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.
5.1 motivation - law of Laplace

5.1.1 motivation - surface tension

Law of Laplace

\[ p_{\text{int}} - p_{\text{out}} = \frac{\pi}{R} \]

Law of Laplace

![Law of Laplace](image)

Figure 5.7: Law of Laplace. The membrane force \( F_{\text{mem}} = \pi \cdot 2\pi R \) is the result of the surface tension \( \pi \) acting on the cell membrane along the circumference \( C = 2\pi R \). It is in equilibrium with the forces \( F_{\text{pore}} \) resulting from the pressure difference \( \Delta p \) acting on the cell area \( A = \pi R^2 \).

Concept of surface tension

- Air: No cohesive forces
- Air-water interface: Cohesive forces from all sides
- Water: Cohesive forces

![Concept of surface tension](image)

Figure 5.13: 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 erg, the force of one dyne exerted for a distance of one cm is equal to gram centimeter squared per second squared g cm²/s² or, equivalently, 10⁻⁷ joules. The surface tension of water at room temperature is \( \gamma_{\text{water}} = 72 \) dynes/cm, ethanol has a lower surface tension of \( \gamma_{\text{ethanol}} = 22 \) dynes/cm and mercury has a surface tension as large as \( \gamma_{\text{mercury}} = 465 \) dynes/cm.

5.2 biomembranes - structural elements
transverse deformation - bending

**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)

**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)

5.2 compare 3.2 biopolymers - energy

**Tension vs Bending - Trusses vs Beams**

Overall deformation = axial + transverse deformation

\[
\varepsilon = U_{11}^{\text{tot}} - z w_{xx}
\]

- Axial deformation \( U(x) \)
- Transverse deformation, scaled rotation of beam axis \( z w(x)_x \)

5.2 compare 3.2 biopolymers - energy

**Tension vs Bending - Membranes vs Shells**

Overall deformation = in plane + transverse deformation

\[
\begin{align*}
U^\text{tot}(x, y, z) &= U(x, y) - z w_x \\
v^\text{tot}(x, y, z) &= V(x, y) - z w_y \\
w^\text{tot}(x, y, z) &= w(x, y)
\end{align*}
\]
tension vs bending - membranes vs shells

Figure 5.18: Von Kármán strains in cross section – constant terms \( \varepsilon^{\text{in}} \) related to in plane strains and linear terms \( \varepsilon^{\text{out}} \) related to out of plane bending

overall strain = \( \text{in plane (constant)} + \text{transverse (linear)} \)

\[
\begin{align*}
\varepsilon_{xx} &= u_x + \frac{1}{2} w_x^2 - z w_{xx} \\
\varepsilon_{yy} &= u_y + \frac{1}{2} w_y^2 - z w_{yy} \\
\varepsilon_{xy} &= \frac{1}{2} (u_x + u_y) + w_x w_y - 2z w_{xy}
\end{align*}
\]

5.2 biomembranes - energy

2d in-plane deformation - tension and shear

...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 \( n_x \) and \( n_y \)

\[
\begin{align*}
\sum f_x &= 0 : \\
&= -n_x d y + [n_{xx} + n_{xx,x} d x] d x - n_{xx,x} d x + [n_{xx} + n_{xx,y} d y] d y = 0 \\
\sum f_y &= 0 : \\
&= -n_y d x + [n_{yy} + n_{yy,y} d y] d y - n_{yy,y} d y + [n_{yy} + n_{yy,x} d x] d x = 0 \\
\sum f_z &= 0 : \\
&= -n_{yy} d x d y + [n_{yy} + n_{yy,x} d x] d x [w_x + w_{yy} d y] \\
&= -n_{yy} d x d y + [n_{yy} + n_{yy,x} d x] d x [w_x + w_{yy} d y] \\
&= -n_{yy} d x d y + [n_{yy} + n_{yy,x} d x] d x [w_x + w_{yy} d y] + p_z d x d y = 0
\end{align*}
\]

membrane equations - in plane deformation

kinematic equations

\[
\begin{align*}
\varepsilon_{xx} &= u_x + \frac{1}{2} w_x^2 \\
\varepsilon_{yy} &= u_y + \frac{1}{2} w_y^2 \\
\varepsilon_{xy} &= \frac{1}{2} (u_x + u_y) + w_x w_y - 2z w_{xy}
\end{align*}
\]

constitutive equations

\[
\begin{align*}
\sigma_{xx} &= \frac{E}{1-\nu^2} \left[ \varepsilon_{xx} + \nu \varepsilon_{yy} \right] \\
\sigma_{yy} &= \frac{E}{1-\nu^2} \left[ \varepsilon_{yy} + \nu \varepsilon_{xx} \right] \\
\sigma_{xy} &= \frac{E}{1+\nu} \varepsilon_{xy}
\end{align*}
\]

stress resultants

\[
\begin{align*}
n_{xx} &= \frac{Eh}{1-\nu^2} \left[ \varepsilon_{xx} + \nu \varepsilon_{yy} \right] \sum f_x = 0 \\
n_{yy} &= \frac{Eh}{1-\nu^2} \left[ \varepsilon_{yy} + \nu \varepsilon_{xx} \right] \sum f_y = 0 \\
n_{xy} &= \frac{Eh}{1+\nu} \varepsilon_{xy} \sum f_z = 0
\end{align*}
\]

5.2 biomembranes - energy

membrane equations - in plane deformation

\[
\begin{align*}
n_{xx} w_{xx} + 2 n_{xy} w_{xy} + n_{yy} w_{yy} + p_z &= 0
\end{align*}
\]

...now, let’s look at some special cases...

