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Biological Membranes

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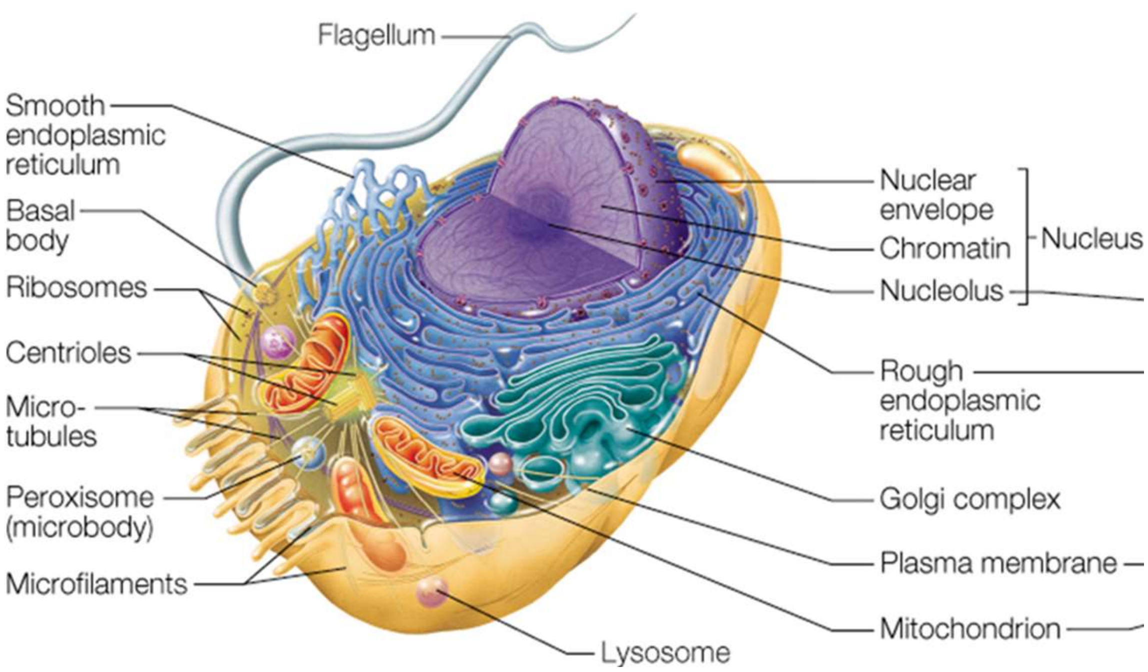
Objectives

- Introduction to lipids
- Structure of biological membranes
- Proteins in the membrane
- Properties of membranes

- Textbook Chapter 10

Eukaryotic cells: several membrane-enclosed organelles (from Lecture 1)



(a) Typical animal cell.

Mitochondria: specialize in oxidative metabolism
Endoplasmic reticulum: where protein synthesis occurs
Golgi complex: secretion and the transport of newly synthesized proteins to their destinations
Nucleus: contains the cell's genetic information, encoded in DNA that is packaged into chromosomes.
Nucleolus: where DNA is subpackaged into a dense region within the nucleus
Nuclear envelope: through which the nucleus and cytoplasm communicate.
Lysosomes: digestive bodies
Basal bodies: anchors for cilia or flagella in animal cells that have these appendages

Cells carry out metabolic reactions

- **Eukaryotic cells** have membrane-surrounded structures (organelles) within the cellular boundary
- During evolution, selective advantage has accrued to systems that were closed off and protected by boundaries, when competing for resources.
- Compartmentation provides protection from environmental fluctuations and maintains high local concentrations of components to increase efficiency of polymerization (e.g. biopolymers) and other chemical reactions (e.g. metabolism, energy generation).

Cellular architecture – Summary

- Compartmentation of cells promotes efficiency of biochemical reactions.
- Metabolic pathways evolved to synthesise biomolecules and generate energy.
- Specialised activities are carried out in different cellular compartments.

What are Biological Membranes?

- Membranes are made of **lipids** and **proteins**
- Lipids are molecules that are either completely hydrophobic or amphipathic (predominantly hydrophobic with a hydrophilic head group)
  - ➢ Mainly amphipathic in membranes
    - ❖ Two main types in membranes are sterols and **phospholipids**
    - ❖ ***Cholesterol*** is the major sterol in humans
    - ❖ Phosphatidic acid is a example of a very simple phospholipid.

