Lectures 16-17:
Biological Membranes: Life in Two Dimensions

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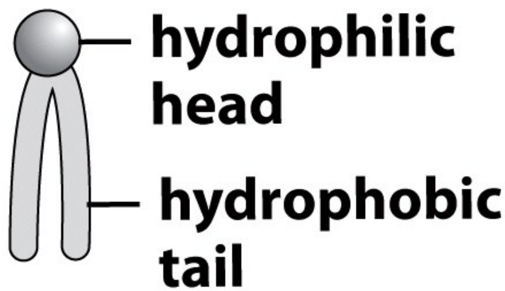
Cells and Cellular Compartments Bound by Membranes

- protect the content of the cell/compartment
- must enable passage of the critical nutrients in and waste out
- must be flexible (to allow cell growth/divison)



Lipid Molecule and Its Assembly Into a Membrane

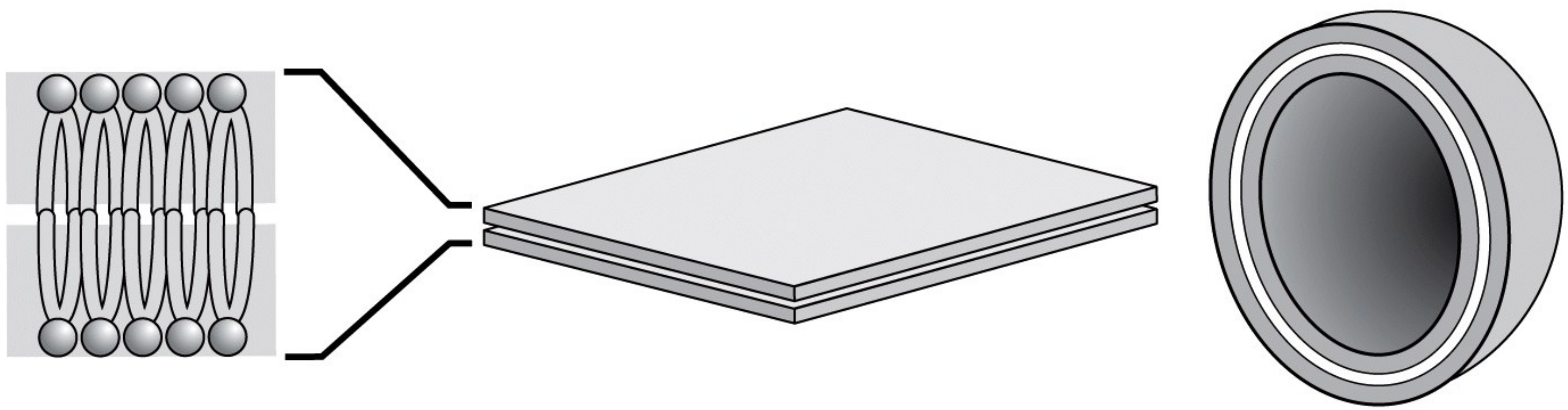


Figure 11.1a Physical Biology of the Cell (© Garland Science 2009)

Within a membrane bilayer:

- **individual lipid molecules diffuse laterally (left) within each of the two *leaflets* as in a 2D liquid;**

→ **membrane proteins also diffuse laterally (center);**

→ **individual lipid molecule may flip over from one leaflet to the other at a very slow rate (right); can be sped up by *flippases***

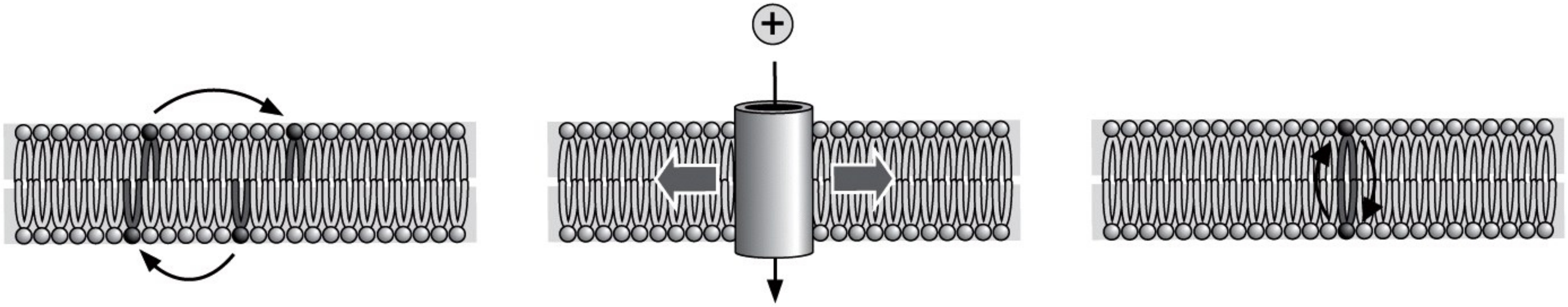


Figure 11.1b Physical Biology of the Cell (© Garland Science 2009)

Membranes change shape due to (i) thermal motion; (ii) external force; (iii) fusion and fission

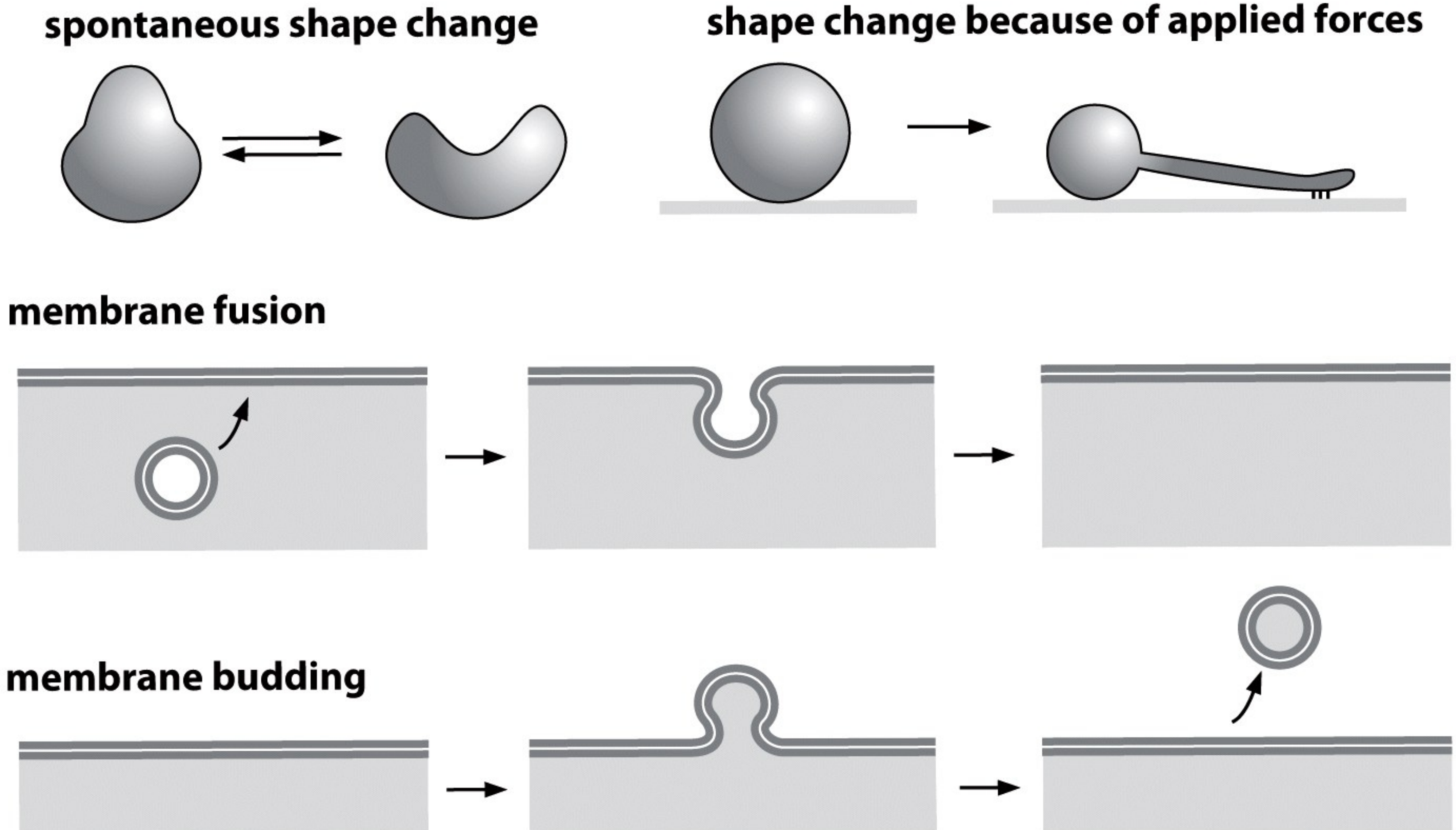


Figure 11.1c Physical Biology of the Cell (© Garland Science 2009)

The geometric feature of membranes is their aspect ratio of their lateral dimension several orders of magnitude larger than their thickness of ~ 5 nm:

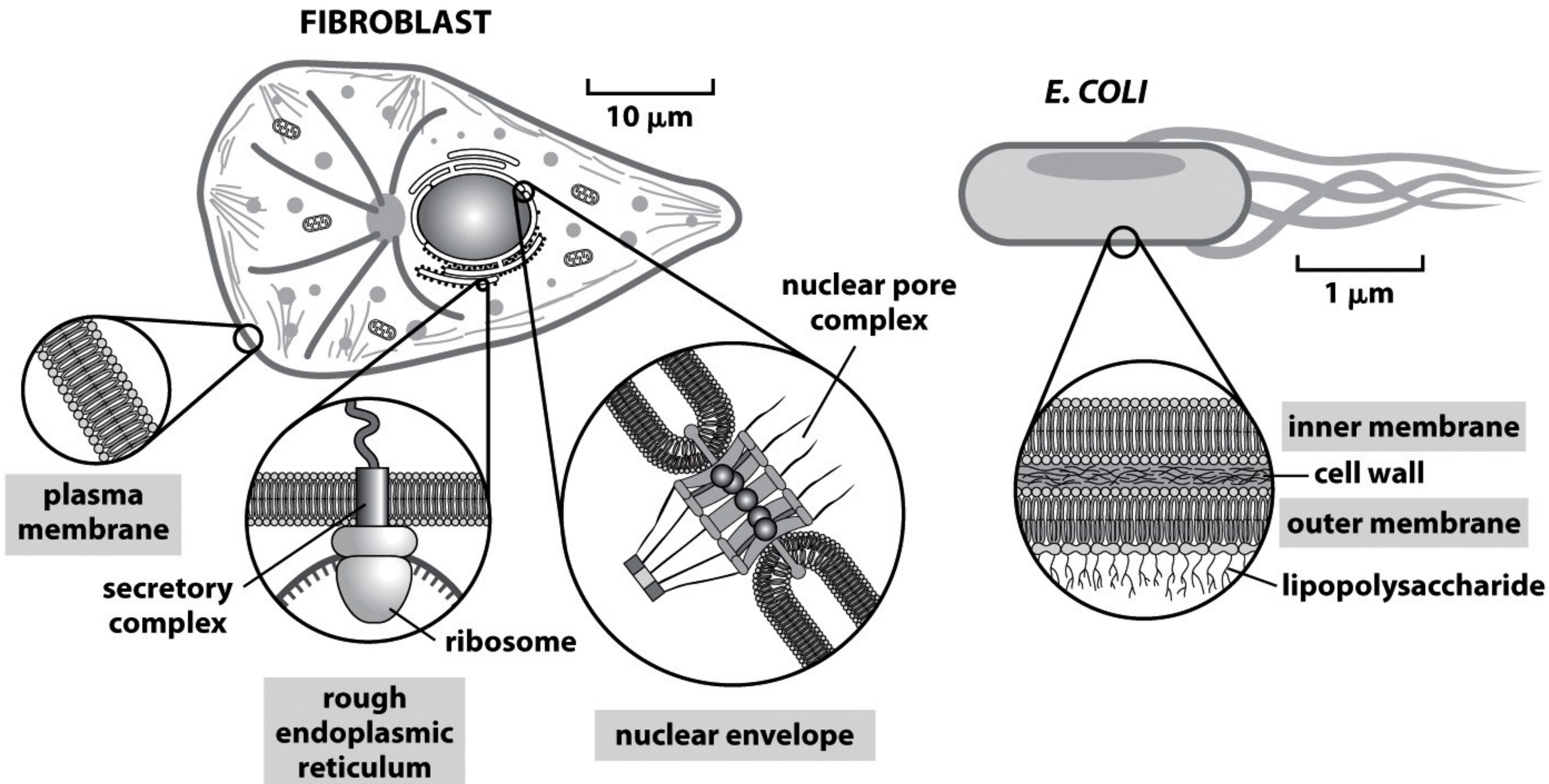


Figure 11.2 Physical Biology of the Cell (© Garland Science 2009)

