5.2 biomembranes - energy

tension, shear, and bending

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day	date		topic	
tue	apr	03	introduction I - cell biology	
thu	apr	05	introduction II - cytoskeletal biology, stem cells	
tue	apr	10	introduction III - structural mechanics	
thu	apr	12	biopolymers I - energy, tension, bending	
thu	apr	12	homework I - biopolymers, directed stem cell differentiation	
tue	apr	17	biopolymers II - entropy, FJC and WLC model	
thu	apr	19	biopolymers III - polymerization kinetics in amoeba	
tue	apr	24	cytoskeletal mechanics I - fiber bundle model for filopodia	
thu	apr	26	cytoskeletal mechanics II - network model for red blood cells	
thu	apr	26	homework II - cytoskeleton, cell mechanics challenges	
tue	may	01	cytoskeletal mechanics III - tensegrity model for generic eukaryotic cells	
thu	may	03	biomembranes I - micropipette aspiration in white blood cells and cartilage cells	
tue	may	08	biomembranes II - lipid bilayer, soap bubble, cell membrane	
thu	may	10	biomembranes III - energy, tension, shear, bending	
tue	may	15	mechanotransduction I - inter- and intracellular signaling, bone cells	
tue	may	15	homework III - micropipette aspiration, final project	
thu	may	17	summary and midterm preparation	
tue	may	22	midterm	
thu	may	24	mechanotransduction II - electrophysiology in nerve cells	
tue	may	29	mechanotransduction III - excitation contraction in skeletal muscle and heart cells	
thu	may	31	final projects I - oral presentations	
tue	jun	05	final projects II - oral presentations	
thu	jun	07	no class	
fri	jun	08	final projects - written projects due	

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homework #2

I just wanted to send you a quick message concerning the last homework. Most of you did really well. For those of you who lost points I'd like to remind you that you can talk to either me or Ellen about the grading, the problems you had with the homework, and ideas for improvement. I try to grade as fair and consistent as I can, if you still feel that something is off, please let me know.

On a different note, I had the impression that to some of you who lost points the **problem was not quiet clear**. If that is the case, please send me an email and ask me for help or clarification the next time. I cannot help once you submitted your homework.

Lastly, I'd like to discuss a few common mistakes. Some of you got **units wrong** and lost points that way. Although you may think that is a minor point and I know what units you meant, I consider units an integral part of the result, so please make sure you double-check. If we do ask for the minimum number please **do not round to the nearest thousand**, we actually would like to see the minimum number.

A problem that seemed more prevalent this time than any other time concerns rounding. When you do work on homework problems, please try to **solve for the unknown variable completely** before you plug in numbers and calculate a numerical value. For problem 1c) I saw a dozen different numbers. All these numbers were derived from the same equations but everybody rounded to a different precision, plugged in numbers at a different stage of their calculation etc.

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final projects

beth	measuring cell traction force
brittany	leukocyte activation
brandon, matthew	vasculogenesis
cesare	metastasis
mengli	bone cells
ernst	adipose cells
juna	skin cells
dee ann, ian, vaishnav	mechanics of cancer cells
livia	dynamics of morphogenesis
alex	artificial red blood cells
kamil	directed stem cell differentiation
elliot, pamon, ben	differentiation of mesenchymal cells
hwee juin	mechanotransduction in intestinal cells
corey, alex	optical stimulation of heart cells
elia, dong hyun, armen	cytoskeletal remodeling in endothelial cells

law of laplace from free body diagram

$$p^{int} - p^{out} = 2\frac{n}{R} \quad \dots \text{ Law of Laplace}$$

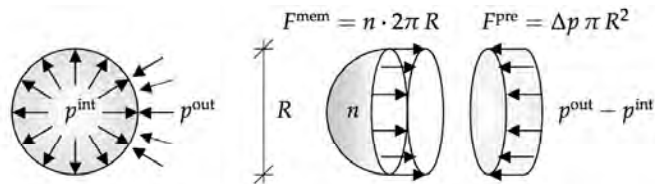$$F^{mem} = n \cdot 2\pi R \qquad F^{pre} = \Delta p\, \pi R^2$$

Figure 5.7: Law of Laplace. The membrane force $F^{mem} = n \cdot 2\pi R$ is the result of the surface tension n acting on the cell membrane along the circumference $C = 2\pi R$. It is in equilibrium with the forces F^{pre} resulting from the pressure difference Δp acting on the cell area $A = \pi R^2$.

5.1 motivation - law of laplace

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law of laplace from energy minimization

$$W(r) = W^{int} - W^{ext}$$
$$W^{int} = \gamma A = \gamma 4\pi r^2$$
$$W^{ext} = \Delta p V = \Delta p \frac{4}{3}\pi r^3$$

$$W(r) \to \min \qquad \delta W(r) \doteq 0$$
$$\delta W^{int} = \gamma 8\pi r$$
$$\delta W^{ext} = \Delta p 4\pi r^2$$

III. *An Essay on the Cohesion of Fluids.* **By Thomas Young**, M. D. For. Sec. R.S.

Read December 20, 1804.

