Topic 7b: Biological Membranes

Overview:

Why does life need a compartment?

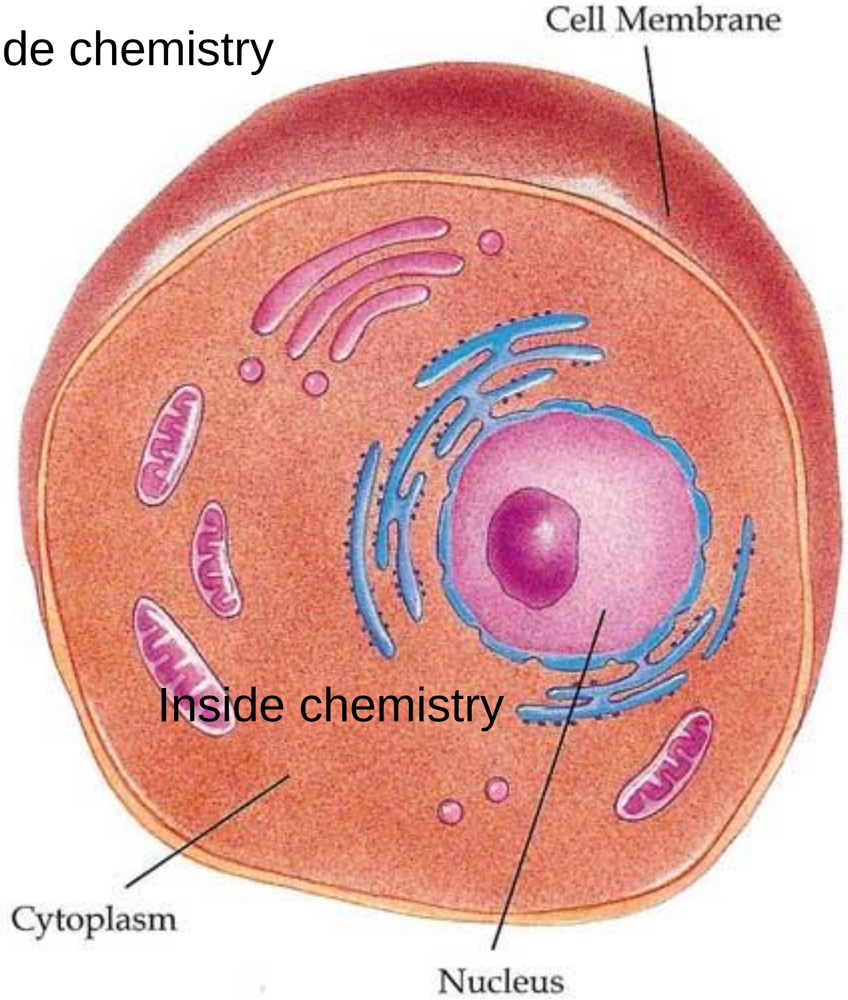
Nature of the packaging – what is it made of? properties?

New types of deformations in 2D

Applications: Stretching membranes, forming vesciles

Importance of packaging:

Outside chemistry



Inside chemistry

Cell can regulate it’s 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

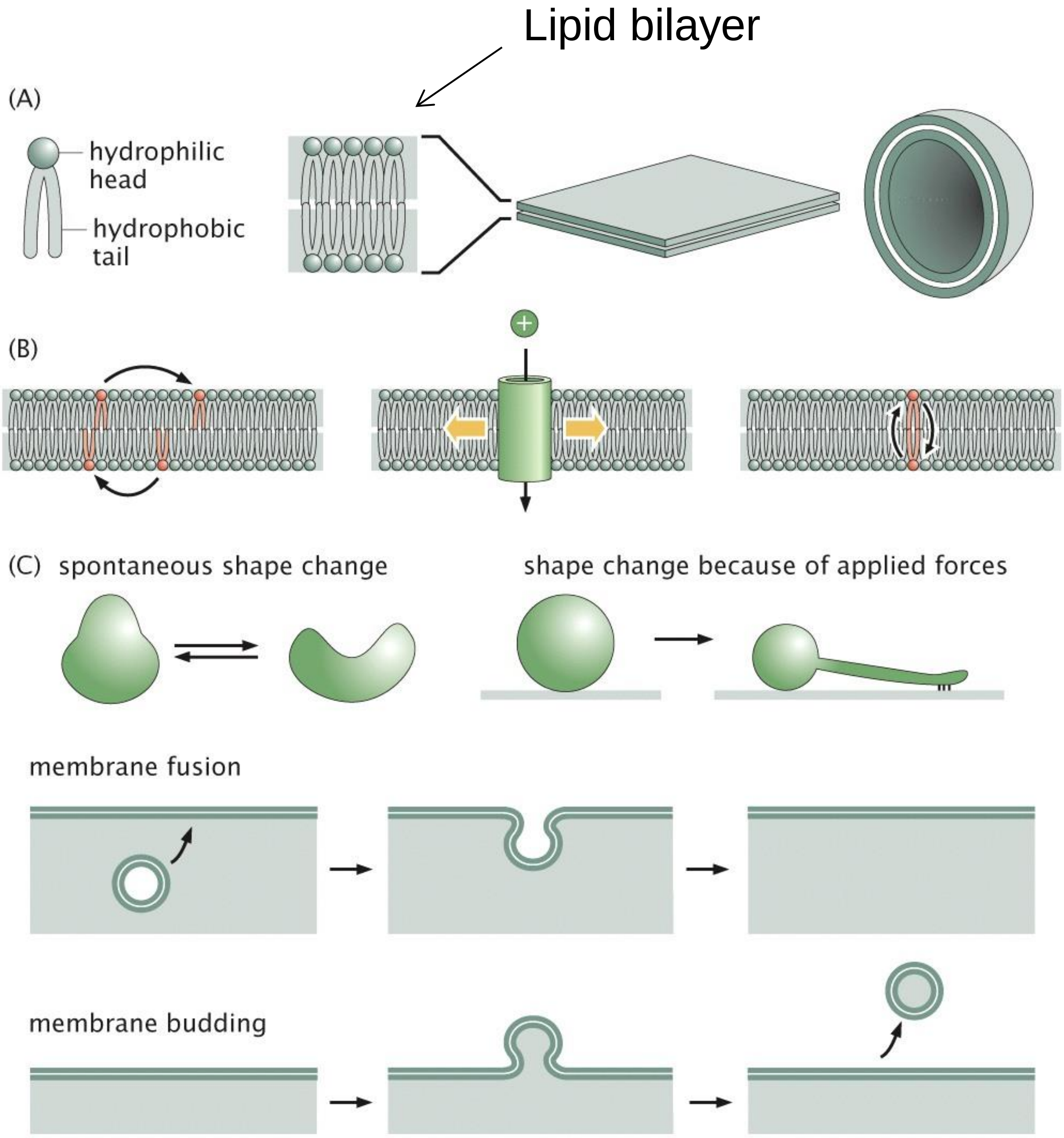


Figure 11.1 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Membrane organization