Electron microscopy images of a variety of membranes:

- **A) *C. crescentus*: membrane layers and cell wall**
- **B) intestinal epithelial cells with dense membrane folds**
- **C) stacks of membranes with photoreceptors in a rod cell**
- **D) mitochondrion surrounded by rough ER**

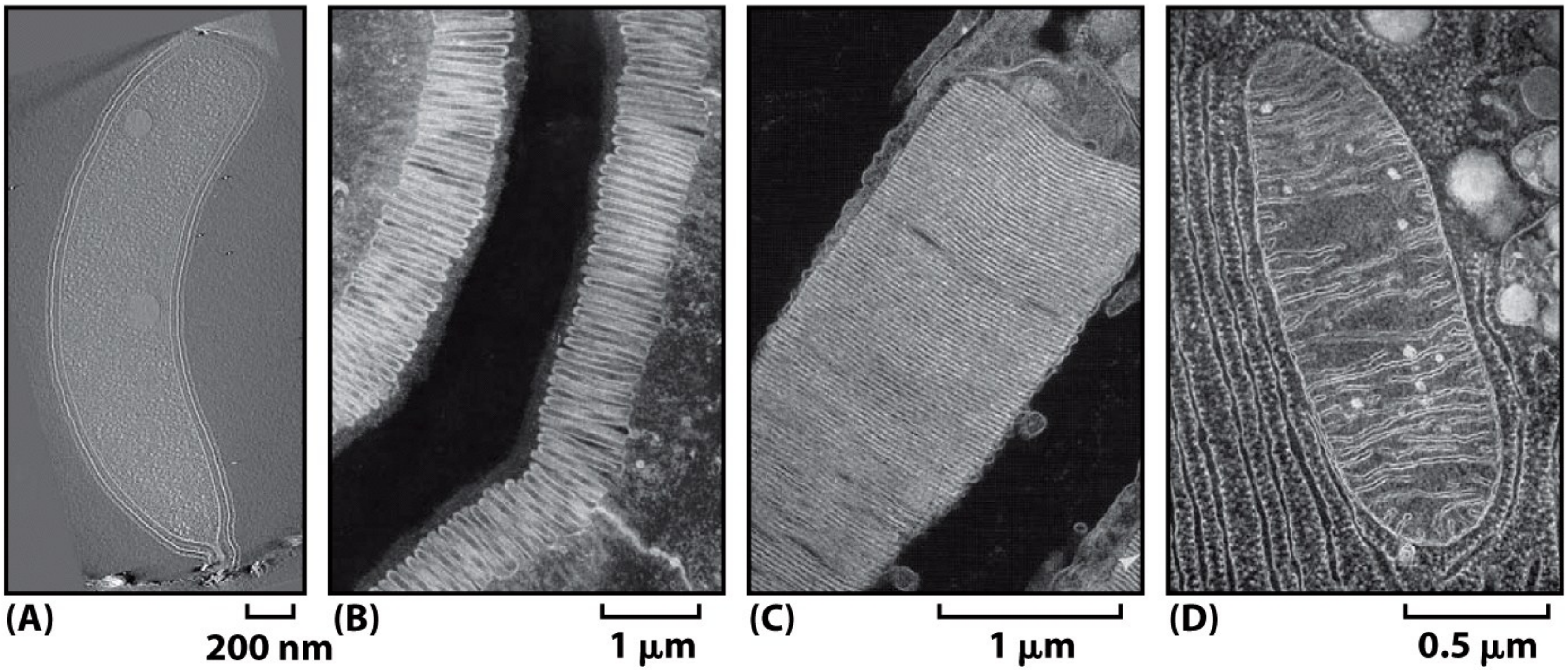


Figure 11.3 Physical Biology of the Cell (© Garland Science 2009)

Lipids are one of the four basic building blocks of cells.

Generic structure of a lipid molecule (*amphipathic*):

- **hydrophilic head (can form HBs with water)**
- **elongated hydrophobic domain (fatty acids)**

Schematic Models of Membranes (right)

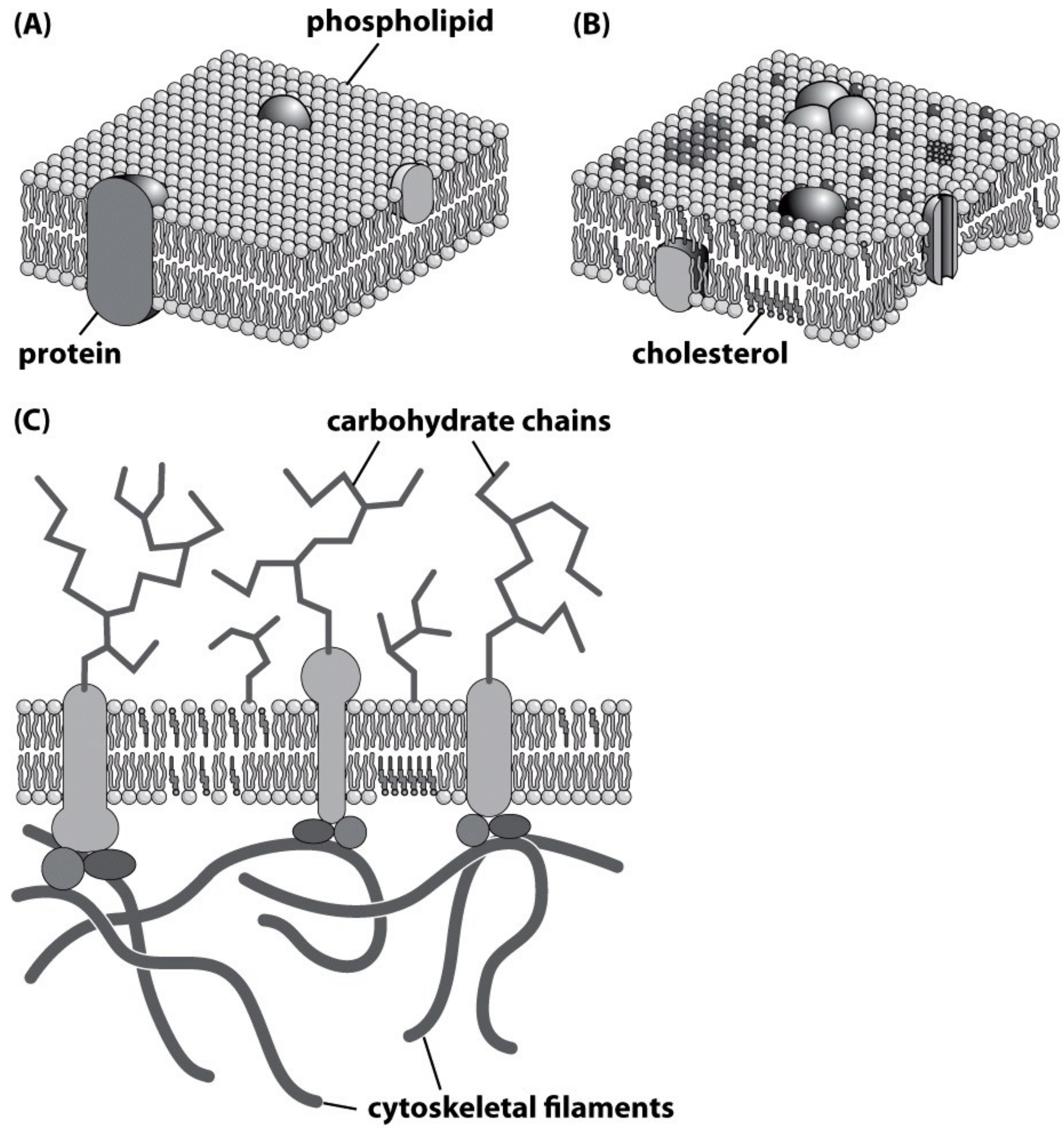


Figure 11.4 Physical Biology of the Cell (© Garland Science 2009)