I. *General Principles.*

IT has already been asserted, by Mr. MONGE and others, that the phenomena of capillary tubes are referable to the cohesive attraction of the superficial particles only of the fluids employed, and that the surfaces must consequently be formed into curves of the nature of linteariæ, which are supposed to be the results of a uniform tension of a surface, resisting the pressure of a fluid, either uniform, or varying according to a given law.

$$\gamma 8\pi r - \Delta p 4\pi r^2 \doteq 0 \qquad \Delta p = 2\gamma\frac{1}{r}$$

young [1805], laplace [1806]

5.1 motivation - energy minimization

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concept of surface tension

air — no cohesive forces

air-water interface

water — cohesive forces from all sides
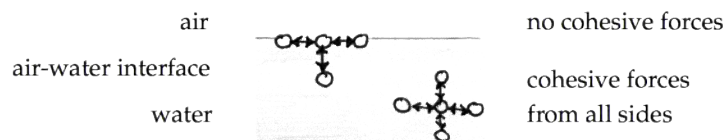
Figure 5.15: Air water interface - molecular interpretation of surface tension

Surface tension Surface tension is typically measured in force per length related to the units dynes per cm. Since 1 dyne = 10 mN, 1 dyne/cm = 1 mN/m. Alternatively, especially in thermodynamics, the notion surface energy is used instead. Surface energy is measured in ergs per length squared, where one eng, the force of one dyne exerted for a distance of one cm is equal to gram centimeter squared per second squared g cm^2/s^2 or, equivalently, 10^{-7} joules. The surface tension of water at room temperature is γ^{water}=72 dynes/cm, ethanol has a lower surface tension of $\gamma^{ethanol}$=22 dynes/cm and mercury has a surface tension as large as $\gamma^{mercury}$=465 dynes/cm.

5.1.motivation - surface tension

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trusses, beams, walls, plates, membranes, shells

	dimension	geometry	loading	deformation	gov eqn
truss	1d straight	$w,h \ll l$	axial	tension	2nd order
beam	1d straight	$w,h \ll l$	transverse	bending	4th order
wall	2d flat	$h \ll w,l$	in plane	tension/shear	2nd order
plate	2d flat	$h \ll w,l$	transverse	bending	4th order
membrane	3d curved	$h \ll w,l$	in plane	tension/shear	2nd order
shell	3d curved	$h \ll w,l$	transverse	bending	4th order

Table 2.1: Classification of structural elements based on dimension, geometry and loading

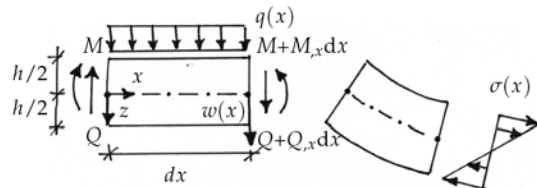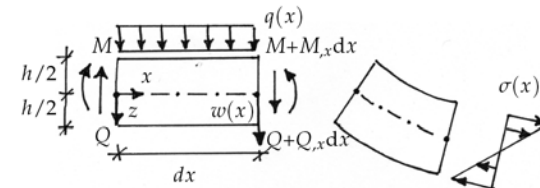**5.2 biomembranes - structural elements**

transverse deformation - bending

Figure 3.2: Transverse loading of one dimensional structure ○ stresses σ vary linearly across the cross section

euler bernoulli beam theory
- normals remain straight (they do not bend)
- normals remain unstretched (they keep the same length)
- normals remain normal (they remain orthogonal to the beam axis)

tension vs bending - trusses vs beams

Figure 3.2: Transverse loading of one dimensional structure ○ stresses σ vary linearly across the cross section

overall deformation = axial + transverse deformation

$$u^{\text{tot}}(x,z) = u(x) - z\,w(x)_{,x}$$
$$\varepsilon = u^{\text{tot}}_{,x} = u_{,x} - z\,w_{,xx}$$

- axial deformation $u(x)$
- transverse deformation, scaled rotation of beam axis $z\,w(x)_{,x}$
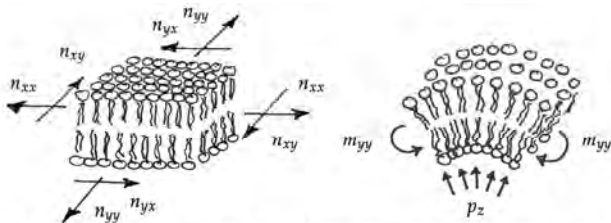
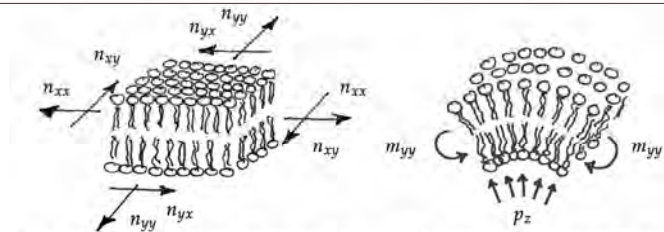## transverse deformation - bending