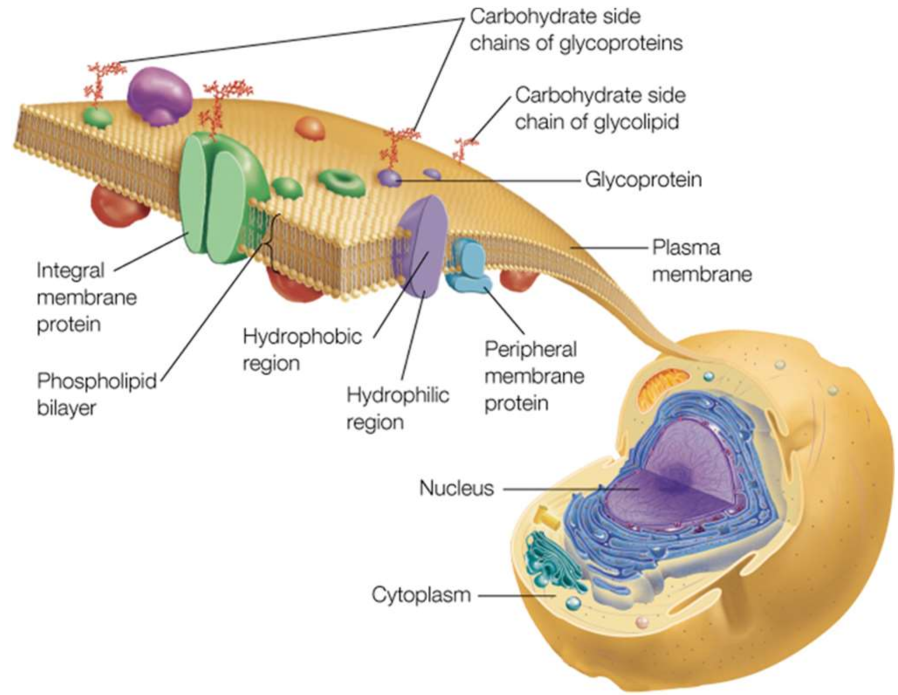
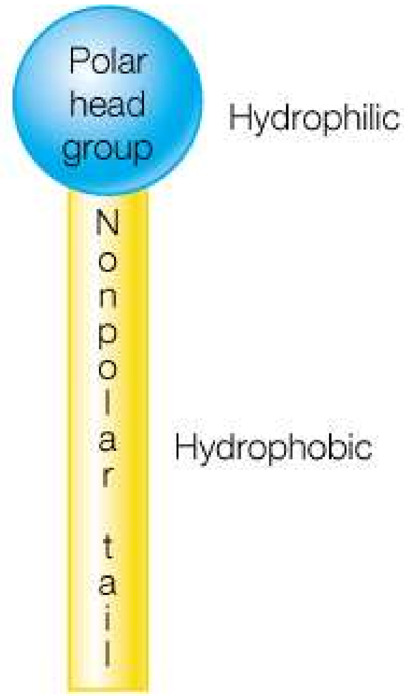


FIGURE 10.9 Structure of a typical cell membrane.

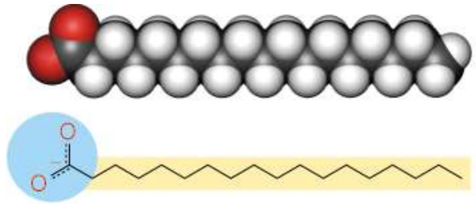
Major Functions and Properties of Lipids

- Major functions of lipids include: energy storage, membrane structure, and signaling
- Unlike carbohydrates, amino acids, nucleotides, or lipids have limited solubility in aqueous media
- Most lipids are amphipathic and they contain both hydrophobic and hydrophilic regions