Key Molecules of the Cell Membrane

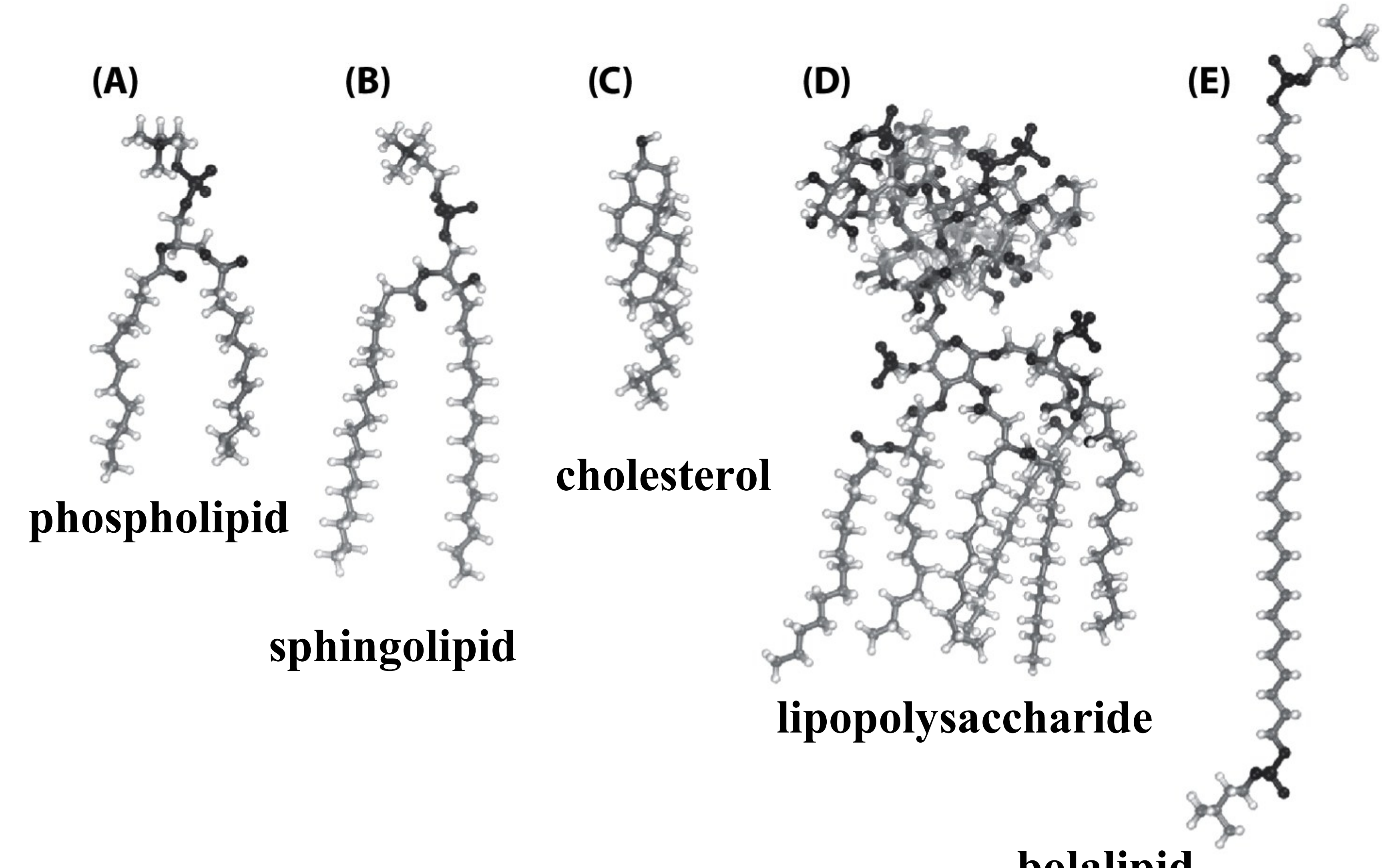
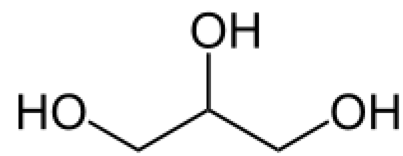
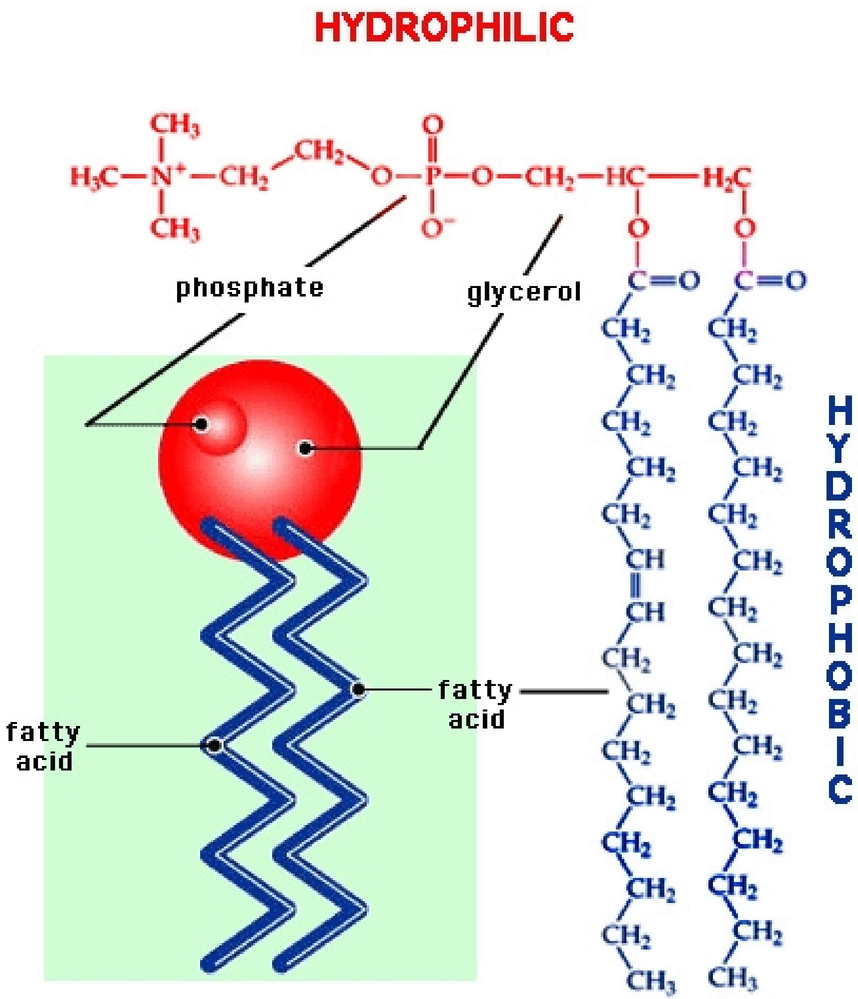
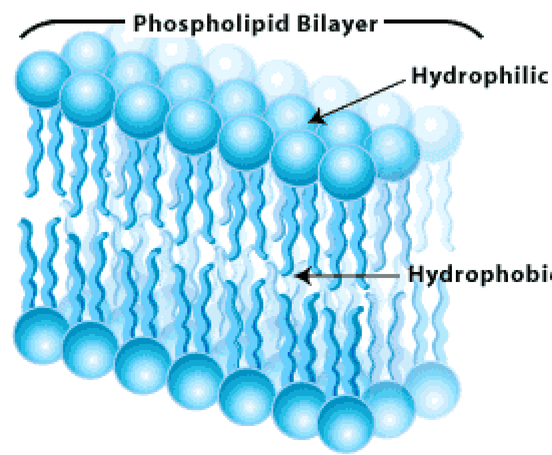


Figure 11.5 Physical Biology of the Cell (© Garland Science 2009)

A phospholipid is built around a *glycerol* (3 carbons and 3 hydroxyl groups)

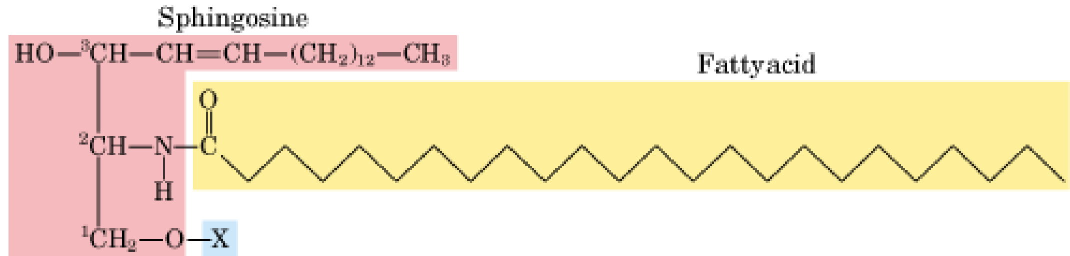


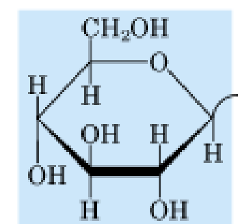
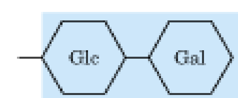
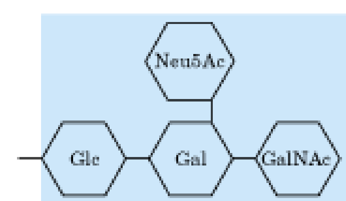




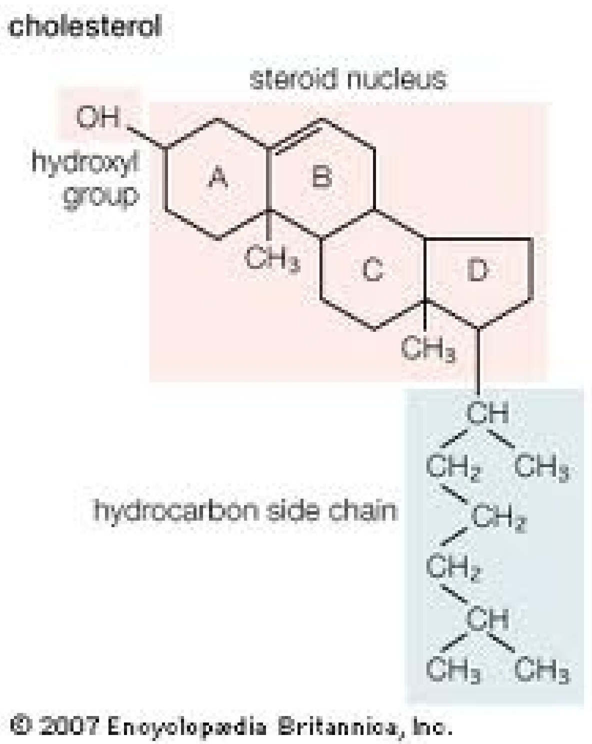
Sphingolipids

Sphingolipid (general structure)

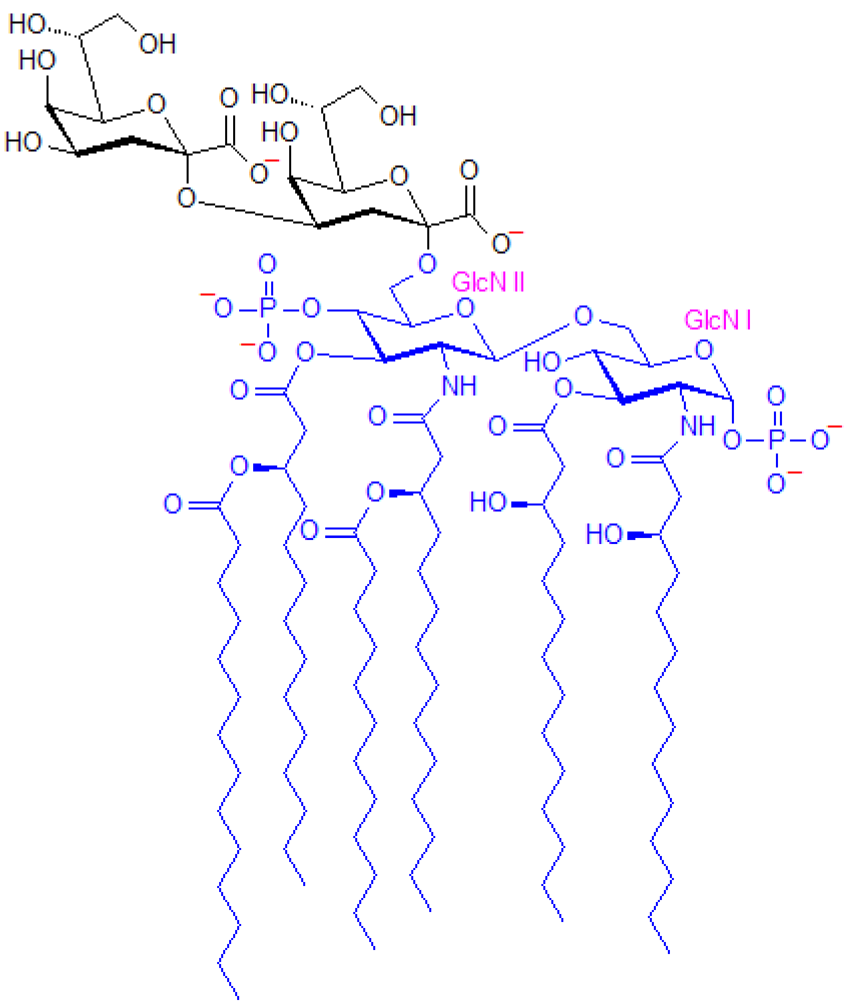


Name of sphingolipid	Name of X	Formula of X
Ceramide	—	$-H$
Sphingomyelin	Phosphocholine	$-P(=O)(O^-)-O-CH_2-CH_2-\overset{+}{N}(CH_3)_3$
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

Cholesterol



Lipopolysaccharide (*E.coli*)



The basic lipopolysaccharide of *E. coli*, incorporating lipid A (blue portion of the structure).