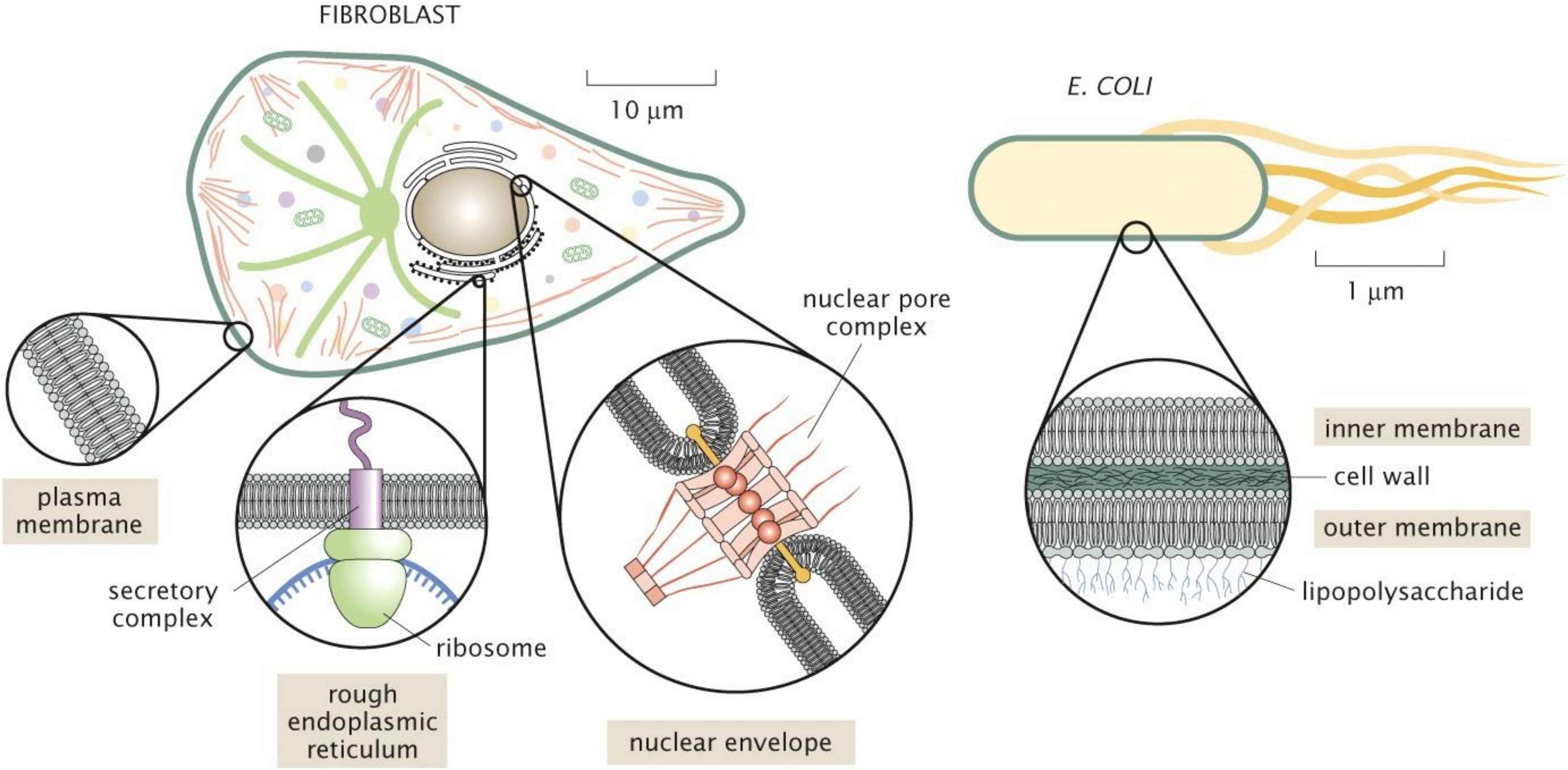


Figure 11.2 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Membranes: complex mixtures

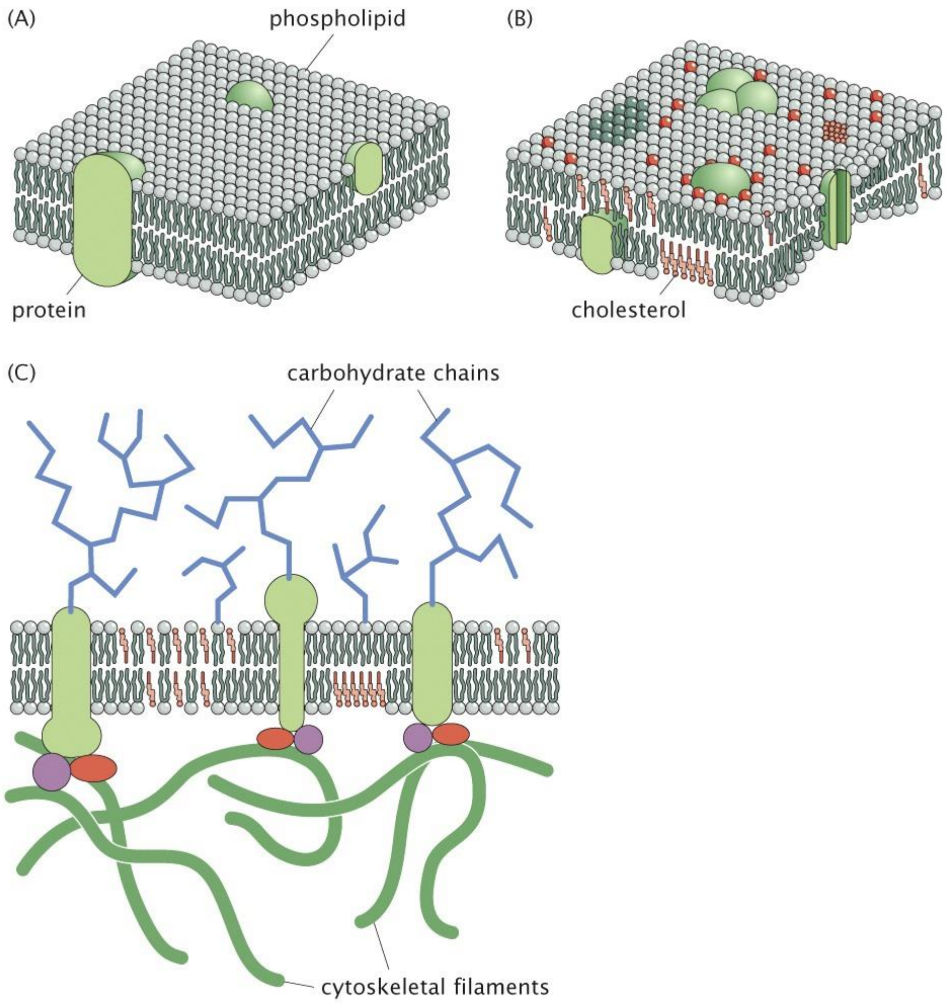


Figure 11.4 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

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

Shapes of Lipids

Lipids come in different shapes that influences the type of membrane structure that they form