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

5.2 biomembranes - energy
membrane equations - in plane deformation

\[ n_{xx} w_{xx} + 2n_{xy} w_{xy} + n_{yy} w_{yy} + p_z = 0 \]

special case of equibiaxial tension (without shear)

\[ \sigma_{xx} = \sigma_{yy} = \sigma, \quad \sigma_{xy} = 0 \]

\[ n_{xx} = n_{yy} = n, \quad n_{xy} = 0 \]

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

\[ p_z = -n \Delta w \quad \text{with} \quad n \ldots \text{surface tension} \]

5.2 biomembranes - energy

energy minimization

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

\[ W^{\text{int}} = \gamma A = \gamma 4\pi r^2 \quad \Delta p = 2\gamma \frac{1}{r} \]

\[ W^{\text{ext}} = \Delta p V = \Delta p \frac{2}{3} \pi r^3 \]

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 \( \sigma_{xy} \) are energetically conjugate to the shear strains \( \varepsilon_{xy} \) or that the normal stress resultants \( n_{xy} \) are conjugate to the corresponding strains \( \varepsilon_{xy}^{\text{ext}} \) 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 \( \delta u, \delta v \) and \( \delta w \). 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.

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 \( u, v, w \). Similar to the soap bubble problem, the minimum of the overall energy \( W \) with respect to variations in displacements \( u, v, w \) can be expressed through the vanishing first variation \( \delta W \) with respect to the individual unknowns.

\[ W(u, v, w) = \min \quad \delta W(u, v, w) = \delta W^{\text{int}} + \delta W^{\text{ext}} = 0 \]

The internal and external virtual work \( \delta W^{\text{int}} \) and \( \delta W^{\text{ext}} \) can then be specified as follows.

\[ \delta W^{\text{int}} = \int_A \int_{-h/2}^{+h/2} \sigma_{xx} \varepsilon_{xx} + 2\tau_{xy} \varepsilon_{xy} + \sigma_{yy} \varepsilon_{yy} \, dA \]

\[ \delta W^{\text{ext}} = \int_A n_{xx} \varepsilon_{xx} + 2n_{xy} \varepsilon_{xy} + n_{yy} \varepsilon_{yy} \, dA \]

\[ \delta W = \int_A \int_{-h/2}^{+h/2} \sigma_{xx} \varepsilon_{xx} + \sigma_{yy} \varepsilon_{yy} \, dA \]

normal force vs strain - extensional stiffness

stress resultants

\[ n_{xx} = \int_{-h/2}^{+h/2} \sigma_{xx} \, dz = \sigma_{xx} \cdot h = \frac{Eh}{[1 - v^2]} [\varepsilon_{xx} + v \varepsilon_{yy}] \]

\[ n_{yy} = \int_{-h/2}^{+h/2} \sigma_{yy} \, dz = \sigma_{yy} \cdot h = \frac{Eh}{[1 - v^2]} [\varepsilon_{yy} + v \varepsilon_{xx}] \]

\[ n_{xx} = K_N [\varepsilon_{xx} + v \varepsilon_{yy}] \quad \text{with} \quad K_N = \frac{Eh}{[1 - v^2]} \ldots \text{tensile stiffness} \]

5.2 biomembranes - energy

5.2 biomembranes - energy

5.2 biomembranes - energy

5.2 biomembranes - energy
normal force vs area strain - area expansion

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

\[ n = \frac{E h}{1 - v^2} [\varepsilon_{xx} + v\varepsilon_{yy}] = \frac{E h}{1 - v^2} [1 + v] \varepsilon = \frac{E h}{2[1 - v]} \frac{\Delta A}{A} \]

special case of equibiaxial tension (without shear)

\[ n_{xx} = n_{yy} = n \quad \varepsilon_{xx} = \varepsilon_{yy} = \varepsilon \]

\[ n = \frac{E h}{1 - v^2} [\varepsilon_{xx} + v\varepsilon_{yy}] = \frac{E h}{1 - v^2} [1 + v] \varepsilon = \frac{E h}{2[1 - v]} \frac{\Delta A}{A} \]

\[ n = K_A \frac{\Delta A}{A} \quad \text{with} \quad K_A = \frac{E h}{2[1 - v]} \quad \ldots \text{area stiffness} \]

shear force vs shear strain - shear stiffness

\[ n_{xy} = \int_{-h/2}^{+h/2} \sigma_{xy} \, dz = \sigma_{xy} \cdot h = \frac{E h}{1 + v} \varepsilon_{xy} \]

special case of shear (without extension)

\[ n_{xy} = K_S \varepsilon_{xy} \quad \text{with} \quad K_S = 2 G h = \frac{E h}{1 + v} \quad \ldots \text{shear stiffness} \]

