Topic 7b: Biological Membranes
Overview:

Why does life need a compartment?

Nature of the packaging – what is it made of? properties?

New types of deformations in 2D

Applications: Stretching membranes, forming vesicles
Importance of packaging:

Cell can regulate its internal chemistry

Differences in concentrations between inside and outside lead to chemical gradients → ability to do work

Protection from bad chemicals

Can organize receptors to respond to those signals that the cell cares about

→ creates an out of equilibrium system
Types of membrane processes: shape changes

- Lipid bilayer
- Hydrophilic head
- Hydrophobic tail
- Spontaneous shape change
- Shape change because of applied forces
- Membrane fusion
- Membrane budding

Figure 11.1 Physical Biology of the Cell, 2nd ed. (© Garland Science 2013)
Membrane organization

Figure 11.2 Physical Biology of the Cell, 2ed. (© Garland Science 2013)
Membranes: complex mixtures

Membranes are made up of an assortment of lipids, cholesterol and different types of proteins.

The different types of lipids phase separate into different domains that possess different properties.

Some phases are ‘ordered’ and others are disordered.

Cholesterol tends to order and make the membrane more rigid.

Figure 11.4 Physical Biology of the Cell, 2ed. (© Garland Science 2013)
Lipids come in different shapes that influence the type of membrane structure that they form.

Mixtures of different lipids can lead to complex shapes.
Types of membrane deformations:

4 ways to deform a membrane

Each has its own spring constant – and hence elastic energy of deformation

Where they occur:

1) stretching → tendril formation
2) bending → action of motors
3) thickness → insertion of protein
4) shear → red blood cell deformation
Stretching a membrane

Stretching: \[ \text{area change} \quad \frac{a}{a+\Delta a} \]

- \( \Delta a(x,y) \) gives area change at \( (x,y) \) in membrane

\[ F_{\text{stretch}} = \frac{k_a}{a^2} \int \left( \frac{\Delta a}{a} \right)^2 dA \]
Describing membrane bending:

Just like for beams, we can look at the radius of curvature of the membrane bend.

Membranes can bend in two directions. Define the membrane height, $h(x,y)$.

It curves in both the $x$ and $y$ directions – $R_1$ and $R_2$. 

*Figure 11.15 Physical Biology of the Cell, 2nd ed. (© Garland Science 2013)*
Small deformations:

For small deformations, we can expand the height function:

\[
h(x,y) = h(x_0,y_0) + \frac{\partial h}{\partial x} \Delta x + \frac{\partial h}{\partial y} \Delta y + \frac{1}{2} \left( \frac{\partial^2 h}{\partial x^2} \Delta x^2 + \frac{\partial^2 h}{\partial x \partial y} \Delta x \Delta y + \frac{\partial^2 h}{\partial y^2} \Delta y^2 \right)
\]
Bending Energy of Membrane

\[
\frac{2^2 h}{2x_1 \partial x_1} = \text{curvature matrix}
\]

\[
= \begin{pmatrix}
K_{xx} & K_{xy} \\
K_{xy} & K_{yy}
\end{pmatrix}
\]

- Eigenvalues/vectors give the principle curvatures & directions = \( K_1 \) & \( K_2 \)

- For a sphere the 2 principle curvatures = \( \frac{1}{R} \)

\[
F_{\text{bend}} = \frac{K_0}{2} \int dA (K_1(x,y) + K_2(x,y))^2
\]
Changing the thickness:

\[ \text{Thickness: } \overline{w_0} \uparrow \overline{w(x,y)} \]

- \( w(x,y) \) is the thickness of membrane at \( (x,y) \)

\[ F_{\text{thickness}} = \frac{K_t}{2} \int dA \left( \frac{w(x,y) - \overline{w_0}}{\overline{w_0}} \right)^2 \]

Figure 11.21: Physical Biology of the Cell, 2nd. (© Garland Science 2013)
Measuring membrane deformations

How can we measure the elastic stretch modulus – $K_A$?

