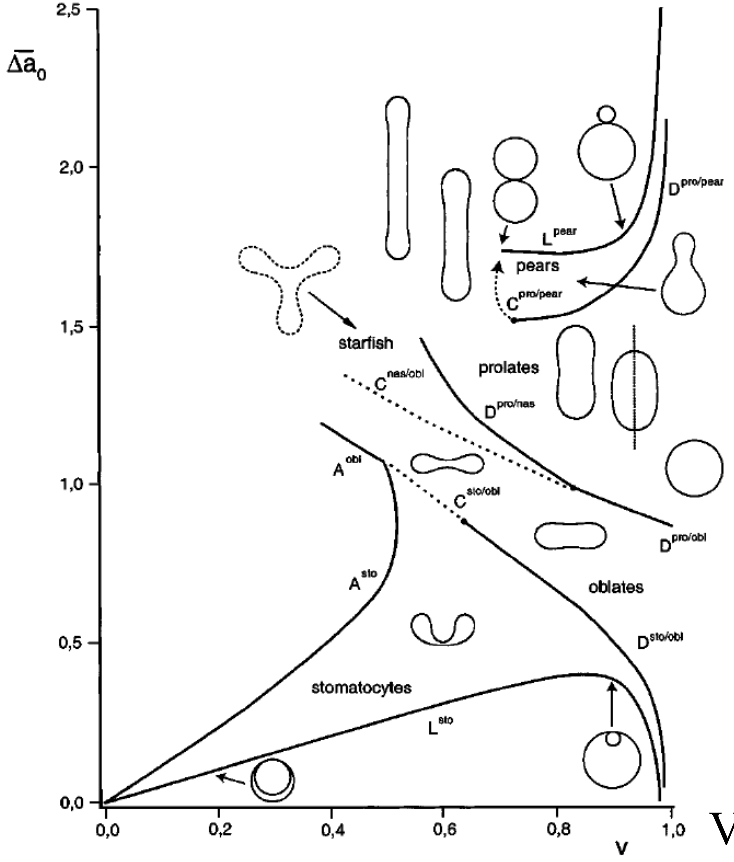
Proteins shape membranes



The springiness of biological membranes

Vesicle shapes: stretch and bend

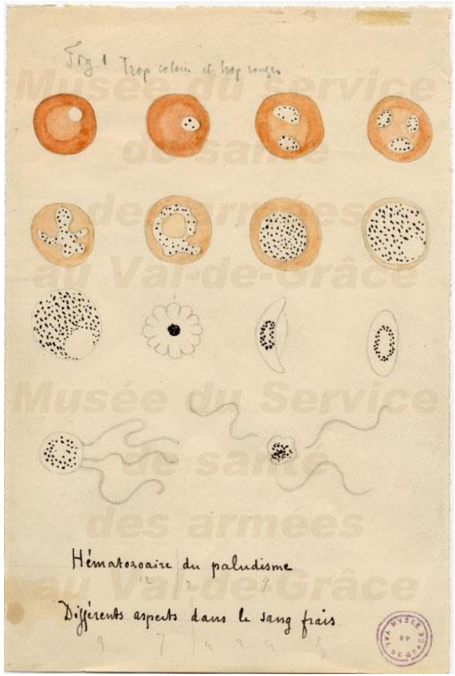
minimize free energy for different volumes, different leaflet area differences (inner/outer)



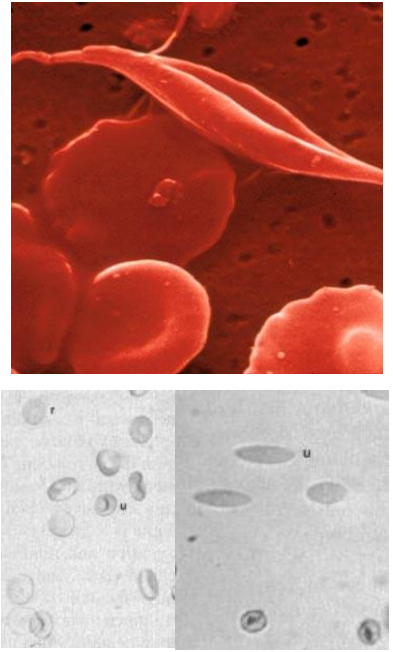
V/V$_{sphere}$

The springiness of biological membranes

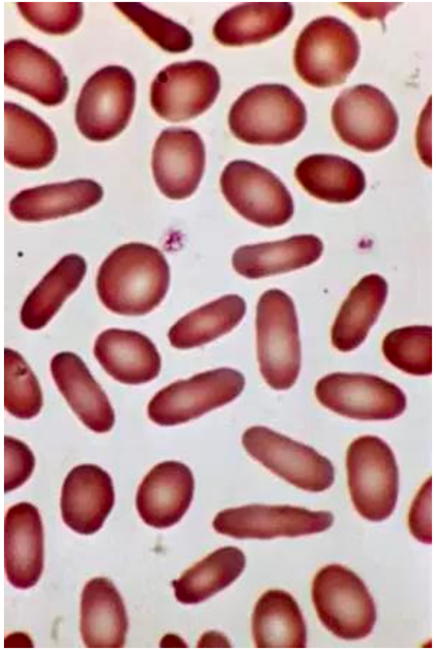
Red blood cell shape and disease



Malaria



Sickle cell anemia

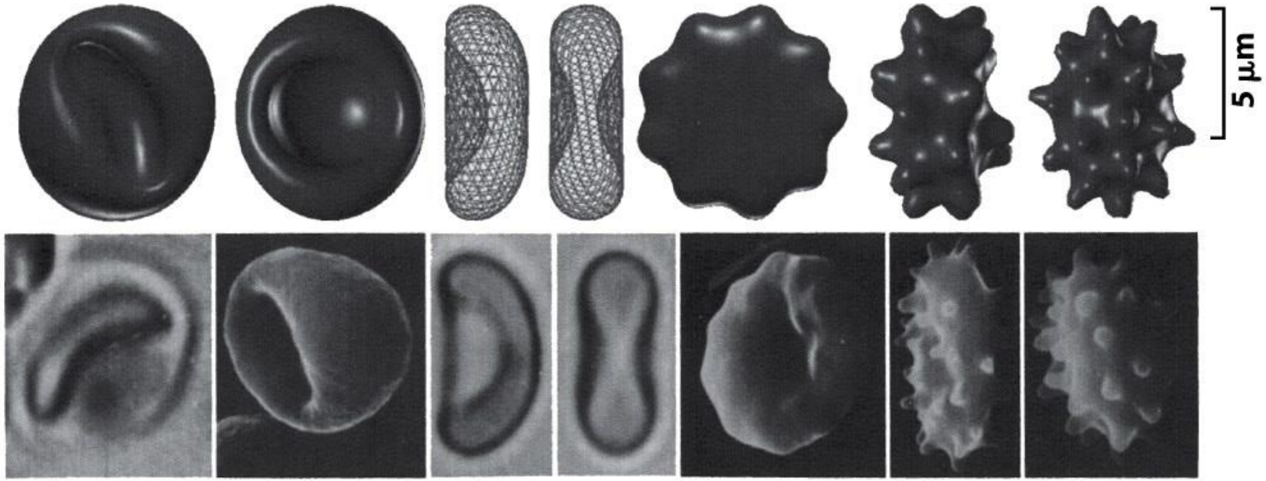


Hereditary elliptocytosis

Biological systems as minimizers

Previously:

Cells as minimizers



changes in area difference between two leaflets of bilayer

states: membrane shapes satisfying geometric constraints (constant area, constant volume)
energy: mechanical (elastic) energy of deformation