Figure 5.12: Infinitesimal element of the cell membrane subject to tension causing in plane deformation and shear (left) and bending causing out of plane deformation (right)

kirchhoff love shell theory
- normals remain straight (they do not bend)
- normals remain unstretched (they keep the same length)
- normals remain normal (they remain orthogonal to the beam axis)

tension vs bending - membranes vs shells

Figure 5.12: Infinitesimal element of the cell membrane subject to tension causing in plane deformation and shear (left) and bending causing out of plane deformation (right)

overall deformation = in plane + transverse deformation

$$u^{\text{tot}}(x,y,z) = u(x,y) - z\,w_{,x}$$
$$v^{\text{tot}}(x,y,z) = v(x,y) - z\,w_{,y}$$
$$w^{\text{tot}}(x,y,z) = w(x,y)$$

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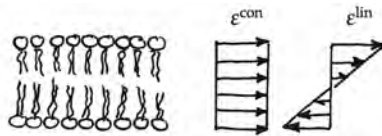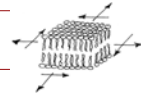
Figure 5.18: Von Kármán strains in cross section – constant terms ε^{con} related to in plain strains and linear terms ε^{lin} related to out of plane bending
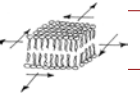
overall strain = in plane (constant) + transverse (linear)

$$\varepsilon_{xx} = u_{,x} + \tfrac{1}{2} w_{,x}^2 - z\, w_{,xx}$$
$$\varepsilon_{yy} = v_{,y} + \tfrac{1}{2} w_{,y}^2 - z\, w_{,yy}$$
$$\varepsilon_{xy} = \tfrac{1}{2} \left[u_{,y} + v_{,x} + w_{,x} w_{,y} - 2z\, w_{,xy} \right]$$

5.2 biomembranes - energy

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kinematic equations

$$\varepsilon_{xx} = u_{,x} + \tfrac{1}{2} w_{,x}^2$$
$$\varepsilon_{yy} = v_{,y} + \tfrac{1}{2} w_{,y}^2$$
$$\varepsilon_{xy} = \tfrac{1}{2} \left[u_{,y} + v_{,x} \right] + w_{,x} w_{,y}$$

constitutive equations

$$\sigma_{xx} = \frac{E}{1-\nu^2} \left[\varepsilon_{xx} + \nu\, \varepsilon_{yy} \right]$$
$$\sigma_{yy} = \frac{E}{1-\nu^2} \left[\varepsilon_{yy} + \nu\, \varepsilon_{xx} \right]$$
$$\sigma_{xy} = \frac{E}{1+\nu} \quad \varepsilon_{xy}$$

stress resultants

$$n_{xx} = \frac{E h}{[1-\nu^2]} \left[\varepsilon_{xx} + \nu\, \varepsilon_{yy} \right]$$
$$n_{yy} = \frac{E h}{[1-\nu^2]} \left[\varepsilon_{yy} + \nu\, \varepsilon_{xx} \right]$$
$$n_{xy} = \frac{E h}{1+\nu} \quad \varepsilon_{xy}$$

equilibrium equations

$$\sum f_x \doteq 0 \quad n_{xx,x} + n_{xy,y} = 0$$
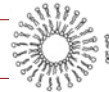$$\sum f_y \doteq 0 \quad n_{yx,x} + n_{yy,y} = 0$$
$$\sum f_z \doteq 0$$

$$n_{xx}\, w_{,xx} + 2\, n_{xy}\, w_{,xy} + n_{yy}\, w_{,yy} + p_z = 0$$

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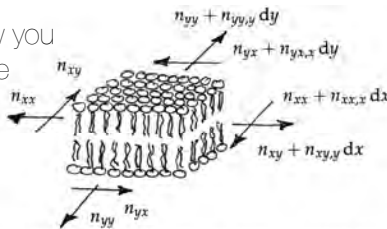…this is just to show you how you could derive the force equilibrium