The geometric properties of lipid molecules (shape) can induce spontaneous curvature and result in various assemblies

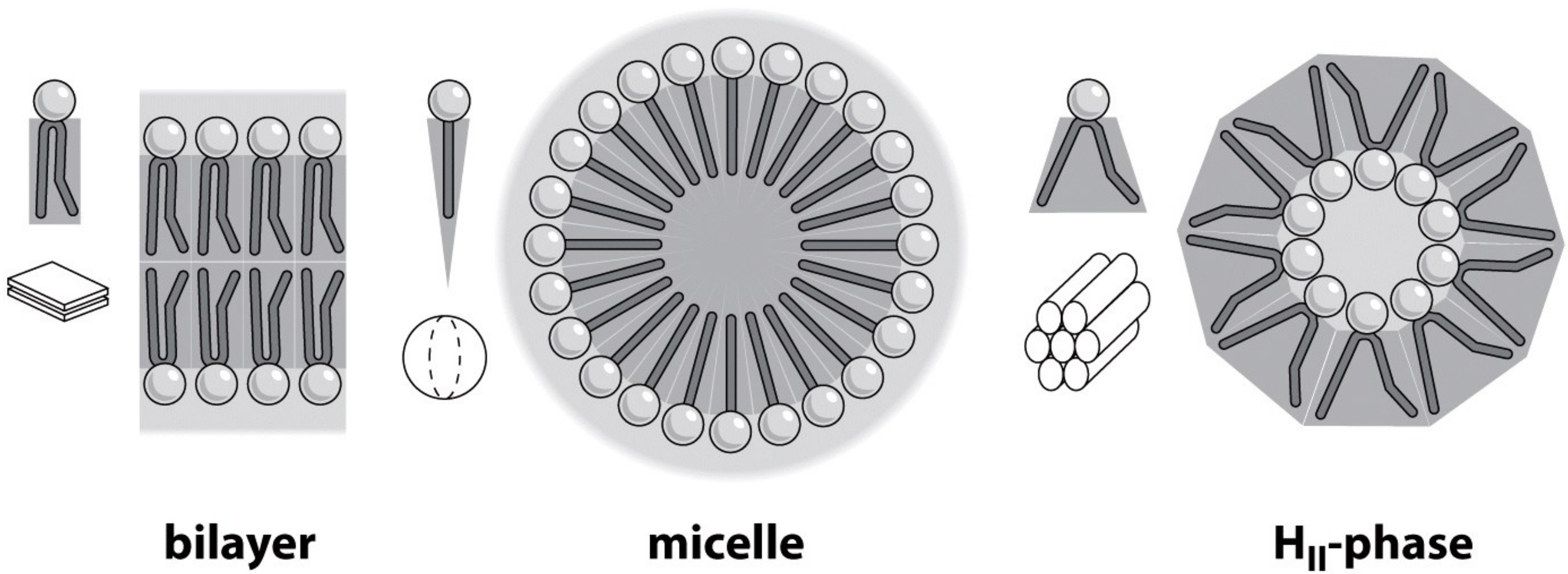


Figure 11.7 Physical Biology of the Cell (© Garland Science 2009)

Structures of multicomponent vesicles at low and high temperature

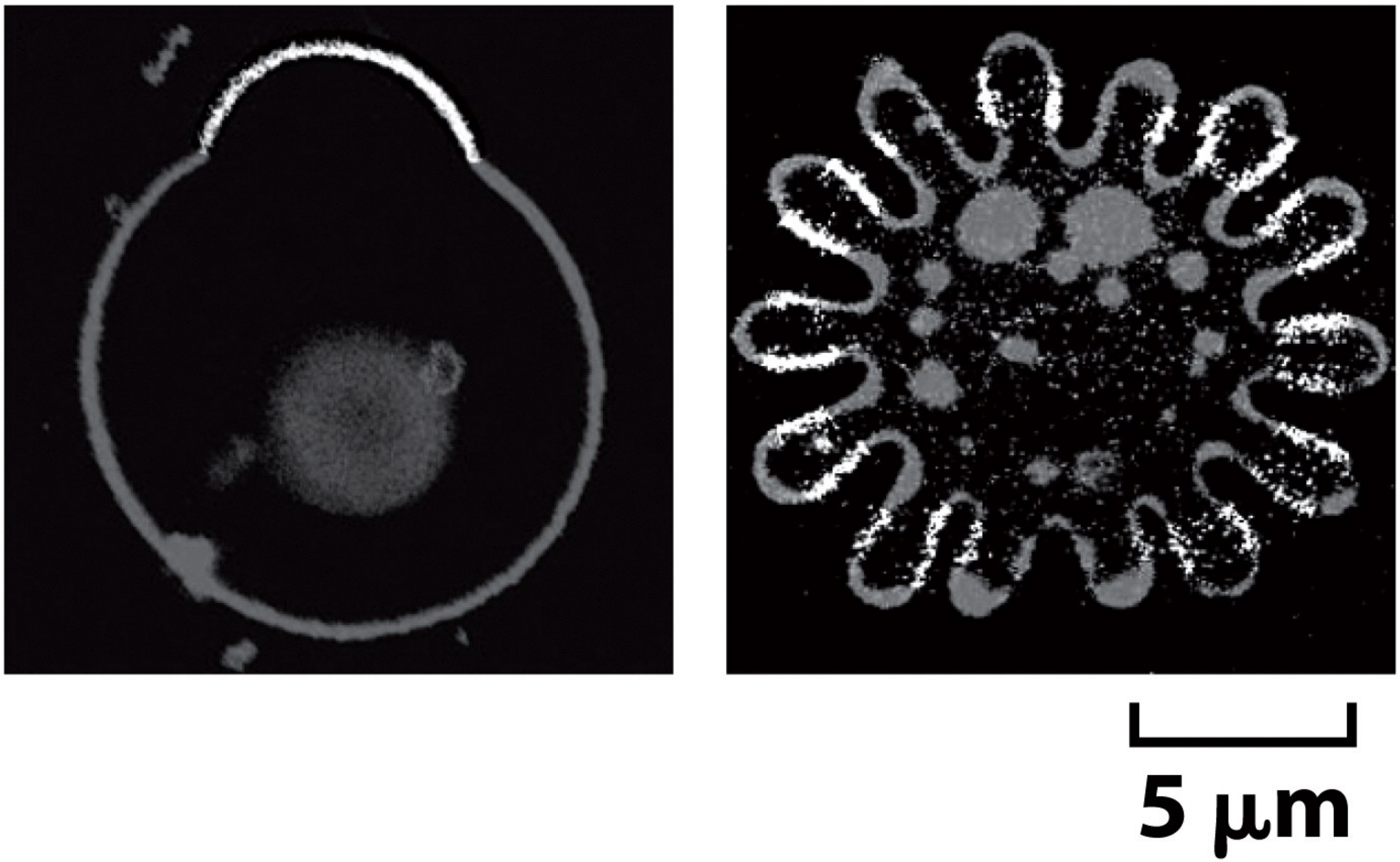


Figure 11.8 Physical Biology of the Cell (© Garland Science 2009)

Membrane Heterogeneity:

- **in *E. coli*: 1/3 of all proteins are membrane proteins:**

  10^6 membrane proteins per cell

- **in *E. coli*: 2 membranes, each with 500,000 proteins**

- **membrane area:** $6\,\mu\text{m}^2$

- **area per protein:** $12\,\text{nm}^2$

- **average spacing between proteins in a membrane:** $3.5\,\text{nm}$

- **mitochondrial membranes: proteins ~ 70% of the total mass**

Various membrane proteins

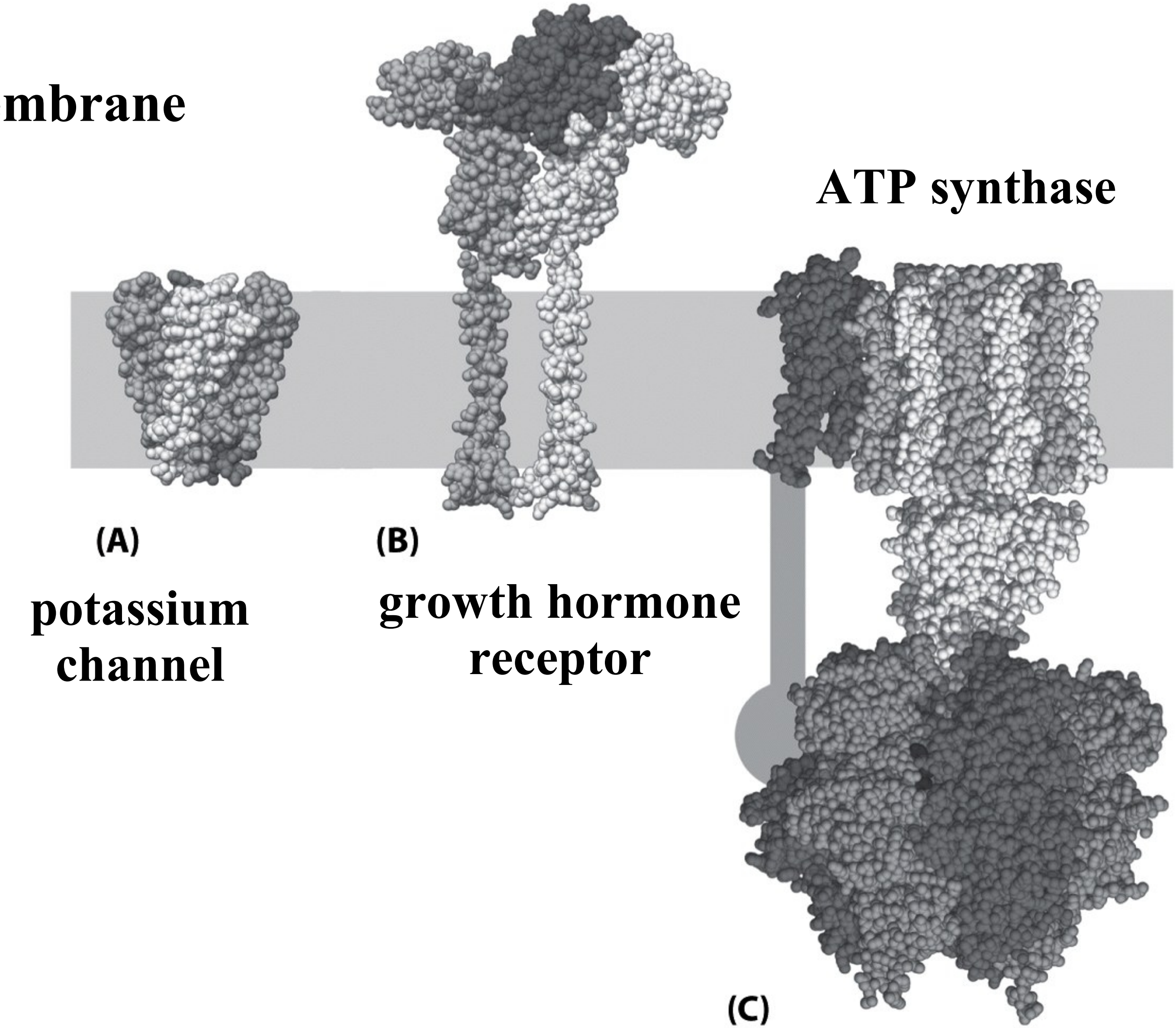


Figure 11.9 Physical Biology of the Cell (© Garland Science 2009)