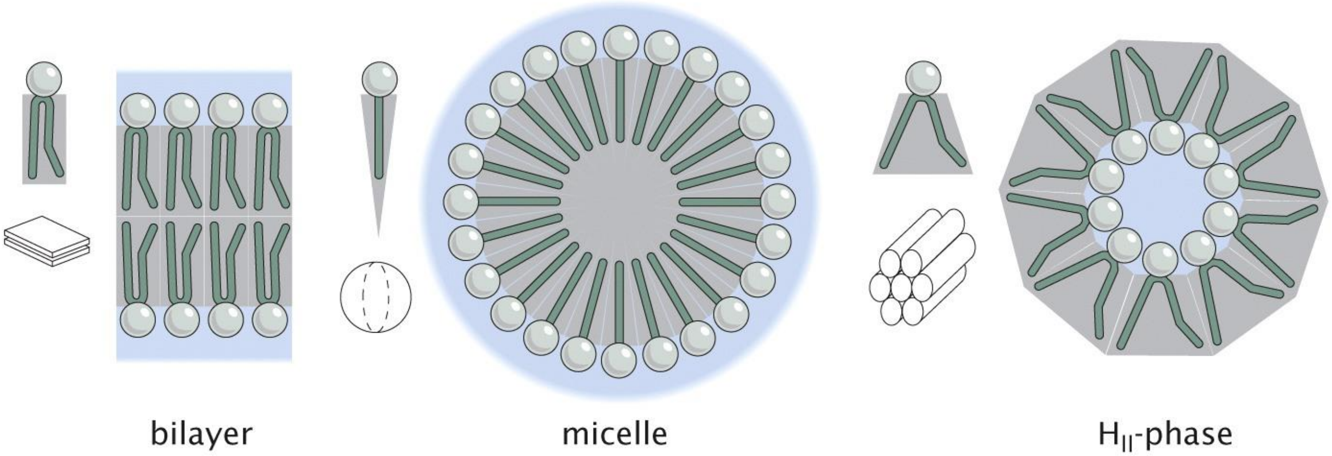
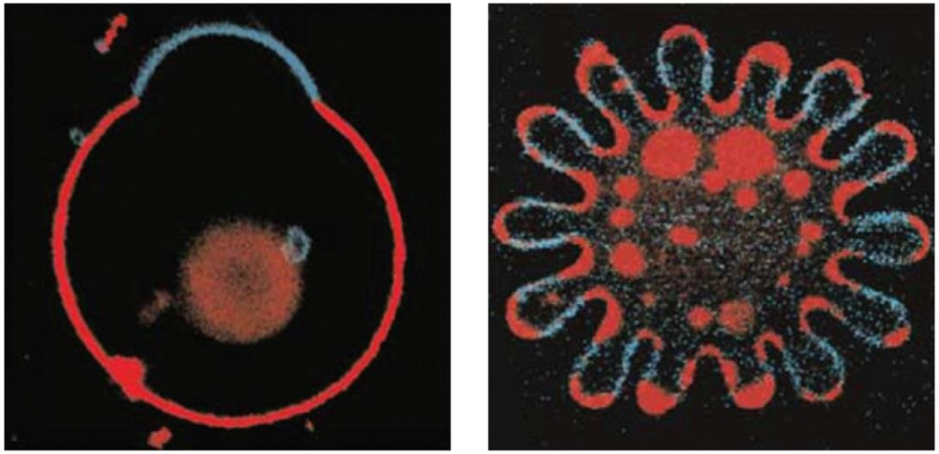


Figure 11.7 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Mixtures of different lipids can lead to complex shapes



Types of membrane deformations:

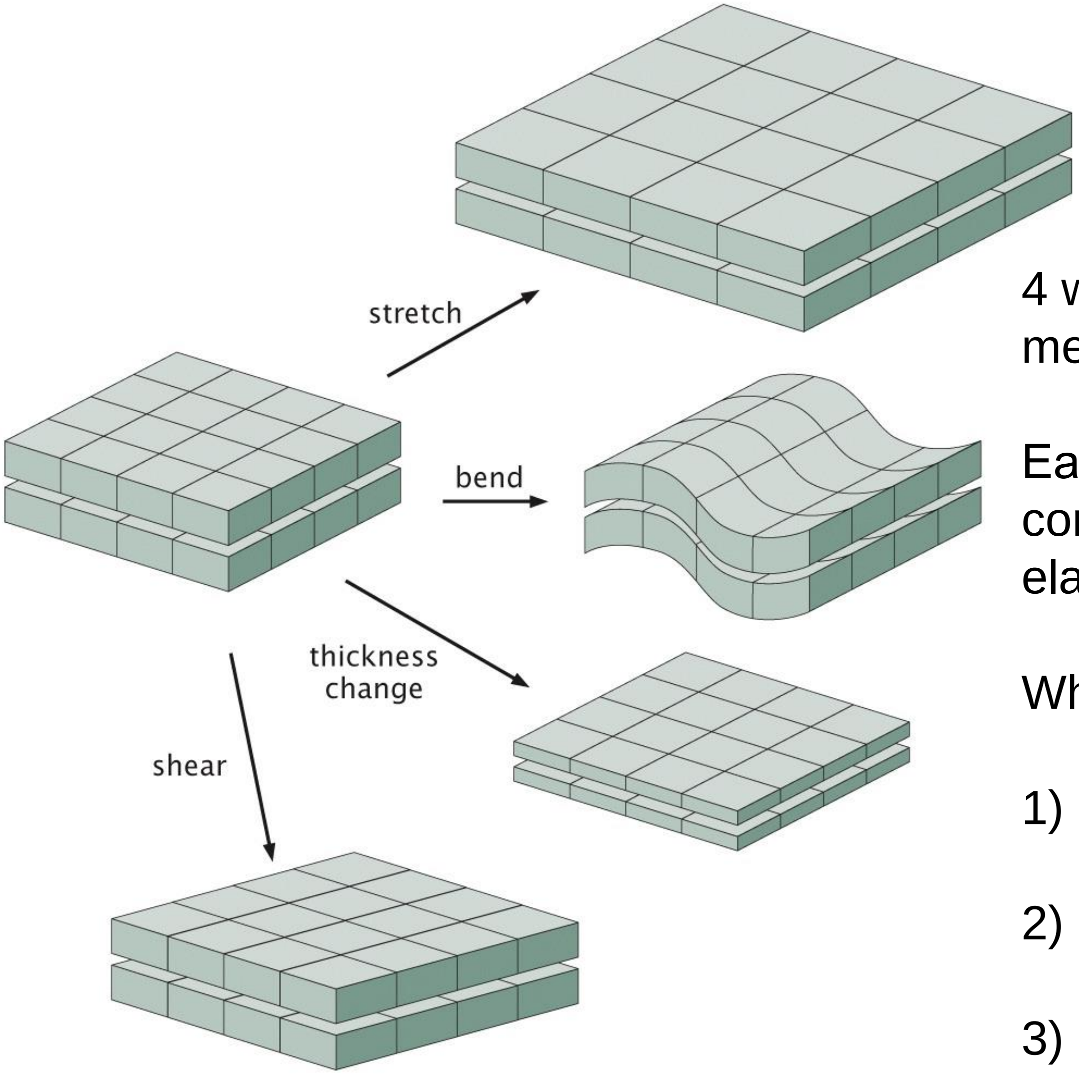


Figure 11.13 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

4 ways to deform a membrane

Each has it's 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

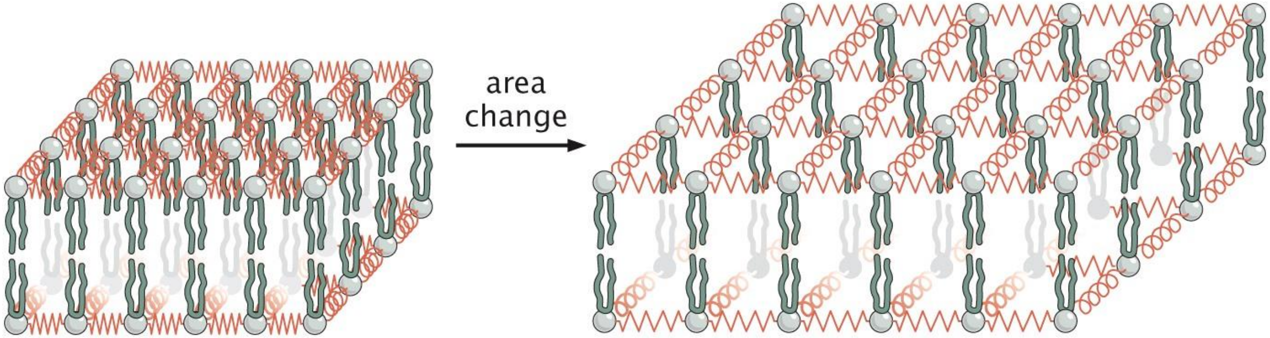
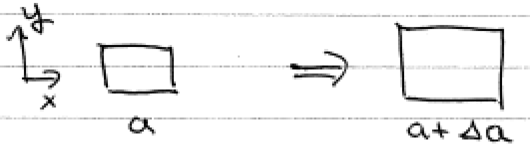