Figure 5.19: Infinitesimal element of the cell membrane with in plane tensile forces n_{xx} and n_{yy}

$$\sum f_x \doteq 0: \quad -n_{xx}dy + [n_{xx} + n_{xx,x}dx]dy - n_{yx}dx + [n_{yx} + n_{yx,y}dy]dx = 0$$
$$\sum f_y \doteq 0: \quad -n_{yy}dx + [n_{yy} + n_{yy,y}dy]dx - n_{xy}dy + [n_{xy} + n_{xy,x}dx]dy = 0$$
$$\sum f_z \doteq 0: \quad -n_{xx}dy\, w_{,x} + [n_{xx} + n_{xx,x}dx]dy[w_{,x} + w_{,xx}dx]$$
$$\qquad -n_{xy}dy\, w_{,y} + [n_{xy} + n_{yx,x}dx]dy[w_{,y} + w_{,xy}dx]$$
$$\qquad -n_{yx}dx\, w_{,x} + [n_{yx} + n_{xy,y}dy]dx[w_{,x} + w_{,xy}dy]$$
$$\qquad -n_{yy}dx\, w_{,y} + [n_{yy} + n_{yy,y}dy]dx[w_{,y} + w_{,yy}dy] + p_z\, dxdy = 0$$

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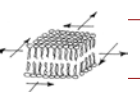
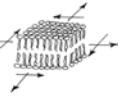$$n_{xx}\, w_{,xx} + 2\, n_{xy}\, w_{,xy} + n_{yy}\, w_{,yy} + p_z = 0$$

now, let's look at some special cases…

- equilibiaxial tension (without shear) > tensile stiffness
- equilibiaxial tension (without shear) > area stiffness
- shear (without extension)   > shear stiffness

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$$n_{xx}\, w_{,xx} + 2\, n_{xy}\, w_{,xy} + n_{yy}\, w_{,yy} + p_z = 0$$

special case of equibiaxial tension (without shear)

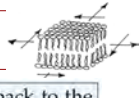$$\sigma_{xx} = \sigma_{yy} = \sigma_. \qquad \sigma_{xy} = 0$$
$$n_{xx} = n_{yy} = n \qquad n_{xy} = 0$$

$$n\left[w_{,xx} + w_{,yy} \right] + p_z = 0 \qquad w_{,xx} + w_{,yy} = \Delta w$$

$$p_z = -n\,\Delta w \qquad \text{with} \qquad n \ \ldots \text{ surface tension}$$

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Energy minimization for the soap bubble problem Let us briefly turn back to the soap bubble problem. Although maybe a bit more cumbersome, we can, of course, derive the equilibrium equations through energy principles as well. We thus want to look for the minimum of the overall energy W with respect to all dependent quantities. Unlike in the bubble example where the kinematic unknown was just the radius r the unknowns in our formulation here are the displacements u, v and w. Similar to the soap bubble problem, the minimum of the overall energy W with respect to variations in displacements u, v and w can be expressed through the vanishing first variation δW with respect to the individual unknowns.

$$W(u,v,w) \to \min \qquad \delta W(u,v,w) = \delta W^{\text{int}} + \delta W^{\text{ext}} \doteq 0$$
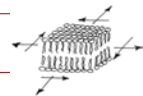
The internal and external virtual work δW^{int} and δW^{ext} can then be specified as follows.

$$
\begin{aligned}
\delta W^{\text{int}} &= \int_A \int_{-h/2}^{+h/2} \sigma_{xx}\,\delta\varepsilon_{xx} + 2\sigma_{xy}\,\delta\varepsilon_{xy} + \sigma_{yy}\,\delta\varepsilon_{yy} \quad \mathrm{d}A \\
&= \int_A n_{xx}\,\delta\varepsilon_{xx}^{\text{con}} + 2n_{xy}\,\delta\varepsilon_{xy}^{\text{con}} + n_{yy}\,\delta\varepsilon_{yy}^{\text{con}} \quad \mathrm{d}z\,\mathrm{d}A \\
\delta W^{\text{ext}} &= \int_A \qquad\qquad p\,\delta w \qquad\qquad \mathrm{d}A
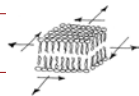\end{aligned}
$$

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compare to young and laplace solution

$$W(r) = W^{\text{int}} - W^{\text{ext}}$$

$$
\begin{aligned}
W^{\text{int}} &= \gamma A = \gamma\, 4\,\pi\, r^2 \\
W^{\text{ext}} &= \Delta p\, V = \Delta p\, \tfrac{4}{3}\pi r^3
\end{aligned}
\qquad \Delta p = 2\gamma\,\frac{1}{r}
$$