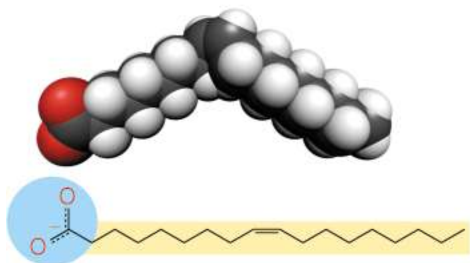


A simplified representation of an amphipathic lipid molecule

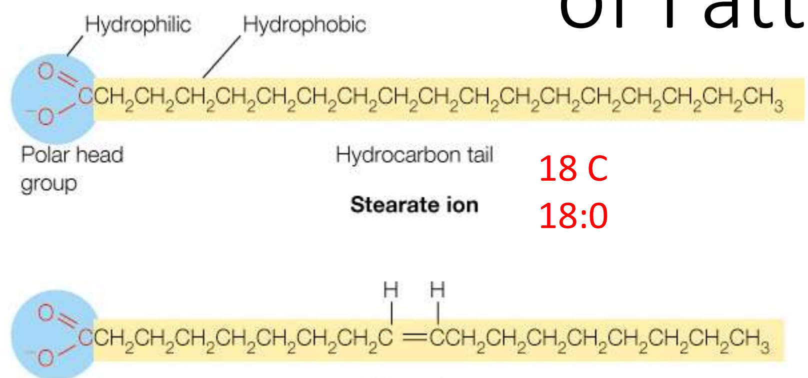
Lipids are made up of Fatty Acids



(a) Stearate ion. Stearate (the anionic, deprotonated form of stearic acid) is a saturated fatty acid.



(b) Oleate ion. Oleate is an unsaturated fatty acid with one *cis* double bond.



(c) Formulas. Alternate representations for (a) and (b).

18 C
18:0

18 C with 1 C=C
18:1*n*-9

FIGURE 10.1 Structures of the ionized forms of two representative fatty acids.

- Fatty acids are major constituents of lipids
- In a fatty acid, a hydrophilic carboxylate group is attached to one end of a hydrocarbon chain (containing typically between 12 and 24 carbons)
- In their hydrocarbon chains, unsaturated fatty acids contain one or more *cis* C=C bonds, whereas saturated fatty acids contain none
- The fluidity of fatty acids decreases as the chain length increases and the number of *cis* double bonds decreases

Example Fatty Acids

TABLE 10.1 Some biologically important fatty acids

Common Name	Systematic Name	Abbreviation	Structure	Melting Point (°C)
Saturated Fatty Acids				
Capric acid	Decanoic acid	10:0	$CH_3(CH_2)_8COOH$	31.6
Lauric acid	Dodecanoic acid	12:0	$CH_3(CH_2)_{10}COOH$	44.2
Myristic acid	Tetradecanoic acid	14:0	$CH_3(CH_2)_{12}COOH$	53.9
Palmitic acid	Hexadecanoic acid	16:0	$CH_3(CH_2)_{14}COOH$	63.1
Stearic acid	Octadecanoic acid	18:0	$CH_3(CH_2)_{16}COOH$	69.6
Arachidic acid	Eicosanoic acid	20:0	$CH_3(CH_2)_{18}COOH$	76.5
Behenic acid	Docosanoic acid	22:0	$CH_3(CH_2)_{20}COOH$	81.5
Lignoceric acid	Tetracosanoic acid	24:0	$CH_3(CH_2)_{22}COOH$	86.0
Cerotic acid	Hexacosanoic acid	26:0	$CH_3(CH_2)_{24}COOH$	88.5
Unsaturated Fatty Acids				
Palmitoleic acid	*cis*-9-Hexadecenoic acid	16:1cΔ9	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	0
Oleic acid	*cis*-9-Octadecenoic acid	18:1cΔ9	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	16
Linoleic acid	*cis*,*cis*-9,12-Octadecenoic acid	18:2cΔ9,12	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	5
Linolenic acid	all-*cis*-9,12,15-Octadecenoic acid	18:3cΔ9,12,15	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	−11
Arachidonic acid	all-*cis*-5,8,11,14-Eicosatetraenoic acid	20:4cΔ5,8,11,14	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_3COOH$	−50

- Fatty acid double bonds are almost always in the *cis* form.
- This puts a rigid 30° bend in the chain which prevents tight packing of chains and lowers the transition (liquid↔gel) temperature of the membrane lipids.

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Fats

- In fat (or triacylglyceride), glycerol is esterified with three fatty acids
    - ‘R’ indicates a long-chain saturated or unsaturated fatty acid chain
    - R groups can be identical (as in the figure) or different
- Fat can be used for metabolic energy storage because its carbon atoms are highly reduced
- Fat can act as a source for energy or heat production, and for thermal insulation in organisms