5.2 biomembranes - energy

different stiffness values

\[ n_{xx} = K_N [\varepsilon_{xx} + v\varepsilon_{yy}] \quad \text{with} \quad K_N = \frac{E h}{[1 - v^2]} \quad \ldots \text{tensile stiffness} \]

\[ n_{yy} = K_N [\varepsilon_{yy} + v\varepsilon_{xx}] \quad \text{with} \quad K_N = \frac{E h}{[1 - v^2]} \quad \ldots \text{tensile stiffness} \]

\[ n = K_A \frac{\Delta A}{A} \quad \text{with} \quad K_A = \frac{E h}{2[1 - v]} \quad \ldots \text{area stiffness} \]

\[ K_A = 0.1 - 1.0 \, \text{N/m} \quad \text{lipid bilayer} \]
\[ K_A = 0.45 \, \text{N/m} \quad \text{red blood cells} \]

\[ n_{xy} = K_S \varepsilon_{xy} \quad \text{with} \quad K_S = 2 G h = \frac{E h}{1 + v} \quad \ldots \text{shear stiffness} \]

\[ K_S = 6 - 9 \cdot 10^{-6} \, \text{N/m} \quad \text{red blood cells} \]

5.2 biomembranes - energy

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 twodimensional 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.
5.2 biomembranes - energy

The fluid mosaic model

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

Summary

A fluid mosaic model is presented for the gross organization and structure of the proteins and lipids of biological membranes. 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 nonpolar core 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 locally analogous to a two-dimensional oriented solution of integral proteins (or lipoproteins) in the various phospholipid bilayer solvents. Recent experi-

shell equations - out of plane deformation

kinematic equations

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

stress resultants

\[ m_{xx} = \frac{E h^2}{12(1-v^2)} [\kappa_{xx} + \nu \kappa_{yy}] \]
\[ m_{yy} = \frac{E h^2}{12(1-v^2)} [\kappa_{yy} + \nu \kappa_{xx}] \]
\[ m_{xy} = \frac{E h^2}{12(1+v)} \kappa_{xy} \]

constitutive equations

\[ \sigma_{xx} = \frac{E}{1-v^2} [\kappa_{xx} + \nu \kappa_{yy}] z \]
\[ \sigma_{yy} = \frac{E}{1-v^2} [\kappa_{yy} + \nu \kappa_{xx}] z \]
\[ \sigma_{xy} = \frac{E}{1+v} \kappa_{xy} z \]

equilibrium equations

\[ q_{xx} + q_{yy} + p_z = 0 \]
\[ m_{xx,x} + m_{yy,y} - q_x = 0 \]
\[ m_{xy,y} + m_{yy,x} - q_y = 0 \]

overall strain

\[ \varepsilon_{xx} = u_x + \frac{1}{2} w_{,xx}^2 - \frac{1}{2} w_{,xx} \]
\[ \varepsilon_{yy} = u_y + \frac{1}{2} w_{,yy}^2 - \frac{1}{2} w_{,yy} \]
\[ \varepsilon_{xy} = \frac{1}{2} (u_y + w_{,x} + w_{,x} w_y) - \frac{1}{2} w_{,xy} \]

5.2 biomembranes - energy

pressure vs bending - bending stiffness

pressure bending relation

\[ p_z = K_B [w_{,xxx} + 2w_{,xyy} + w_{,yyy}] \]

\[ p_z = K_B \Delta^2 w \quad \text{with} \quad K_B = \frac{E h^3}{12(1-v^2)} \ldots \text{membrane stiffness} \]

\[ K_B = 10^{-19} \text{Nm} \quad \text{red blood cells} \]
red blood cells

5.2 biomembranes - energy

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 $\lambda$ 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 conditions.

\[
\frac{K_B}{n \lambda^2} \ll 1 \quad \text{tension dominated}
\]

\[
\frac{K_B}{n \lambda^2} \gg 1 \quad \text{bending dominated}
\]

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 $K_B / n \lambda^2 = 0.02$ which would indicate that in biological cells, membrane effects are typically dominant over bending.

5.2 biomembranes - red blood cells

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 $A/V$
- **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.

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.
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.

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 $A = 140 \mu m^2$, $A/V = 1.56/\mu m$
- A sphere of an identical volume of $V = 90 \mu m^3$, it would have a surface area of only $A = 98 \mu m^2$, $A/V = 1.09/\mu m$

The biconcave shape provides approximately 40 $\mu m^2$ of excess surface area, an extra 43%, that allows the red cell to undergo large deformations without rupturing.

**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. Blocked blood vessels can cause pain, serious infections, and organ damage.

**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.
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]