Energy considerations can sometimes be very illustrative. They immediately provide information about the so called energy conjugate pairs. For example, from the above expression, you can easily see that the shear stresses σ_{xy} are energetically conjugate to the shear strains ε_{xy} or that the normal stress resultants n_{xx} are conjugate to the corresponding strains $\varepsilon_{xx}^{\text{con}}$ which are constant over the thickness. The entire set of equilibrium equations (1.2.10) can be extracted from the energy formulation by making use of the kinematic equations and expressing the strains through the displacements. Then we would perform an integration by parts and sort all contributions with respect to δu, δv and δw. Each related term would then represent one of the equilibrium equations stated in equation (1.2.10). In this context, the equilibrium equations would be referred to as the Euler-Lagrange equations.
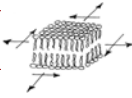
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stress resultants

$$
\begin{aligned}
n_{xx} &= \int_{-h/2}^{+h/2} \sigma_{xx}\,\mathrm{d}z = \sigma_{xx}\cdot h = \frac{E\,h}{[1-\nu^2]}\left[\varepsilon_{xx} + \nu\,\varepsilon_{yy}\right] \\
n_{yy} &= \int_{-h/2}^{+h/2} \sigma_{yy}\,\mathrm{d}z = \sigma_{yy}\cdot h = \frac{E\,h}{[1-\nu^2]}\left[\varepsilon_{yy} + \nu\,\varepsilon_{xx}\right]
\end{aligned}
$$

$$
\begin{aligned}
n_{xx} &= K_N\left[\varepsilon_{xx} + \nu\,\varepsilon_{yy}\right] \\
n_{yy} &= K_N\left[\varepsilon_{yy} + \nu\,\varepsilon_{xx}\right]
\end{aligned}
\qquad \text{with} \quad K_N = \frac{E\,h}{[1-\nu^2]} \quad \ldots \text{ tensile stiffness}
$$

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$$\frac{\Delta A}{A} = \frac{a - A}{A} = \frac{[1+\varepsilon]^2 L^2 - L^2}{L^2} = 2\varepsilon + \varepsilon^2 \approx 2\varepsilon$$

$$n = \frac{E\,h}{1-\nu^2}\left[\varepsilon_{xx} + \nu\,\varepsilon_{yy}\right] = \frac{E\,h}{1-\nu^2}\left[1+\nu\right]\varepsilon = \frac{E\,h}{2\left[1-\nu\right]}\frac{\Delta A}{A}$$

special case of equibiaxial tension (without shear)

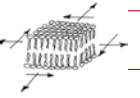$$n_{xx} = n_{yy} = n \qquad \varepsilon_{xx} = \varepsilon_{yy} = \varepsilon$$

$$n = \frac{E\,h}{1-\nu^2}\left[\varepsilon_{xx} + \nu\,\varepsilon_{yy}\right] = \frac{E\,h}{1-\nu^2}\left[1+\nu\right]\varepsilon = \frac{E\,h}{2\left[1-\nu\right]}\frac{\Delta A}{A}$$

$$n = K_A\,\frac{\Delta A}{A} \quad \text{with} \quad K_A = \frac{E\,h}{2\left[1-\nu\right]} \qquad \text{… area stiffness}$$

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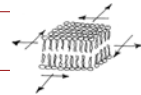
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special case of shear (without extension)

$$n_{xy} = \int_{-h/2}^{+h/2} \sigma_{xy}\,\mathrm{d}z = \sigma_{xy}\cdot h = \frac{E\,h}{1+\nu}\,\varepsilon_{xy}$$

$$n_{xy} = K_S\,\varepsilon_{xy} \quad \text{with} \quad K_S = 2\,G\,h = \frac{E\,h}{1+\nu} \qquad \text{… shear stiffness}$$

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$$\begin{aligned} n_{xx} &= K_N\left[\varepsilon_{xx} + \nu\,\varepsilon_{yy}\right] \\ n_{yy} &= K_N\left[\varepsilon_{yy} + \nu\,\varepsilon_{xx}\right] \end{aligned} \quad \text{with} \quad K_N = \frac{E\,h}{\left[1-\nu^2\right]} \ \text{… tensile stiffness}$$

$$n = K_A\,\frac{\Delta A}{A} \quad \text{with} \quad K_A = \frac{E\,h}{2\left[1-\nu\right]} \qquad \text{… area stiffness}$$

$$K_A = 0.1 - 1.0\,\mathrm{N/m} \qquad \text{lipid bilayer}$$
$$K_A = 0.45\,\mathrm{N/m} \qquad \text{red blood cells}$$

$$n_{xy} = K_S\,\varepsilon_{xy} \quad \text{with} \quad K_S = 2\,G\,h = \frac{E\,h}{1+\nu} \qquad \text{… shear stiffness}$$
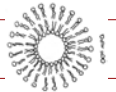
$$K_S = 6 - 9 \cdot 10^{-6}\,\mathrm{N/m} \qquad \text{red blood cells}$$