Mobility of Proteins in the Mitochondrial Membrane

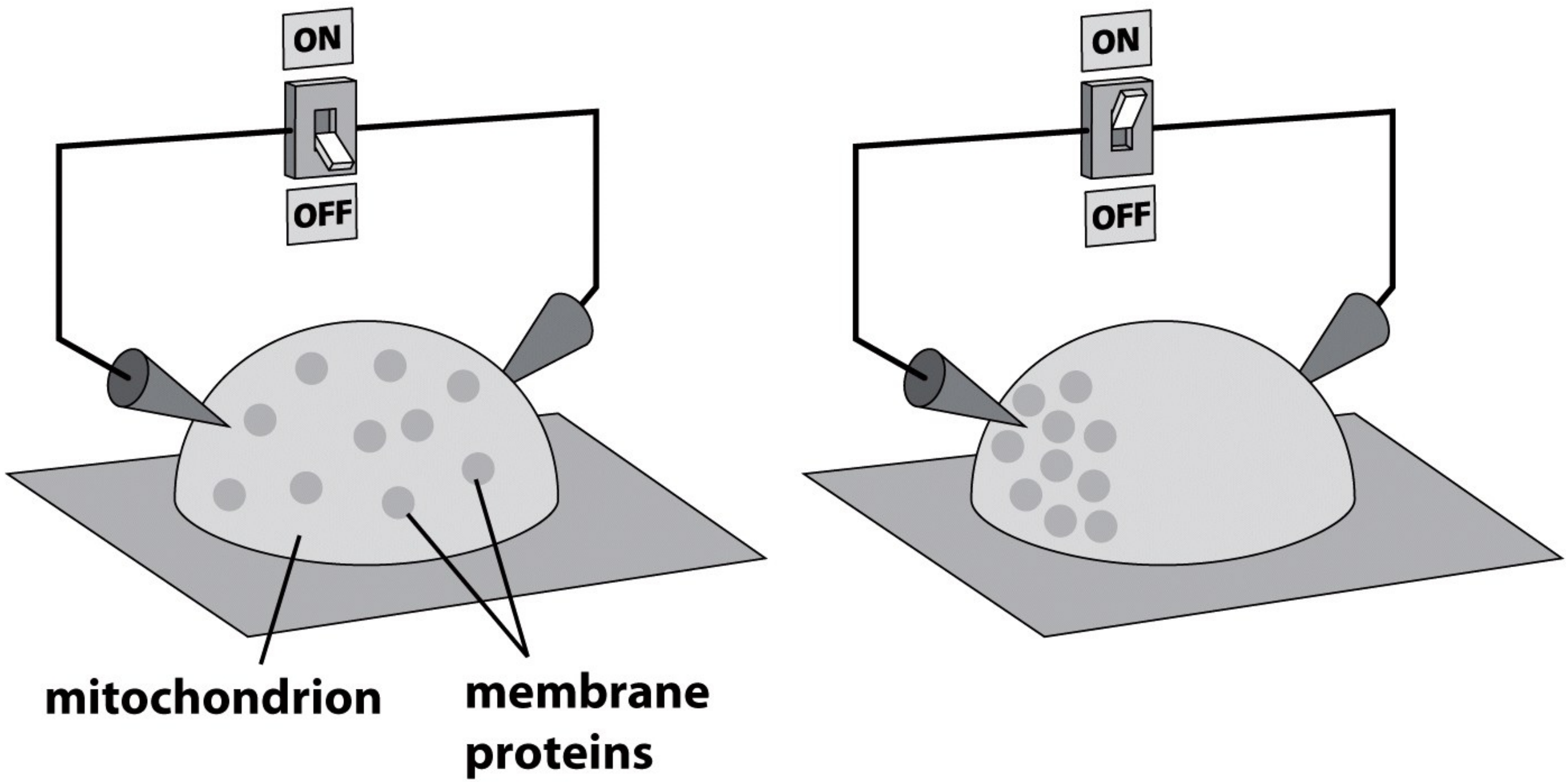


Figure 11.10a Physical Biology of the Cell (© Garland Science 2009)

Freeze Fracture Flectron Microscopy: Membrane proteins in mitochondirial membrane

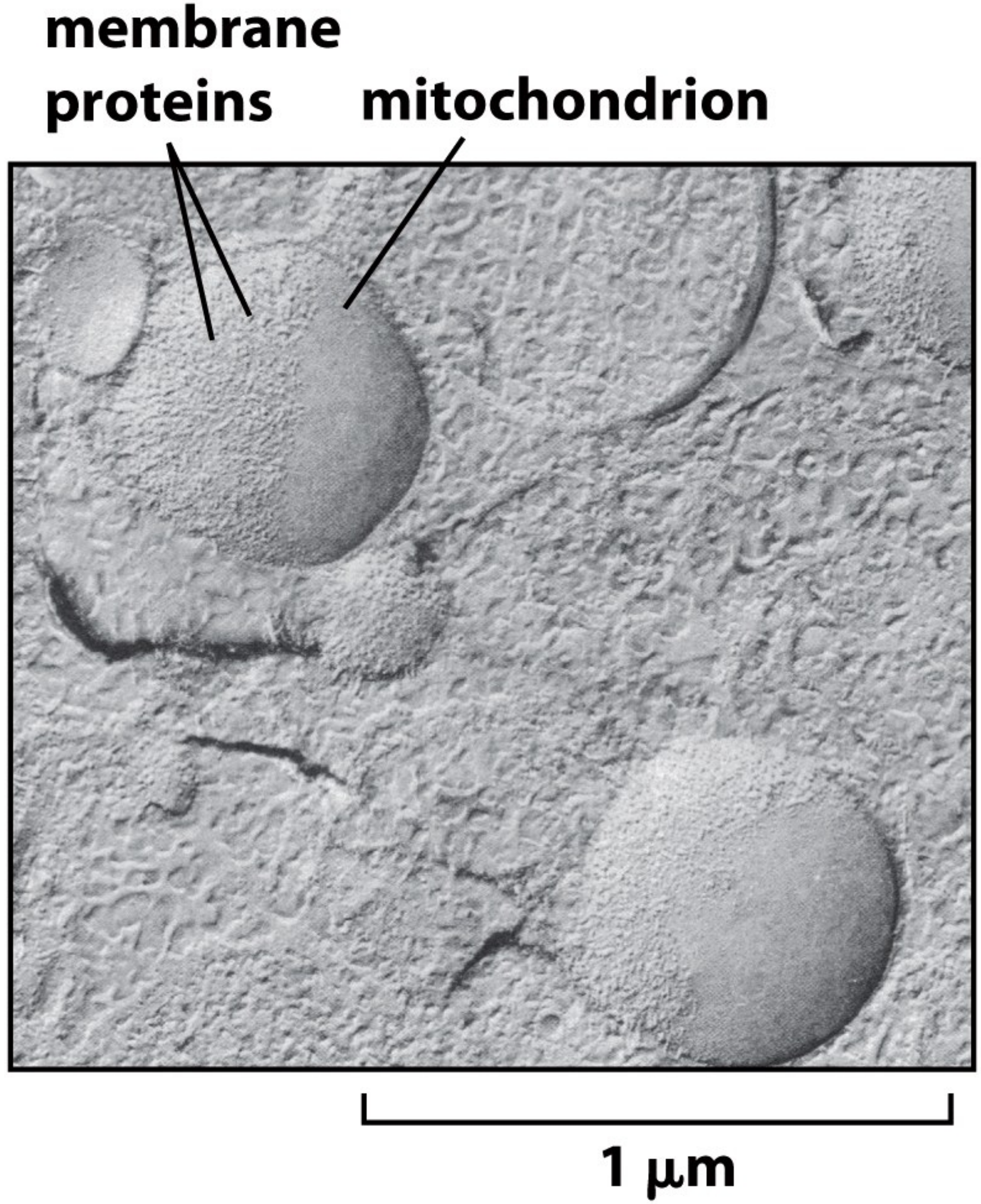


Figure 11.10b Physical Biology of the Cell (© Garland Science 2009)

Membrane proteins help transport mass across the membrane:

- **membrane *permeability cofficient P* is defined as following:**

$$\text{flux} = P(c_{\text{INSIDE}} - c_{\text{OUTSIDE}})$$
$$\text{flux} \ldots [m^{-2}s^{-1}] \qquad P[m/s]$$
$$c_{\text{INSIDE}} \ldots \text{ion conc. 'inside}$$
$$c_{\text{OUTSIDE}} \ldots \text{ion conc. 'outside}$$

- **permeability depends on the molecule crossing the membrane (right)**
  - **-water has the highest permeability**
  - **-ions have a rather low permeability**

- **Transporter proteins act as channels that selectively increase *P* for the particular ion/molecule**

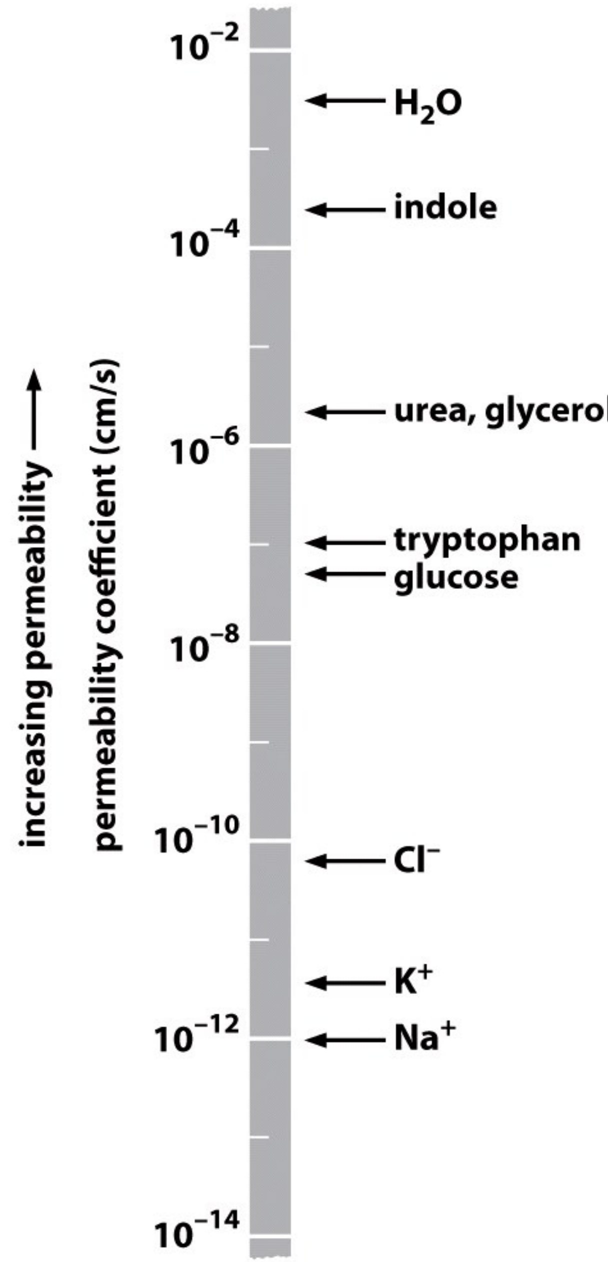


Figure 11.11 Physical Biology of the Cell (© Garland Science 2009)

Growth factor attaches to the receptor extracellularly and initiates microtubule formation inside the neuron (dendrites, axon growth)