Figure 11.19 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

stretching:



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

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

Describing membrane bending:

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

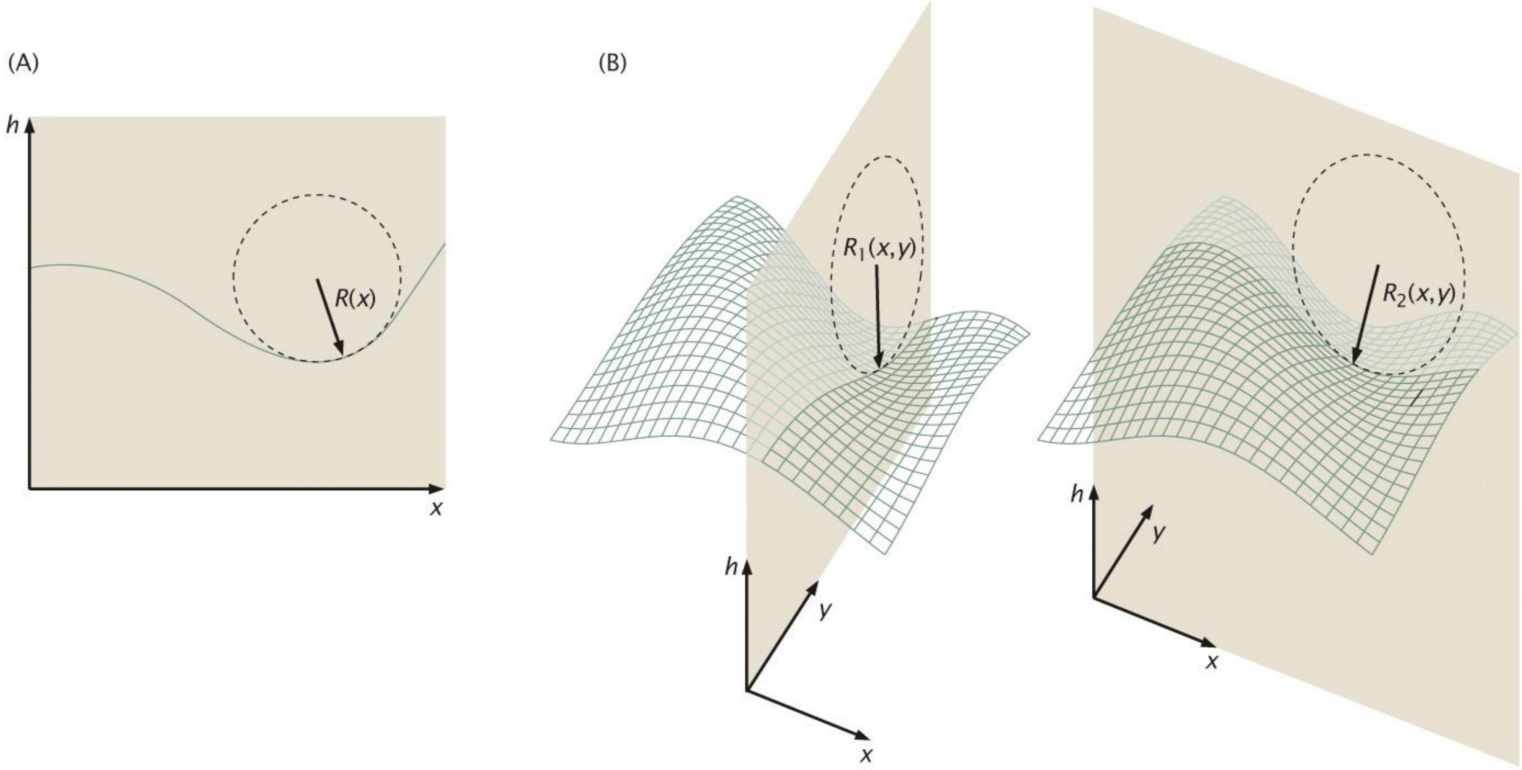


Figure 11.15 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

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

It curves in both the x and y directions – R1 and R2

Small deformations:

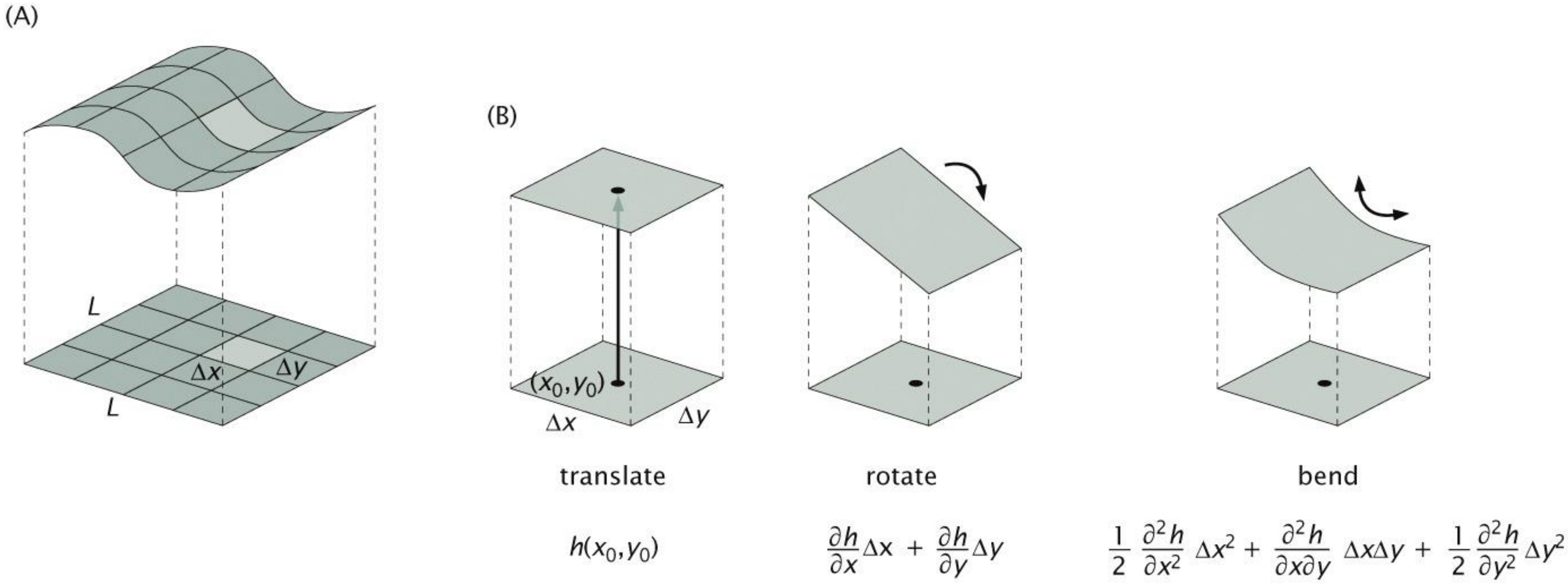
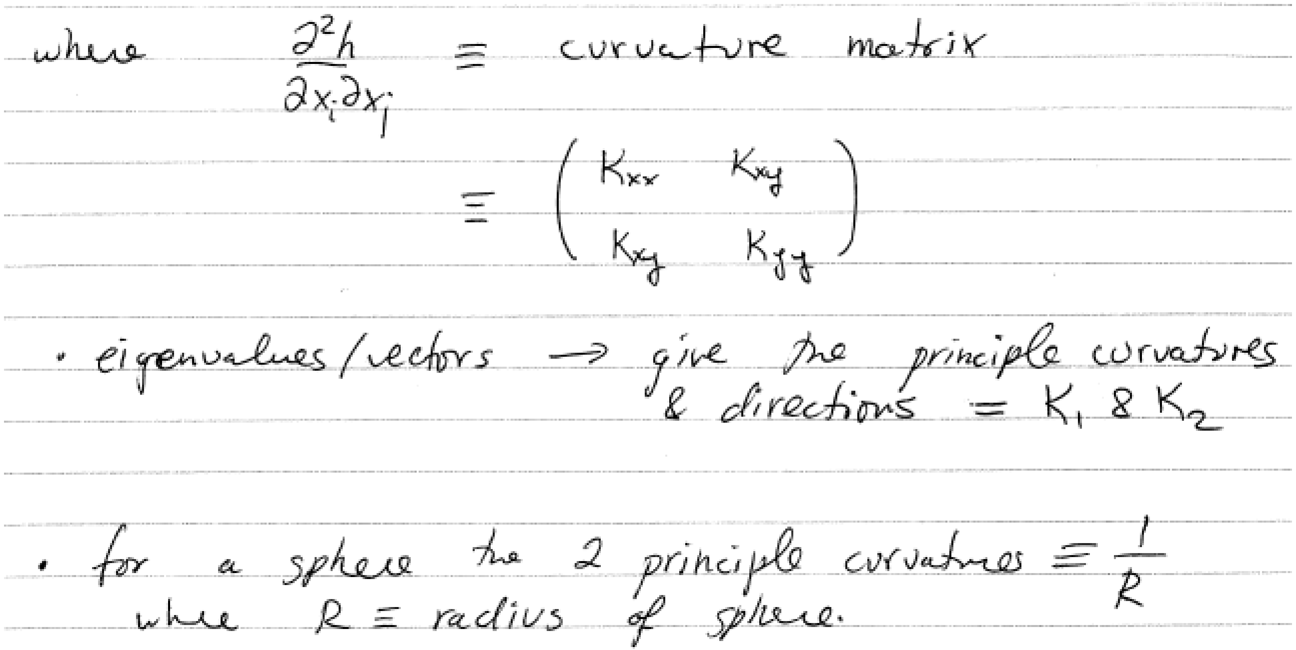