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The fluid mosaic model   What does a low shear stiffness mean for a cell? We have seen that different biological membranes have different functions depending on the proteins associated with their membrane. The low shear resistance indicates that membrane proteins and lipids can easily diffuse laterally or sideways throughout the membrane, giving it its characteristic appearance of a fluid rather than a solid. This property was first recognized by Singer and Nicolson in 1972 who coined the notion of the fluid mosaic model [42]. The fluid mosaic model of lipid bilayer membranes is a two-dimensional fluid, or liquid crystal, in which the hydrophobic integral components such as lipids and membrane proteins are constrained within the plane of the membrane, but are free to diffuse laterally. From a mechanics point of view, biomembranes can thus be understood as fluids as they bear very little resistance to shear.

singer & nicolson [1972]

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Cell membranes are viewed as two-dimensional solutions of oriented globular proteins and lipids.
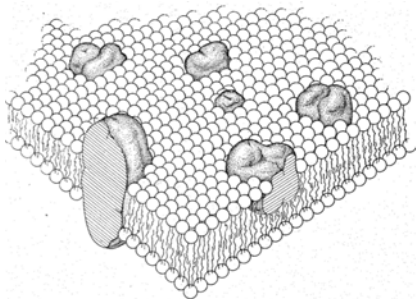

Fig. 3. The lipid-globular protein mosaic model with a lipid matrix (the fluid mosaic model); schematic three-dimensional and cross-sectional views. The solid bodies with stippled surfaces represent the globular integral proteins, which at long range are randomly distributed in the plane of the membrane. At short range, some may form specific aggregates, as shown.

singer & nicolson [1972]

Summary

A fluid mosaic model is presented for the gross organization and structure of the proteins and lipids of biological membranes. The model is consistent with the restrictions imposed by thermodynamics. In this model, the proteins that are integral to the membrane are a heterogeneous set of globular molecules, each arranged in an *amphipathic* structure, that is, with the ionic and highly polar groups protruding from the membrane into the aqueous phase, and the nonpolar groups largely buried in the hydrophobic interior of the membrane. These globular molecules are partially embedded in a matrix of phospholipid. The bulk of the phospholipid is organized as a discontinuous, fluid bilayer, although a small fraction of the lipid may interact specifically with the membrane proteins. The fluid mosaic structure is therefore formally analogous to a two-dimensional oriented solution of integral proteins (or lipoproteins) in the viscous phospholipid bilayer solvent. Recent experi-
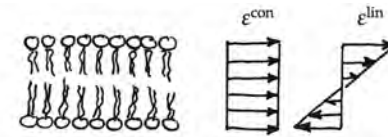
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Figure 5.18: Von Kármán strains in cross section – constant terms ε^{con} related to in plain strains and linear terms ε^{lin} related to out of plane bending

overall strain = in plane (constant) + transverse (linear)

$$\varepsilon_{xx} = u_{,x} + \tfrac{1}{2} w_{,x}^2 - z\,w_{,xx}$$
$$\varepsilon_{yy} = v_{,y} + \tfrac{1}{2} w_{,y}^2 - z\,w_{,yy}$$
$$\varepsilon_{xy} = \tfrac{1}{2}\left[u_{,y} + v_{,x} + w_{,x}w_{,y}\right] - 2z\,w_{,xy}$$

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kinematic equations

$$\varepsilon_{xx} = -w_{,xx}\,z = \kappa_{xx}\,z$$
$$\varepsilon_{yy} = -w_{,yy}\,z = \kappa_{yy}\,z$$
$$\varepsilon_{xy} = -w_{,xy}\,z = \kappa_{xy}\,z$$

constitutive equations

$$\sigma_{xx} = \frac{E}{1-\nu^2}\left[\kappa_{xx} + \nu\,\kappa_{yy}\right]z$$
$$\sigma_{yy} = \frac{E}{1-\nu^2}\left[\kappa_{yy} + \nu\,\kappa_{xx}\right]z$$
$$\sigma_{xy} = \frac{E}{1+\nu}\qquad \kappa_{xy}\qquad z$$

stress resultants

$$m_{xx} = \frac{E h^3}{12\left[1-\nu^2\right]}\left[\kappa_{xx} + \nu\,\kappa_{yy}\right]$$
$$m_{yy} = \frac{E h^3}{12\left[1-\nu^2\right]}\left[\kappa_{yy} + \nu\,\kappa_{xx}\right]$$
$$m_{xy} = \frac{E h^3}{12\left[1+\nu\right]}\qquad \kappa_{xy}$$

equilibrium equations

$$q_{x,x} \quad + \quad q_{y,y} \quad + \quad p_z = 0$$
$$m_{xx,x} + m_{yx,y} - q_x = 0$$
$$m_{yy,y} + m_{xy,x} - q_y = 0$$

$$p_z = K_B\left[w_{,xxxx} + 2\,w_{,xxyy} + w_{,yyyy}\right]$$

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pressure bending relation
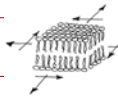$$p_z = K_B\left[w_{,xxxx} + 2\,w_{,xxyy} + w_{,yyyy}\right]$$

$$p_z = K_B\,\Delta^2 w \quad \text{with} \quad K_B = \frac{E h^3}{12\left[1-\nu^2\right]} \quad \dots \text{ membrane stiffness}$$

$$K_B = 10^{-19}\,\text{Nm} \quad \text{red blood cells}$$

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$$n\,[\,w_{,xx} + w_{,yy}\,] - K_B\,[\,w_{,xxxx} + 2\,w_{,xxyy} + w_{,yyyy}\,] + p_z = 0$$