GTP (guanosine tri-phosphate) molecules

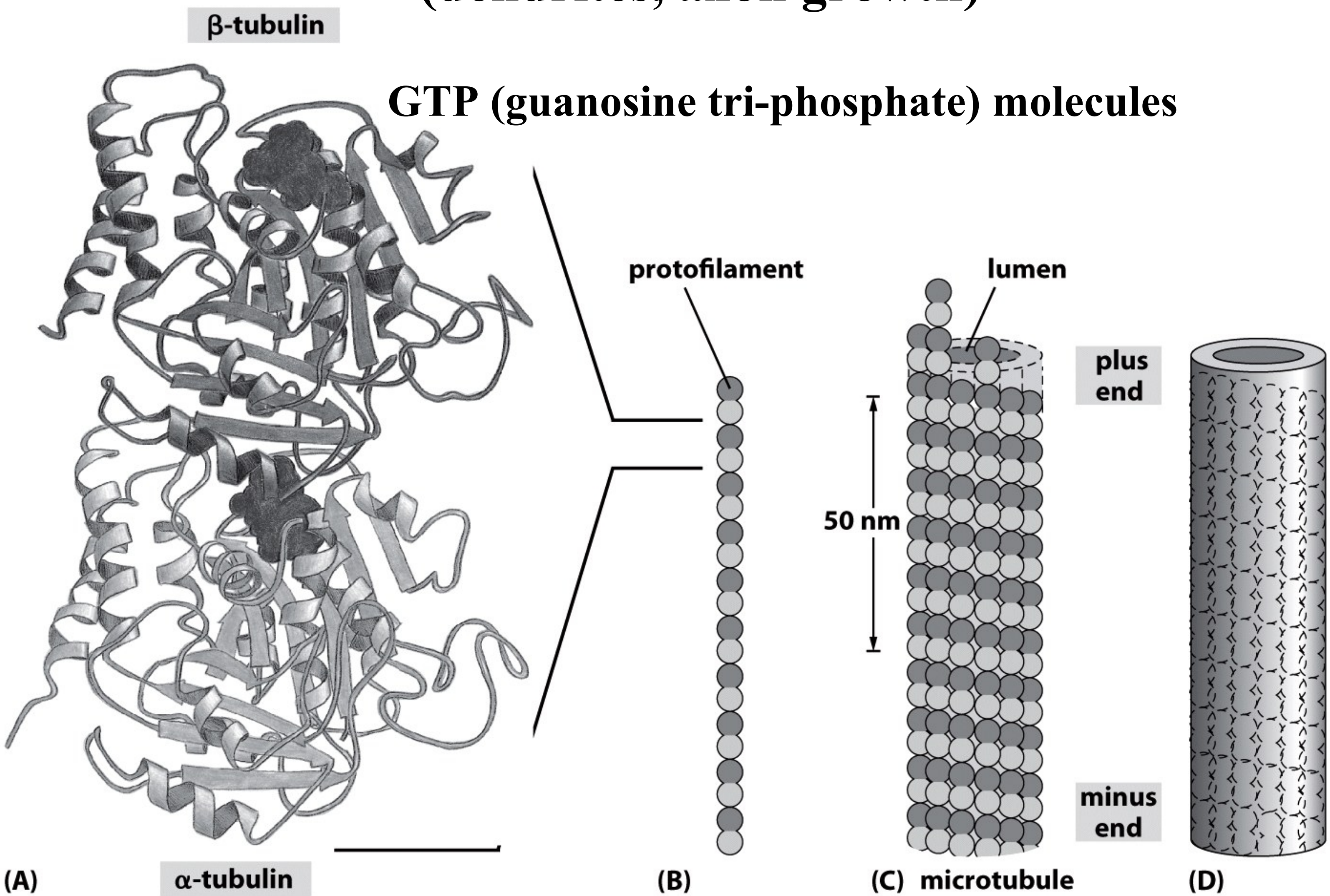


Figure 10.27 Physical Biology of the Cell (© Garland Science 2009)

Examples of Important Membrane Proteins

ATP synthase: **a molecular machine that converts a transmembrane H+ gradient into ATP using ADP and inorganic phosphate**

Bacteriorhodopsin: **pumps protons across the membrane in response to light**

When ATP synthase and bacteriorhodopsin are reconstructed in artificial phospholipid vesicles, they adopt a symbiotic relationship:

- **bacteriorhodopsin creates proton gradient using light**
- **ATP synthase uses the proton gradient to create ATPs**

Together, they form a minimalistic green plant that converts light into ATP chemical energy!

Bacteriorhodopsin and ATP synthase in an artificial vesicle

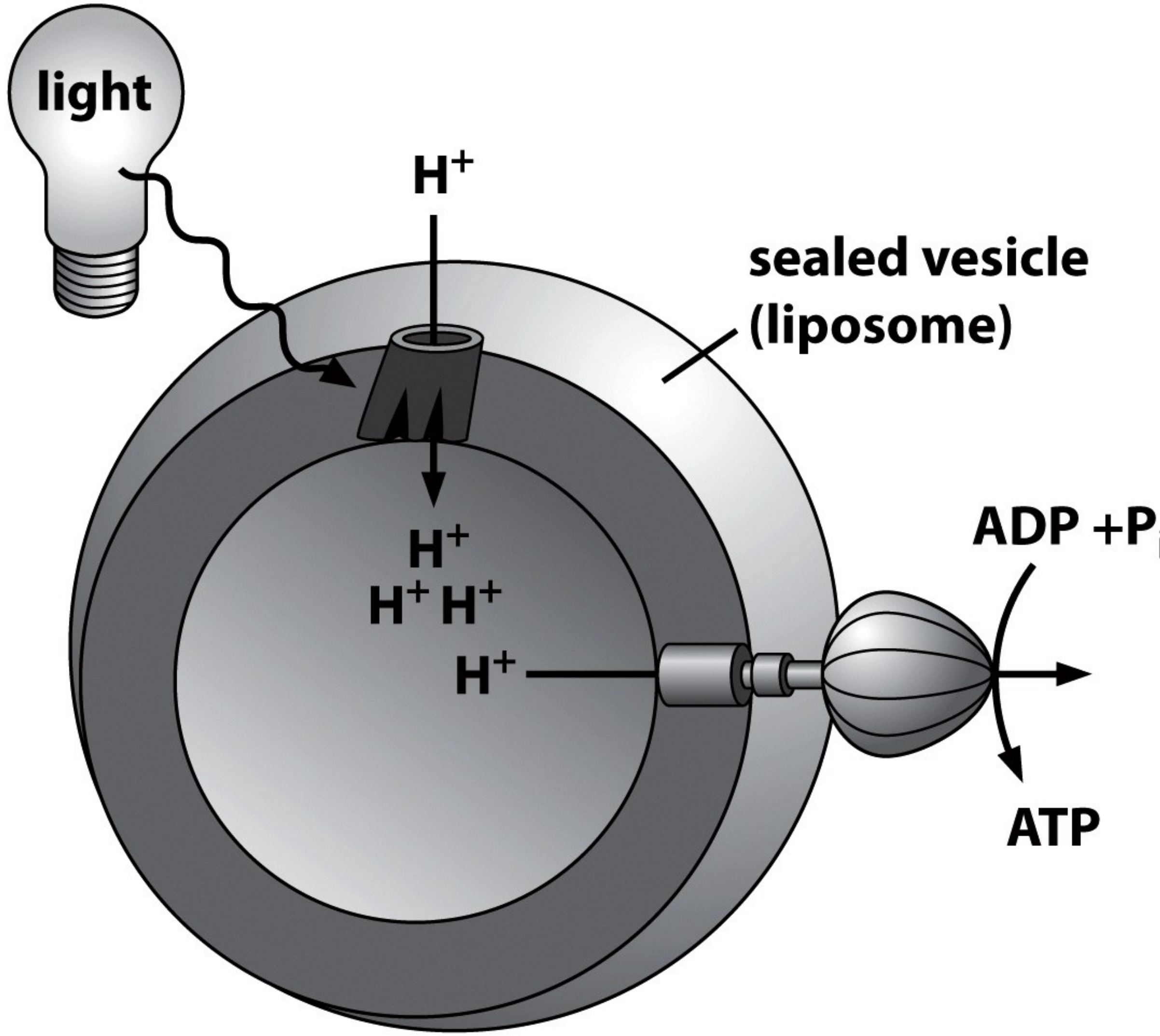


Figure 11.12 Physical Biology of the Cell (© Garland Science 2009)

Four types of membrane deformations:

- **Stretch**
- **Bend**
- **Thickness Change**
- **Shear**

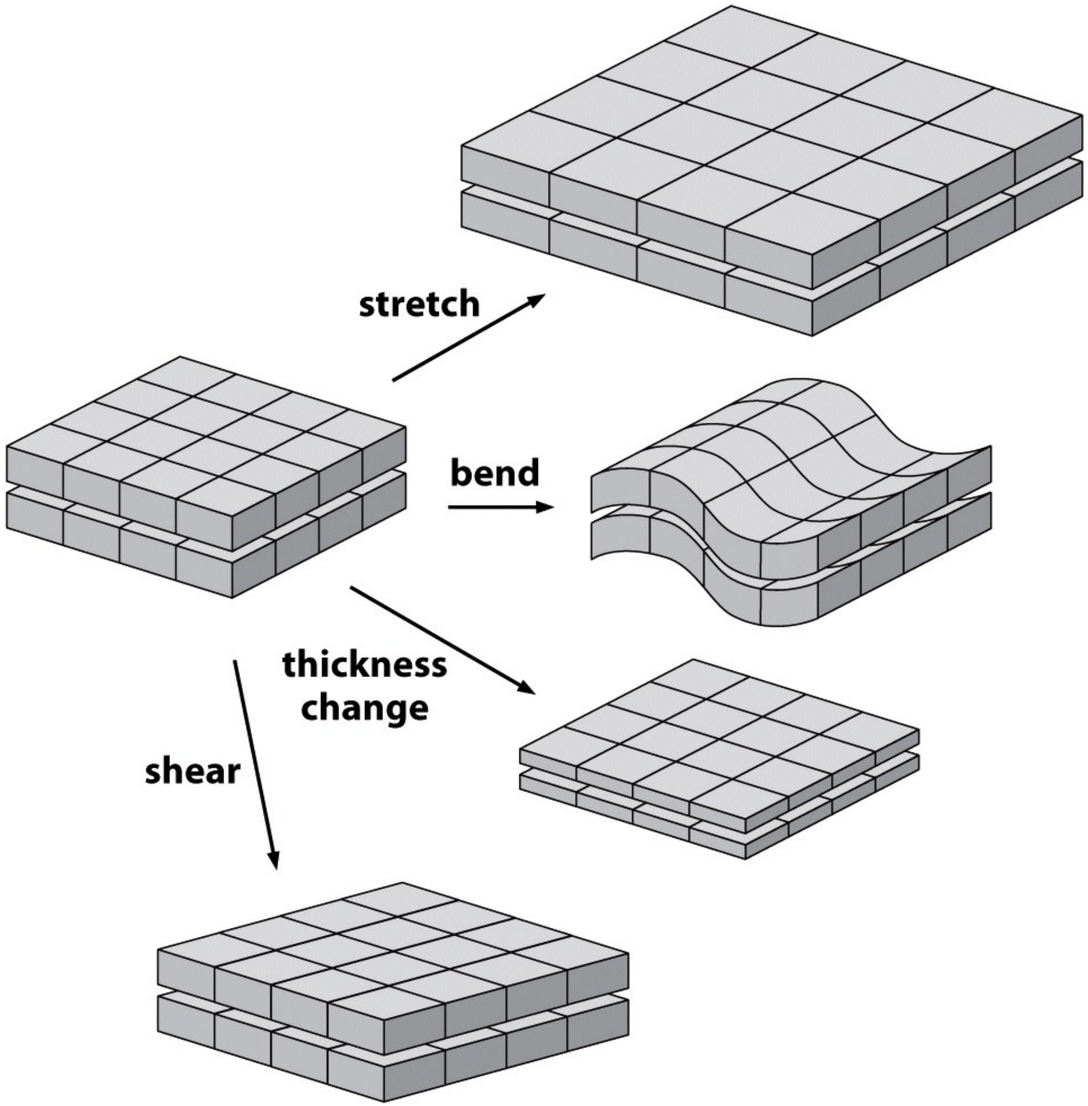


Figure 11.13 Physical Biology of the Cell (© Garland Science 2009)

Mathematical description of stretching, bending, compression, and shear of the membrane

Consider a patch of membrane described in the (x,y) plane:

- **Stretching:** $\Delta a(x,y)$... change of the local area
- **Bending:** $h(x,y)$... height of the local area
- **Compression:** $w(x,y)$... thickness of the local area
- **Shear:**