Figure 11.17 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

For small deformations, we can expand the height function:

$$h(x,y) = h(x_0,y_0) + \frac{\partial h}{\partial x}\Delta x + \frac{\partial h}{\partial y}\Delta y + \frac{1}{2}\left(\frac{\partial^2 h}{\partial x^2}\Delta x^2 + 2\frac{\partial^2 h}{\partial x \partial y}\Delta x \Delta y + \frac{\partial^2 h}{\partial y^2}\Delta y^2\right)$$

Bending Energy of Membrane



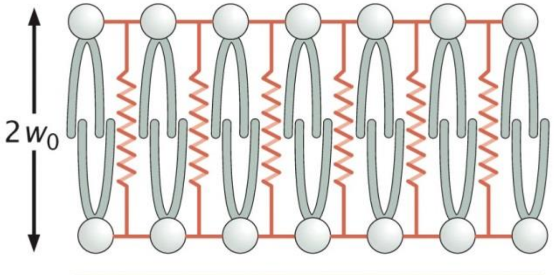
where $\frac{\partial^2 h}{\partial x_i \partial x_j} \equiv$ curvature matrix

$$\equiv \begin{pmatrix} K_{xx} & K_{xy} \\ K_{xy} & K_{yy} \end{pmatrix}$$

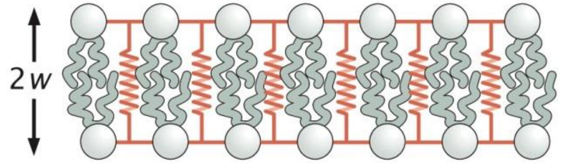
- eigenvalues/vectors → give the principle curvatures & directions $= K_1$ & K_2
- for a sphere the 2 principle curvatures $\equiv \frac{1}{R}$ where $R \equiv$ radius of sphere.

$$F_{bend} = \frac{K_b}{2} \int dA \left(K_1(x,y) + K_2(x,y) \right)^2$$

Changing the thickness:



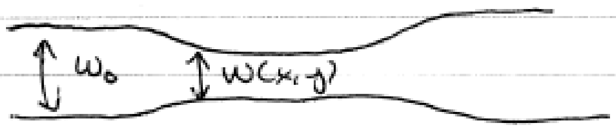
equilibrium bilayer thickness



deformed bilayer

Figure 11.21 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Thickness:



- $w(x,y)$ is the thickness of membrane @ (x,y)

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

Measuring membrane deformations

How can we measure the elastic stretch modulus – K_A?

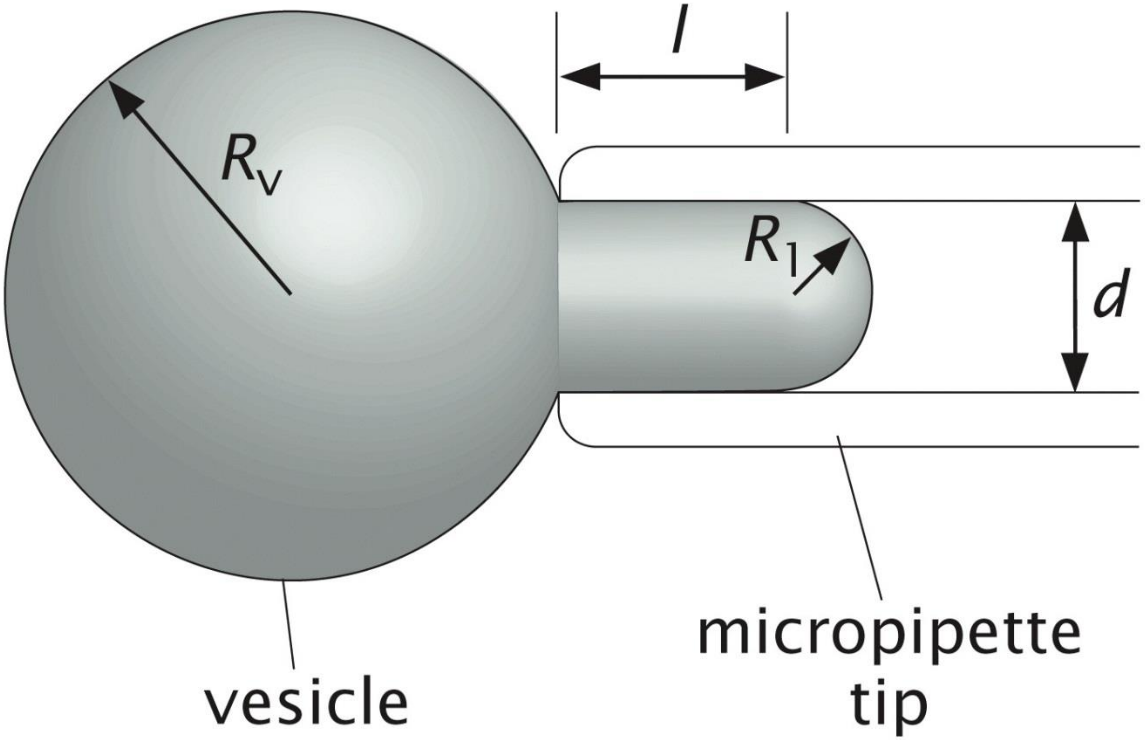


Figure 11.22 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

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 → K_A

Micropipette experiments:

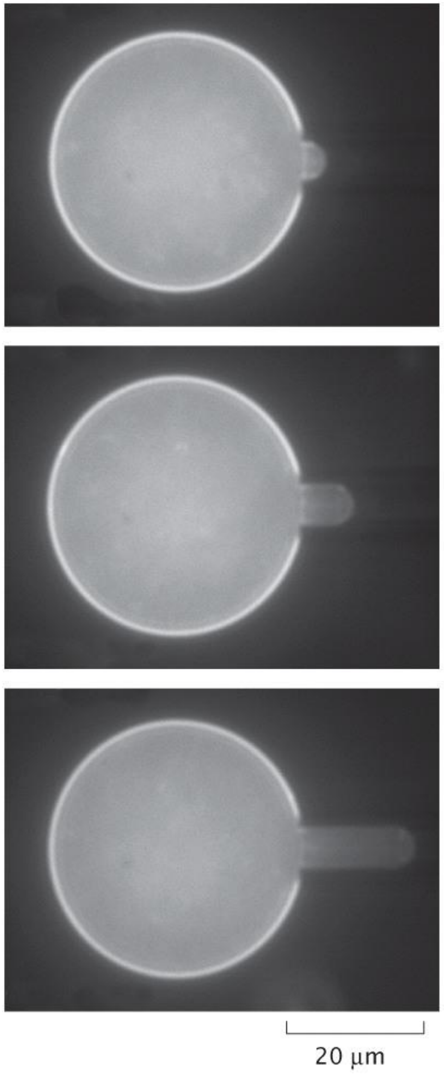


Figure 11.23 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

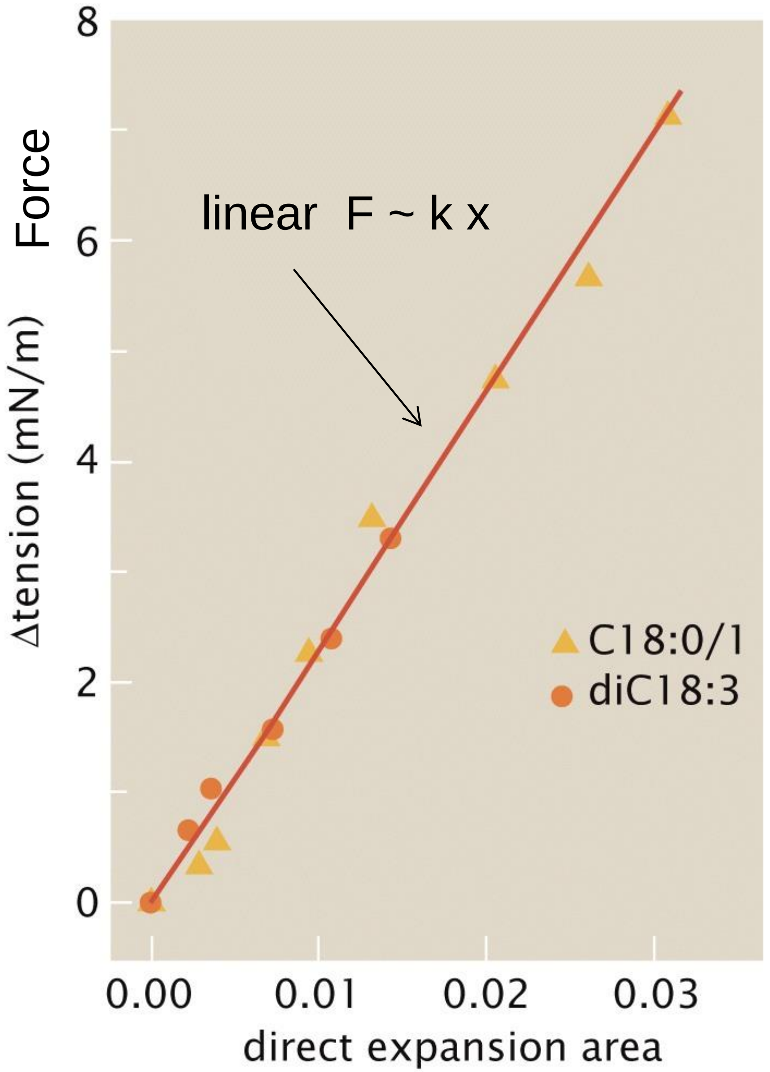


Figure 11.24a Physical Biology of the Cell, 2ed. (© Garland Science 2013)

Calculating the response:

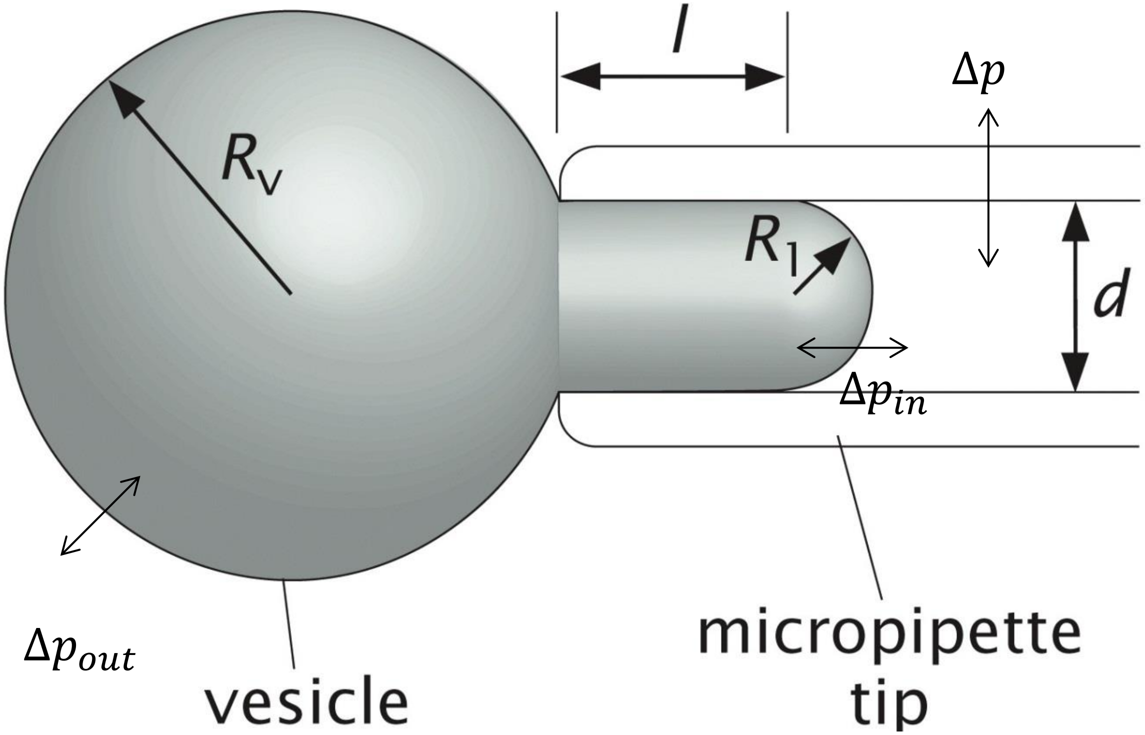


Figure 11.22 Physical Biolo

Relating the geometry to the pressure:

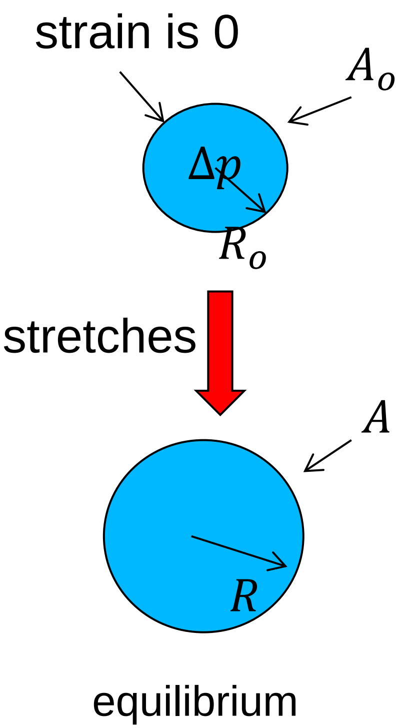
$\Delta p_{out} \equiv$ difference in pressure between inside and outside of vesicle

$\Delta p_{in} \equiv$ diff in pressure between inside & outside of bleb

$$\Delta p = \Delta p_{in} - \Delta p_{out} = (p_{out} - p) - (p_{in} - p) = p_{out} - p_{in}$$

Aside: Some soap bubble physics:

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



Energy:

$$G_{stretch}(R) = \frac{K_A}{2}\left(\frac{A(R) - A_0}{A_0}\right)^2 \quad \text{(for a sphere)}$$

$$G_{work}(R) = -\Delta p\left(\frac{4}{3}\pi R^3\right)$$

so

$$G_{tot}(R) = G_{stretch}(R) + G_{work}(R)$$

Equilibrium R from $\partial G/\partial R = 0$

$$\frac{\partial G_{tot}}{\partial R} = K_A\frac{(A-A_0)}{A_0}\frac{dA}{dR} - 4\pi\Delta p R^2$$

$$= \underbrace{K_A\frac{(A-A_0)}{A_0}}_{=\text{ tension, }\tau}(8\pi R) - 4\pi R^2\Delta p$$

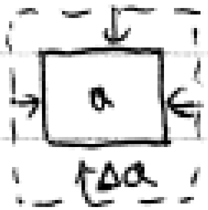
$$= 8\pi R\tau - 4\pi R^2\Delta p = 0$$

so

Laplace-Young relation → $\boxed{\Delta p = \frac{2\tau}{R}}$ $\left(\text{or } R = \frac{2\tau}{\Delta p}\right)$

Aside: Tension

Recall: for an elastic rod $\underset{\underset{\text{stress}}{\uparrow}}{\sigma} = E\, \underset{\underset{\text{strain}}{\uparrow}}{\varepsilon}$ where $\varepsilon = \Delta L/L$

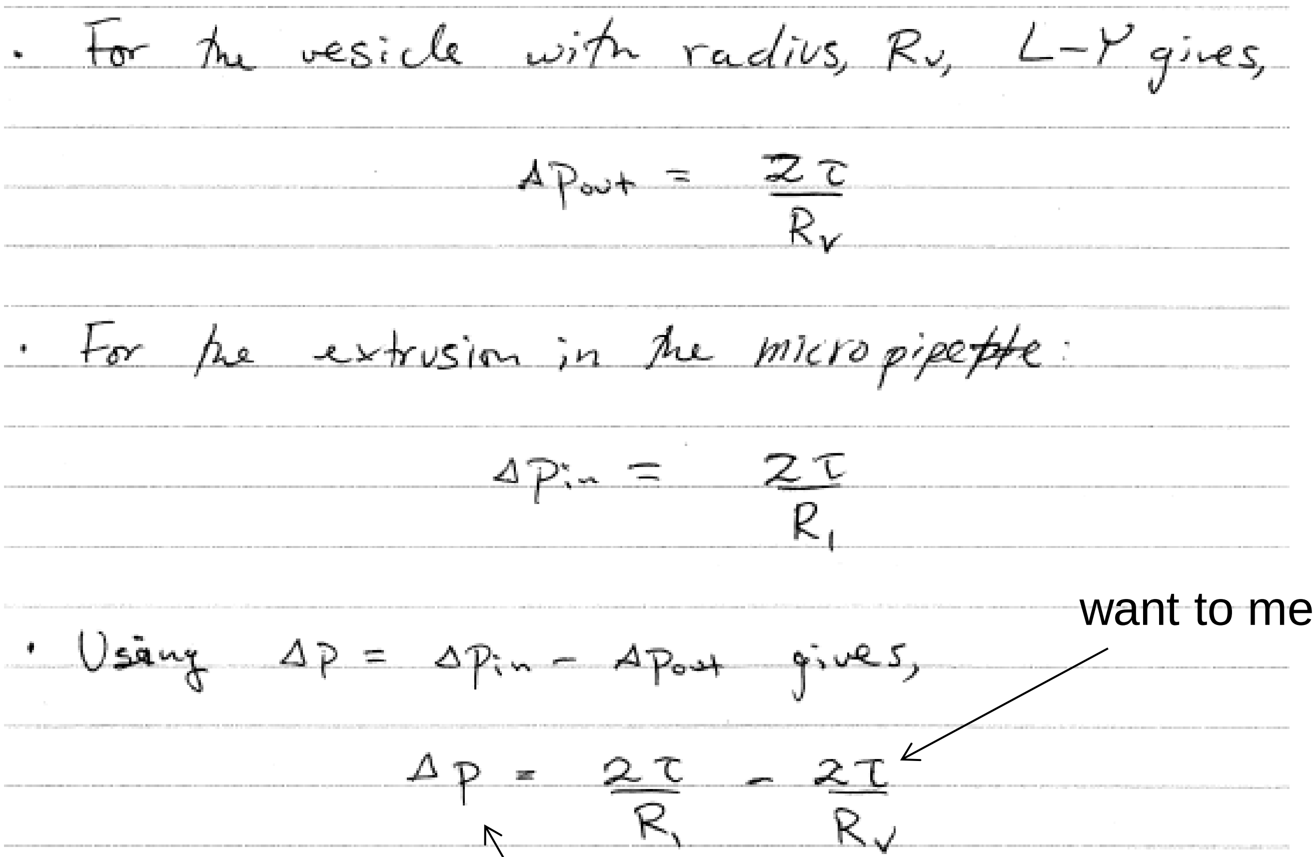


$$\underset{\underset{\text{tension}}{\uparrow}}{\tau} = K_A\left(\frac{\Delta a}{a}\right) \qquad \left[\frac{N}{m}\right]$$

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,

$$\Delta P_{out} = \frac{2\tau}{R_v}$$

- For the extrusion in the micropipette:

$$\Delta P_{in} = \frac{2\tau}{R_1}$$

- Using $\Delta P = \Delta P_{in} - \Delta P_{out}$ gives,

$$\Delta P = \frac{2\tau}{R_1} - \frac{2\tau}{R_v}$$

want to measure this

can measure all these

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

Micropipette experiment continued…

Solving for the tension:

$$\tau = \frac{\Delta p}{2} \frac{R_1}{1 - \frac{R_1}{R_v}} \equiv y\text{-axis}$$