The ratio between the two constants n and K_B would then immediately tell us which of the two phenomena is dominant. Let w be the transverse displacement and λ be a characteristic length over which these transverse displacements may vary. The membrane term would thus scale with $n\,w\,/\,\lambda^2$ while the bending term scales with $K_B\,w\,/\,\lambda^4$. The ratio of these scaling factors $K_B\,/\,[n\,\lambda^2]$ could give us an indication of whether tension or bending is relevant under the given conditons.

$$\frac{K_B}{n\,\lambda^2} \ll 1 \qquad \text{tension dominated}$$
$$\frac{K_B}{n\,\lambda^2} \gg 1 \qquad \text{bending dominated}$$

A typical value for cells at $K_B = 10^{-18}$Nm, $n = 5 \cdot 10^5$N/m and $\lambda = 1\mu$m would be $\frac{K_B}{n\,\lambda^2} = 0.02$ which would indicate that in biological cells, membrane effects are typically dominant over bending.

5.2 biomembranes - energy

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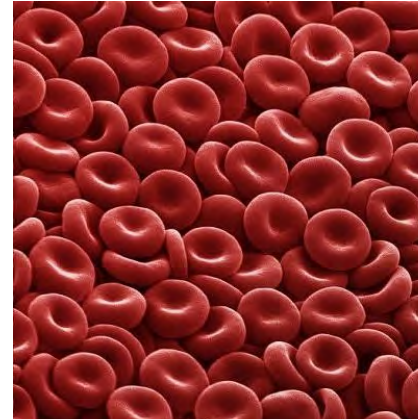
erythrocytes, red blood cells are essential to deliver oxygen to the body via the blood flow through the circulatory system. they take up oxygen in the lungs and release it while squeezing through the body's capillaries. adult humans have about 2-3 10^{13}, 20-30 trillion, red blood cells comprising about a quarter of the total amount of cells in the human body.

5.2 biomembranes - red blood cells

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during its passage through the circulation, an erythrocyte that is **7 to 8 um in diameter** must elongate and deform to pass through **3 um diameter capillaries**. thus, during its **120-day life span**, the erythrocyte must undergo extensive passive deformation and must be mechanically stable to resist fragmentation.

red cell stiffness is influenced by three distinct cellular components:

- **cell shape**, which determines the surface to volume ratio A/V
  higher values of A/V facilitate deformation
- **cytoplasmic viscosity**, regulated by mean corpuscular hemoglobin concentration
  influenced by alterations in cell volume
- **membrane stiffness**, which are regulated by multiple membrane properties,
  influenced by **area stiffness**, **shear stiffness** and **bending stiffness**

directly or indirectly, membrane components and their organization play an important role in regulating each of the factors that influence **cellular deformability**

5.2 biomembranes - red blood cells

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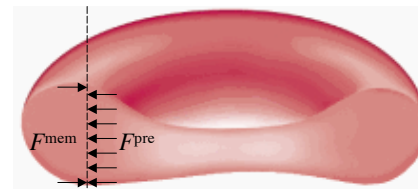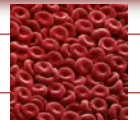
free body diagram
- from vertical force balance
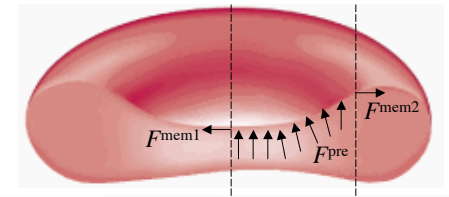$$F^{\text{pre}} = 0$$
- from horizontal force balance
$$F^{\text{mem1}} = F^{\text{mem2}}$$
- from momentum balance
$$F^{\text{mem1}} = F^{\text{mem2}} = 0$$

free body diagram

$$F^{\text{mem}} = n \cdot 2\pi R \qquad F^{\text{pre}} = \Delta p\,\pi\,R^2$$

$$p^{\text{int}} - p^{\text{out}} = 2\frac{n}{R}$$
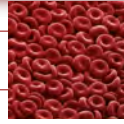
5.2 biomembranes - red blood cells

- unlike other cells, at rest, the red blood cell is **in a stress free state**
- it cannot compensate deformation through prestress requirements upon deformation