Using a micropipette we can stretch the membrane a fixed amount under a controlled force – the amount that the area expands due to the applied force $\rightarrow K_A$
Micropipette experiments:

\[
\text{linear } F \sim k x
\]

**Figure 11.23** Physical Biology of the Cell, 2ed. (© Garland Science 2013)

**Figure 11.24a** Physical Biology of the Cell, 2ed. (© Garland Science 2013)
Calculating the response:

$$\Delta p_{\text{out}} = \Delta p_{\text{in}} - \Delta p_{\text{in}}$$

Relating the geometry to the pressure:

$$\Delta p_{\text{out}} = \text{difference in pressure between inside and outside of vesicle}$$

$$\Delta p_{\text{in}} = \text{differential pressure between inside and outside of bleb}$$

$$\Delta p = \Delta p_{\text{in}} - \Delta p_{\text{out}} = (p_{\text{out}} - p) - (p_{\text{in}} - p) = p_{\text{out}} - p_{\text{in}}$$
Aside: Some soap bubble physics:

Q: What radius does a soap bubble take under a given pressure difference?

\[ \Delta p \]

**Strain is 0**

\[ R_o \]

\[ A_o \]

\[ \Delta p \]

**Strain is 0**

\[ A \]

\[ R \]

**Equilibrium**

\[ \frac{\partial E_{\text{tot}}}{\partial R} = 0 \]

\[ E_{\text{stretch}}(R) = \frac{K_A}{2} \left( \frac{A(R) - A_o}{A_o} \right)^2 \]

\[ E_{\text{work}}(R) = -\Delta p \left( \frac{4}{3} \pi R^3 \right) \]

\[ E_{\text{tot}}(R) = E_{\text{stretch}}(R) + E_{\text{work}}(R) \]

\[ E_{\text{tot}}(R) = K_A \left( \frac{A(R) - A_o}{A_o} \right) \frac{dA}{A_o} - 4\pi \Delta p R^2 \]

\[ = K_A \left( \frac{A(R) - A_o}{A_o} \right) (8\pi R) - 4\pi R^2 \Delta p \]

\[ = \frac{K_A}{A_o} \left( 8\pi R \right) - 4\pi R^2 \Delta p \]

\[ \Delta p = \frac{2\tau}{R} \]

(or \( R = \frac{2\tau}{\Delta p} \))
Aside: Tension

Recall: for an elastic rod $\sigma = E \varepsilon$ where $\varepsilon = \Delta L/L$

Surface tension is isotropic, it’s a force per unit length of stretch
Back to micropipette experiment…

Applying the L-Y relation to the micropipette experiment:

- For the vesicle with radius, \( R_v \), L-Y gives:

\[
\Delta P_{\text{out}} = \frac{2T}{R_v}
\]

- For the extrusion in the micropipette:

\[
\Delta P_{\text{in}} = \frac{2T}{R_i}
\]

Using \( \Delta P = \Delta P_{\text{in}} - \Delta P_{\text{out}} \) gives:

\[
\Delta P = \frac{2T}{R_i} - \frac{2T}{R_v}
\]

want to measure this

so we can apply a pressure difference using micropipette and measure the tension

can measure all these
Micropipette experiment continued...

Solving for the tension:

\[
\tau = \frac{4 \pi R_l}{2 \left( 1 - \frac{R_l}{R_v} \right)} \equiv y \text{- axis}
\]

But we also know that tension is given by, \( \tau = K_A \frac{\Delta a}{a} \)

For micropipette the area change can be found from geometry:

\[
\Delta a = 2 \pi R_l l + 2 \pi R_l^2
\]

\[
\frac{\Delta a}{a} = \frac{2 \pi R_l l + 2 \pi R_l^2}{4 \pi R_v^2} = \frac{R_l^2 \left( 1 + l/R_l \right)}{2 R_v^2}
\]

\[\tau = K_A \left[ \frac{R_l^2 \left( 1 + l/R_l \right)}{2 R_v^2} \right] \equiv x \text{- axis}
\]

\[K_A = 55 \, kT/\text{nm}^2\]
Bending membranes: Making vesicles for transport

The energy cost is associated with bending the flat membrane into a sphere with
\[ K_1 = K_2 = \frac{1}{R} \]

Free energy cost for deformation:

Thus no matter what the vesicle size there is a fixed cost to make the deformation

For most membranes \( K_B \sim 250 \ kT \sim 10 \) ATP molecules there are motor proteins which aid the vesicle formation.
There are 4 ways to deform a membrane: stretch, bend, expand and shear

Each has its own elastic response that depends linearly on the extent of the deformation

Using biophysical techniques we can measure these elastic properties to determine the elastic moduli

Application: used soap bubble physics to analyze the stretching of a membrane using a micropipette

found that the energy to form spherical vesicles by bending the membrane of a cell costs a fixed energy regardless of how big the vesicle is.