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

$$\Delta a = 2\pi R_1 \ell + 2\pi R_1^2$$

$$\frac{\Delta a}{a} = \frac{2\pi R_1 \ell + 2\pi R_1^2}{\underset{\substack{\uparrow \\ \text{assume } R_v \\ \text{doesn't change}}}{4\pi R_v^2}} = \frac{R_1^2(1 + \ell/R_1)}{2R_v^2}$$

y-axis

$$\tau = K_A \left[\underbrace{\frac{R_1^2(1 + \ell/R_1)}{2R_v^2}}_{x\text{-axis}} \right]$$

slope

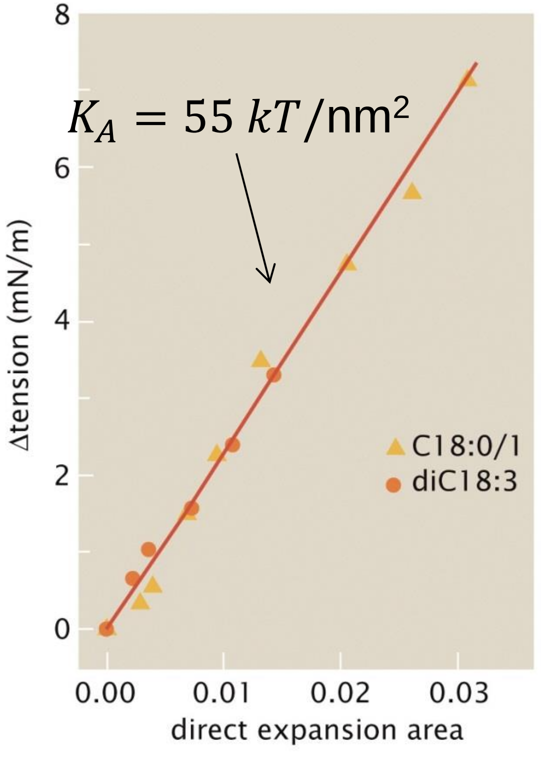
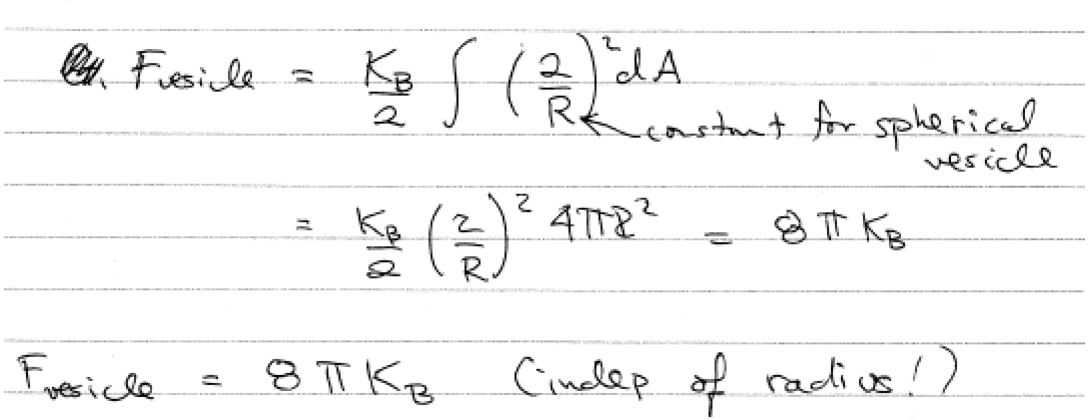

$K_A = 55\ kT/\text{nm}^2$

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

Bending membranes: Making vesicles for transport

The energy cost is associated with bending the flat membrane into a sphere with $K_1 = K_2 = 1/R$

Free energy cost for deformation:



$$F_{vesicle} = \frac{K_B}{2} \int \left(\frac{2}{R}\right)^2 dA$$

constant for spherical vesicle

$$= \frac{K_B}{2} \left(\frac{2}{R}\right)^2 4\pi R^2 = 8\pi K_B$$

$F_{vesicle} = 8\pi K_B$ (indep of radius!)

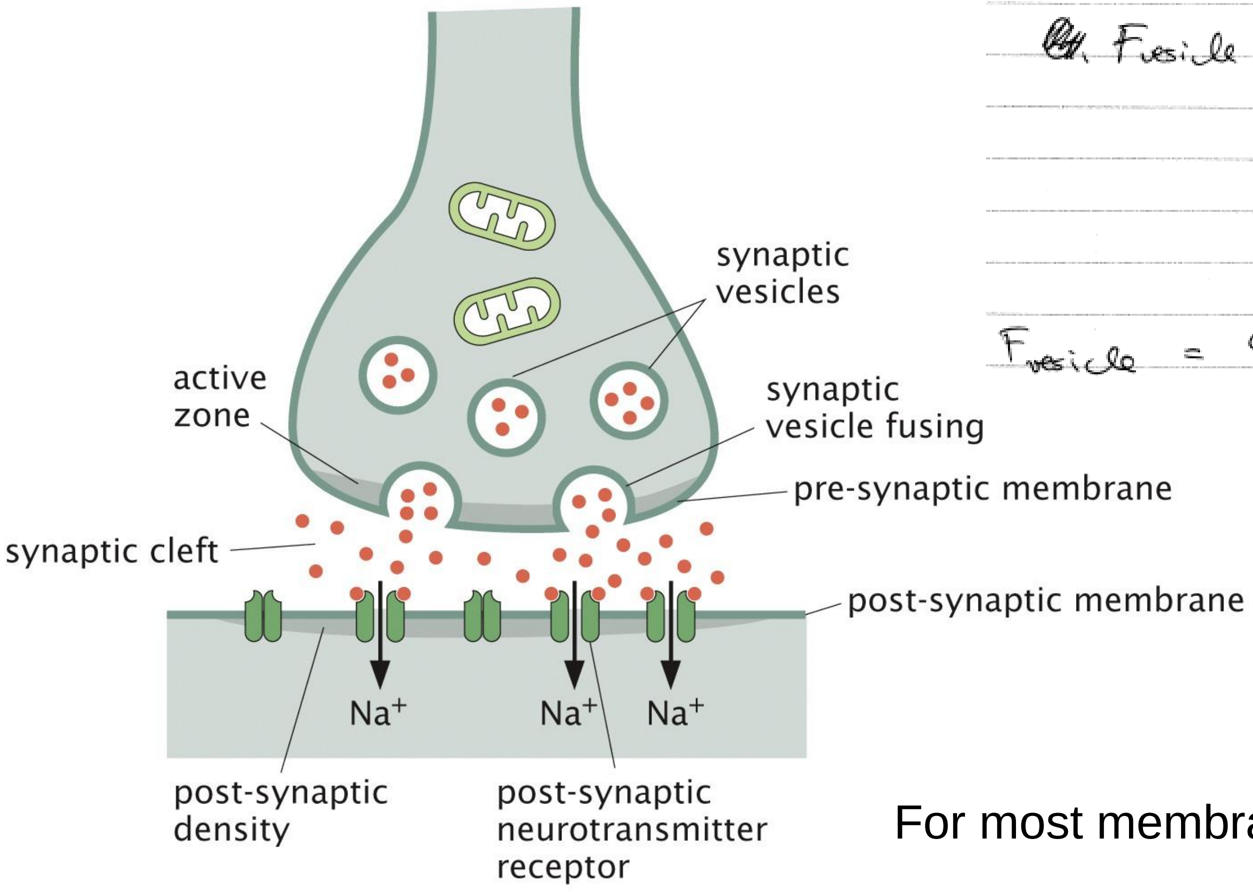


Figure 11.28 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

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

For most membranes $K_B \sim 250\ kT$ ~ 10 ATP molecules

there are motor proteins which aid the vesicle formation

Summary:

There are 4 ways to deform a membrane: stretch, bend, expand and shear

Each has it's 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.