$\theta(x,y)$... shear angle of the local area

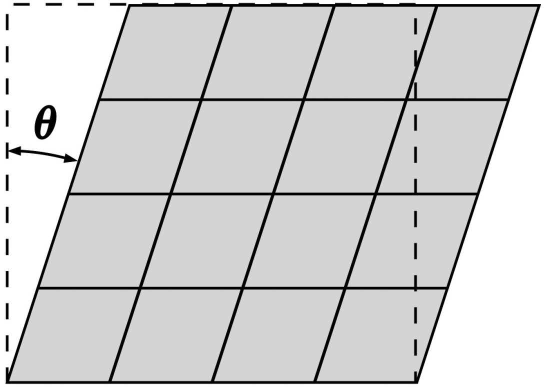


Figure 11.18 Physical Biology of the Cell (© Garland Science 2009)

Description of bending geometry by a height function

$$h(x, y)$$

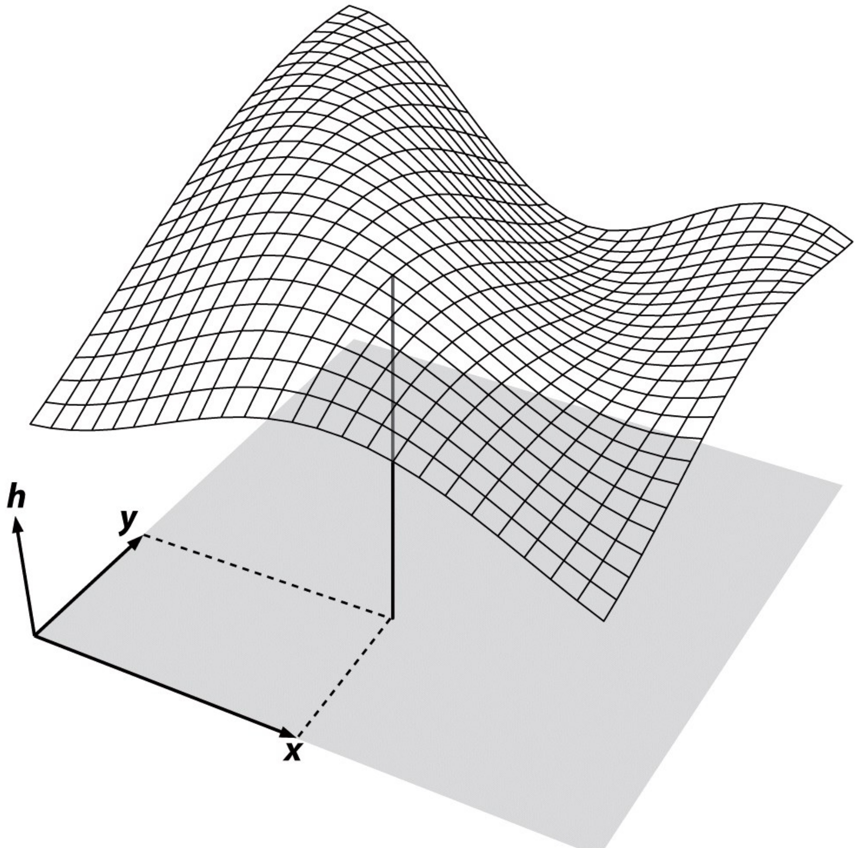


Figure 11.14 Physical Biology of the Cell (© Garland Science 2009)

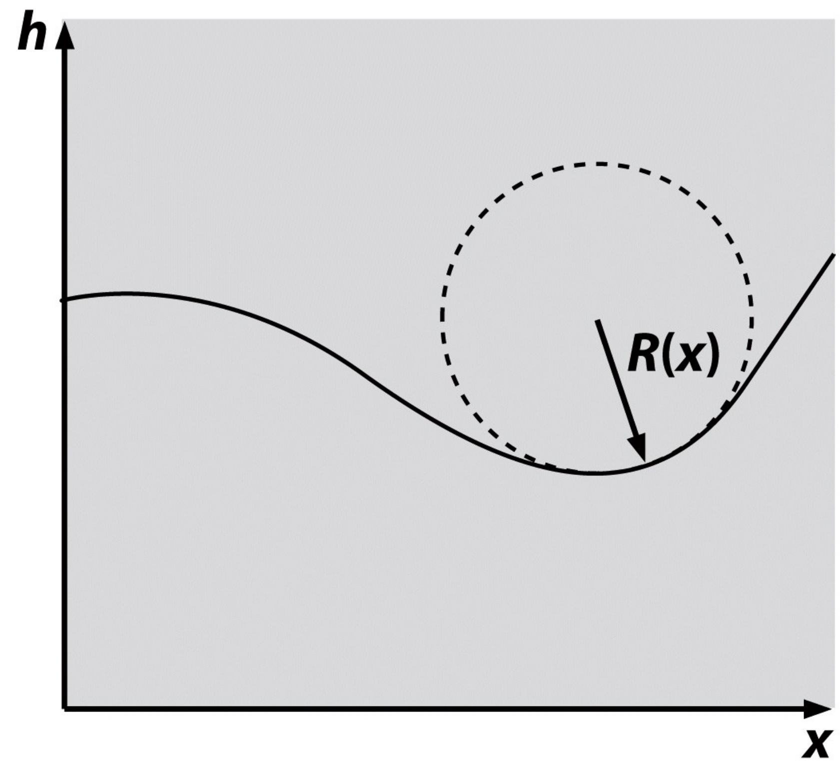


Figure 11.15a Physical Biology of the Cell (© Garland Science 2009)

Local curvature depends on the angle of intersection between the plane and the membrane

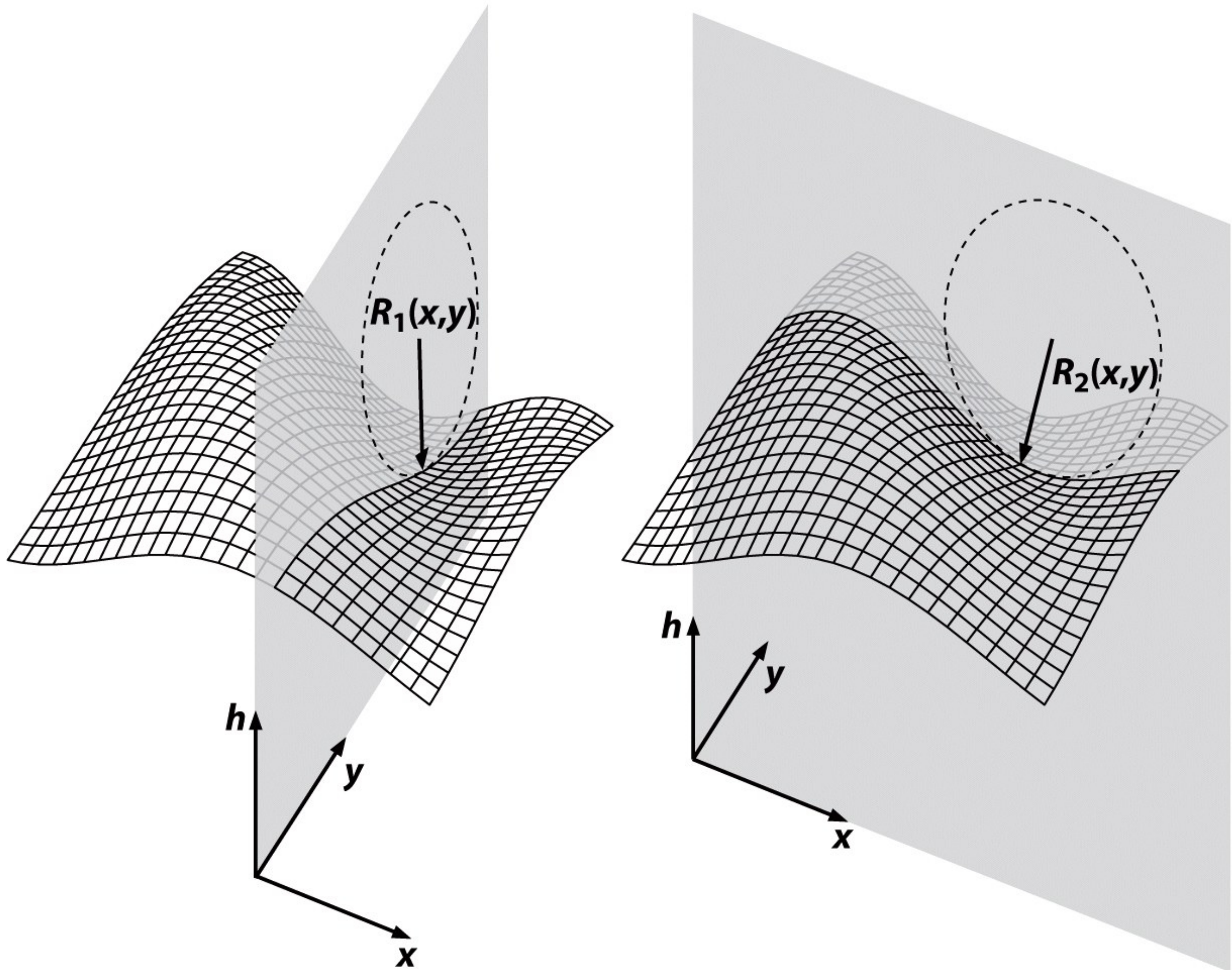


Figure 11.15b Physical Biology of the Cell (© Garland Science 2009)

How do we calculate a curvature of a membrane at (x, y)?

- **Construct the tangent plane at the point (x, y)**

- **Expand the height h in powers of x and y around the origin**

$$h(x,y) = \kappa_{11} x^2 + \kappa_{12} x y + \kappa_{21} y x + \kappa_{22} y^2$$

$$\kappa = \begin{pmatrix} \kappa_{11} & \kappa_{12} \\ \kappa_{21} & \kappa_{22} \end{pmatrix}$$

$$\kappa_{11} = \frac{\partial^{٢} h}{\partial x \partial x} \qquad \kappa_{12} = \frac{\partial^2 h}{\partial x \partial y}$$

$$\kappa_{21} = \frac{\partial^2 h}{\partial y \partial x} \qquad \kappa_{٢٢} = \frac{\partial^2 h}{\partial y \partial y}$$

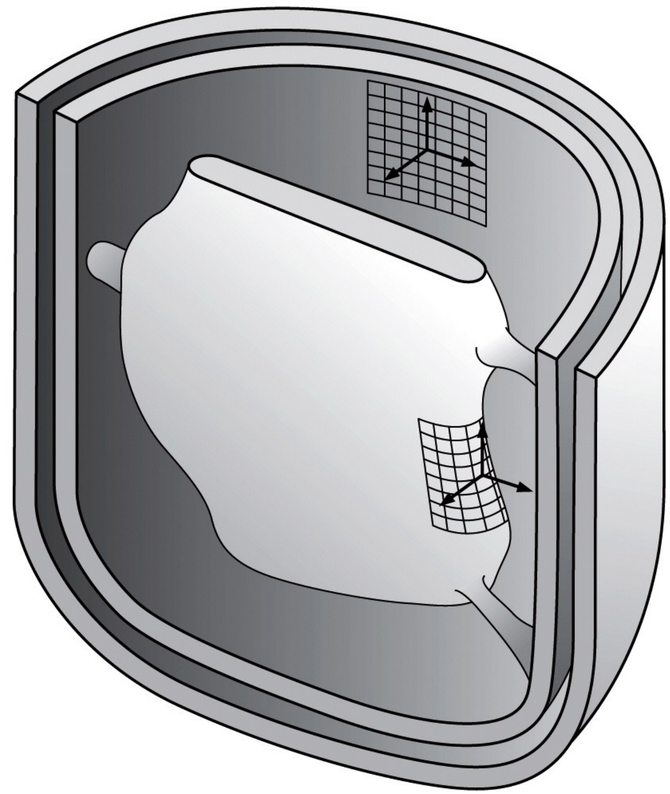


Figure 11.16 Physical Biology of the Cell (© Garland Science 2009)

- **the eigenvalues of this matrix are the two principal curvatures and the eigenvectors correspond to the the axes of the largest and smallest curvatures (principal values)**