- **membrane cannot stretch** beyond 4% (cell lysis)
- **volume cannot change** (incompressible cytoplasm)

- for spherical cells, there is no deformation mode to satisfy both criteria
- for **biconcave cells**, there is an infinite number of deformations

$$F^{mem1} = F^{mem2} = 0$$

F^{mem1} F^{mem2} F^{pre}
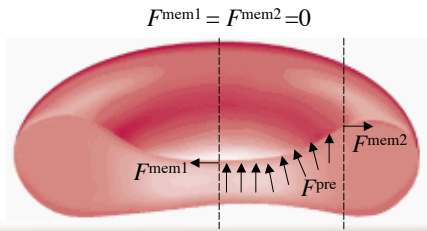
5.2 biomembranes - red blood cells

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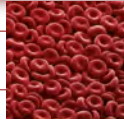
the **biconcave shape** of the normal red cell creates an advantageous **surface-to-volume ratio**, allowing the red cell to undergo large deformation while maintaining a constant surface area.

- the normal human adult red blood cell has a volume of $V=90\mu m^3$ and a surface area of $A=140\mu m^2$, $A/V=1.56/um$
- a sphere of an identical volume of $V=90\mu m^3$, it would have a surface area of only $A=98\mu m^2$, $A/V=1.09/um$

the bioconcave shape provides approximately 40 μm^2 of excess surface area, **an extra 43%**, that allows the red cell to **undergo large deformations without rupturing**.

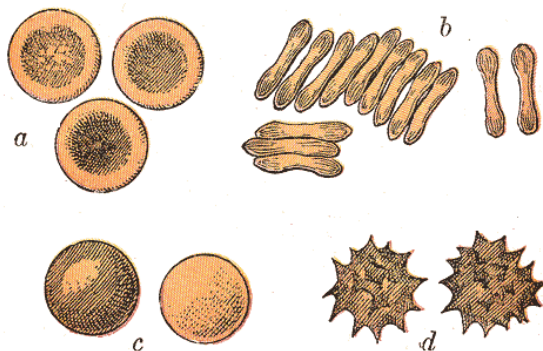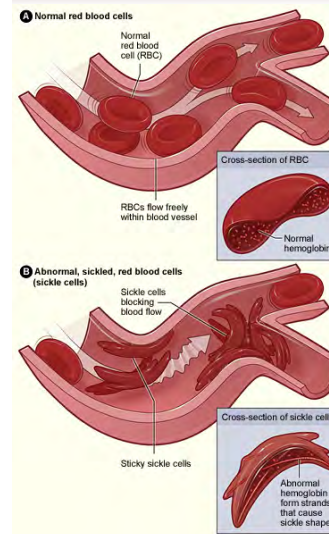## 5.2 biomembranes - red blood cells

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fig. 453 human red blood corpuscles. highly magnified. a. seen from the surface. b. seen in profile and forming rouleaux. c. rendered spherical by water. d. rendered crenate by salt solution.

henry gray "anatomy of the human body" [1918]

5.2 biomembranes - red blood cells

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sickle cell anemia is the most common form of sickle cell disease. this is a serious disorder in which the body makes **sickle-shaped** red blood cells. sickle-shaped means that the red blood cells are shaped like a crescent.

normal red blood cells are **disc-shaped** and look like doughnuts without holes in the center. they **move easily** through your blood vessels. red blood cells contain hemoglobin, an iron-rich protein that gives blood its red color. hemoglobin carries oxygen from the lungs to the rest of the body.

sickle cells contain abnormal hemoglobin that causes the cells to have a sickle, or crescent, shape. These cells don't move easily through your blood vessels. they're **stiff** and **sticky** and tend to form **clumps** and get stuck in the blood vessels.

the clumps of sickle cells block blood flow in the blood vessels in the limbs and organs. blocked blood vessels can cause pain, serious infections, and organ damage.

5.2 biomembranes - red blood cells

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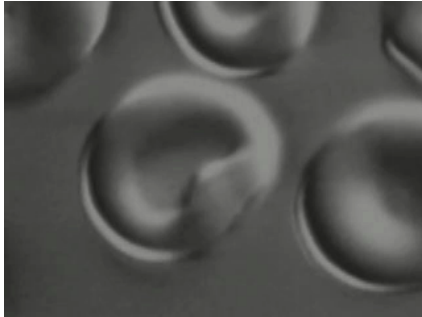
red blood cells must deform when they squeeze through small blood vessels. In this experiment, a red blood cell is pushed and deformed with laser tweezers. it quickly springs back to its original shape because it has an extremely tough cytoskeleton to which the plasma membrane is anchored. when the cell is placed in high salt solution, however, the shape changes dramatically. driven by the difference in osmotic pressure, water rushes out of the cell causing spikelike protrusions to form as the cell collapses.   alberts et al. [2008]