Follow Taylor expansion of $h(x, y)$ around $(x_{0,} y_0)$

$$h(x,y) = h(x_{0,} y_0) + \frac{\partial h}{\partial x}\Delta x + \frac{\partial h}{\partial y}\Delta y$$

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

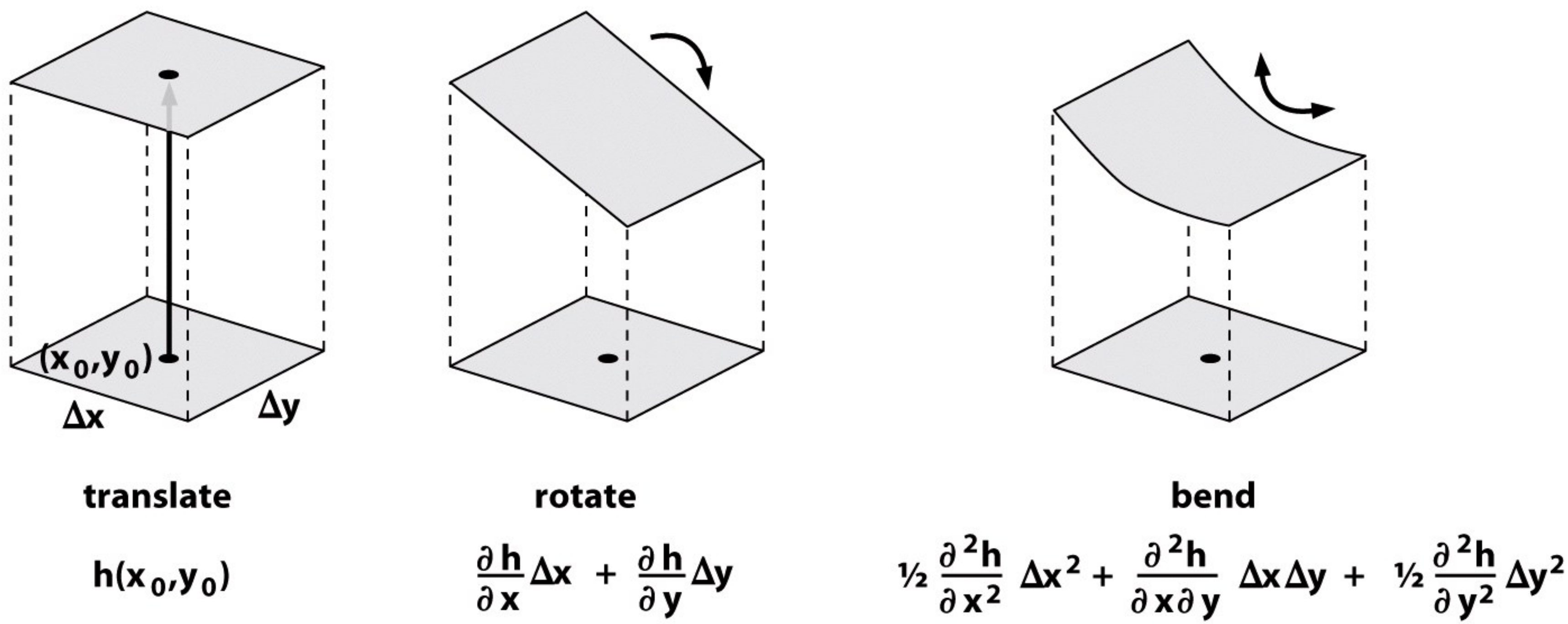


Figure 11.17b Physical Biology of the Cell (© Garland Science 2009)

Free Energy Penalty due to Area Change

$$G_{stretch} = \frac{K_a}{2} \int \left(\frac{\Delta a}{a_0}\right)^2 da$$

K_a ... area stretch modulus $[55-70\ k_B T/m^2]$

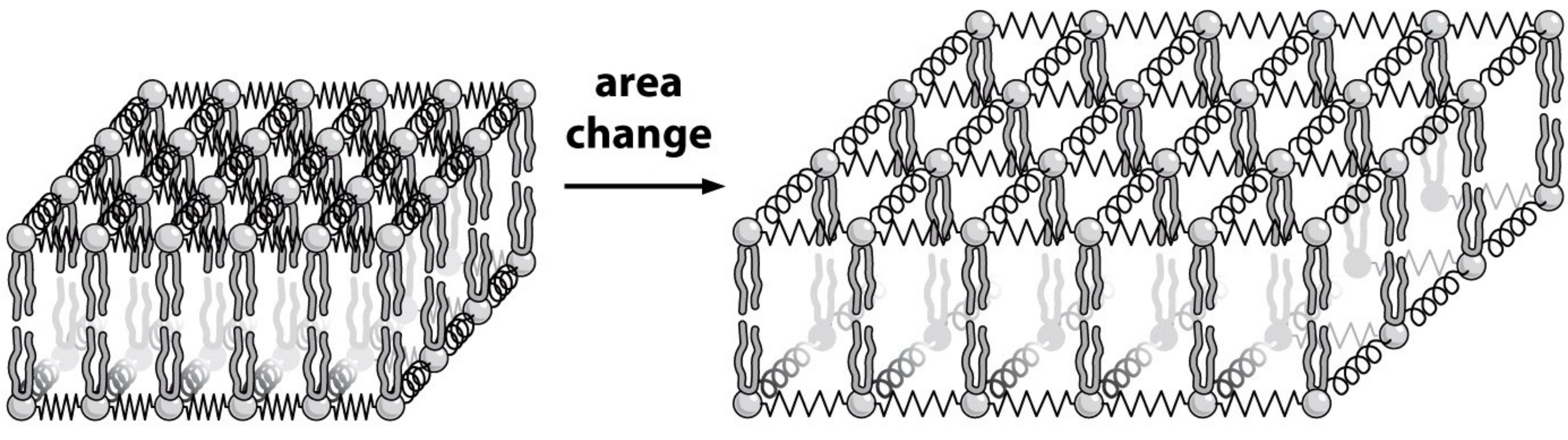


Figure 11.19 Physical Biology of the Cell (© Garland Science 2009)

Free Energy Penalty due to Bilayer Bending: Helfrich-Canham-Evans Free Energy

$$G_{bend} = \frac{K_b}{2} \int da \left(\kappa_1 + \kappa_2\right)^2$$

K_b ... bending rigidity $[10 - 20\ k_B T]$

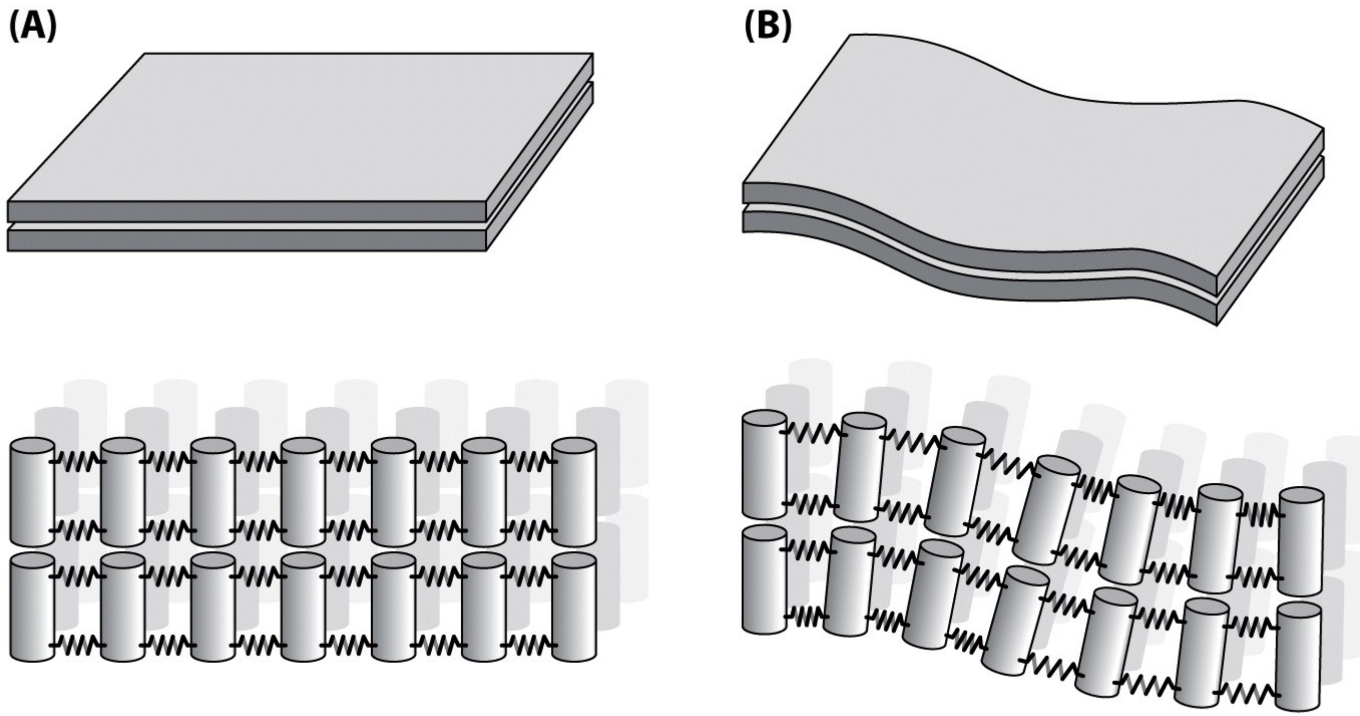


Figure 11.20 Physical Biology of the Cell (© Garland Science 2009)

Free Energy Penalty due to Bilayer Thickness Change

$$G_{compression} = \frac{K_t}{2} \int da \left(\frac{w(x,y) - w_0}{w_0} \right)^2$$

K_t ... stiffness $[60\ k_B T/nm^2]$

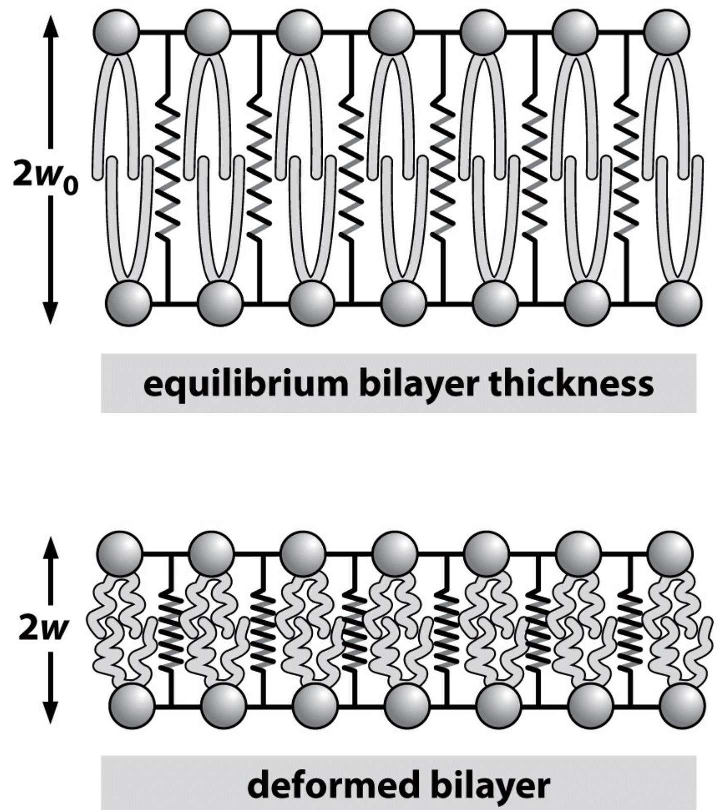


Figure 11.21 Physical Biology of the Cell (© Garland Science 2009)