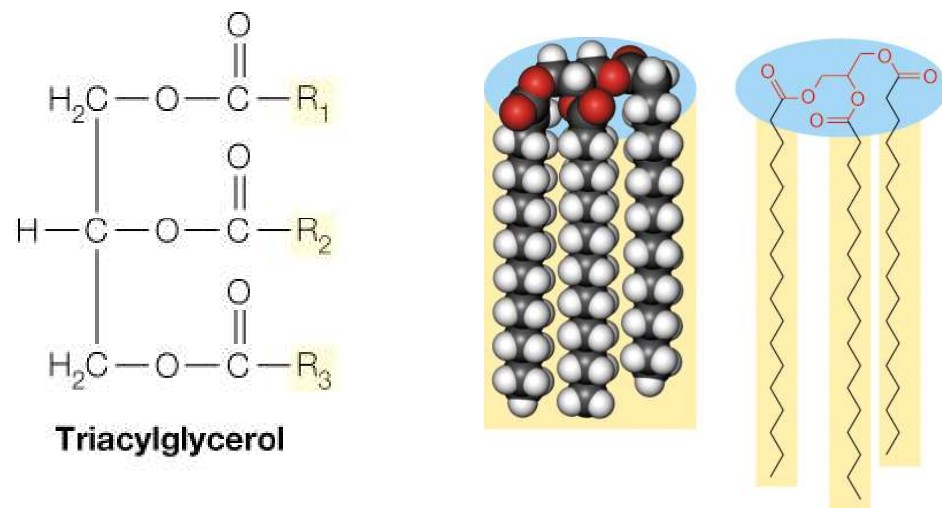
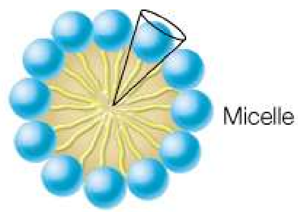


FIGURE 10.2 The structure of tristearin, a simple fat.

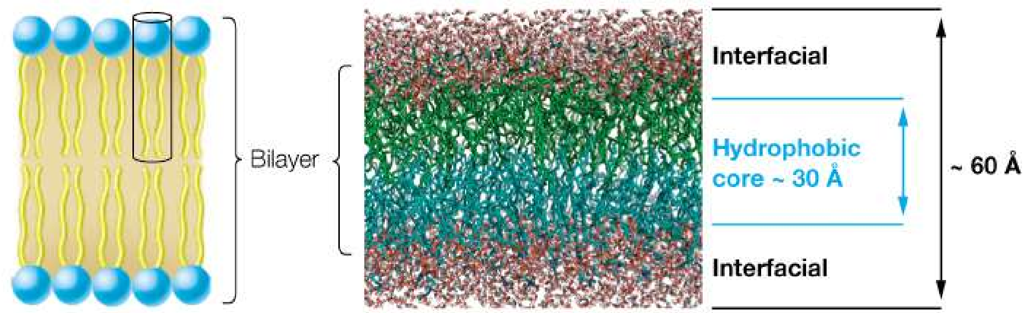
Lipids, Micelles, Bilayers

- Lipids are major constituents of all biological membranes
  1. Fatty acids tend to form spherical micelles
  2. Lipids with one hydrophilic head group and two hydrophobic tails (hydrocarbon chains) promote the formation of a bilayer, the structure seen in biological membranes
- The major classes of membrane-forming lipids are
  a. glycerophospholipids,
  b. glycoglycerolipids,
  c. sphingolipids, and
  d. glycerosphingolipids



Polar or charged groups face the solvent

(a) Fatty acids are wedge-shaped and tend to form spherical micelles.



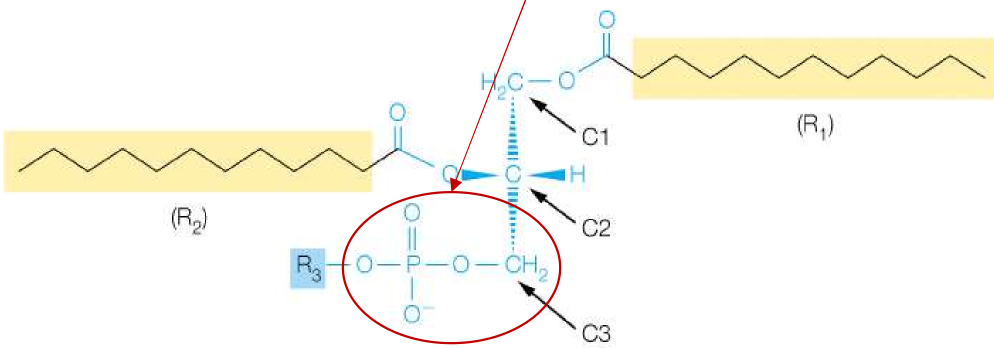
(b) Phospholipids are more cylindrical and pack together to form a bilayer structure.

(c) A computer simulation of a phospholipid bilayer showing approximate boundaries for the hydrophobic core, the interface regions, and the bulk water (above and below the interfacial regions). Water is shown in white and red. The hydrocarbon portions of the bilayer lipids are shown in green and cyan.

FIGURE 10.5 Phospholipids and membrane structure.

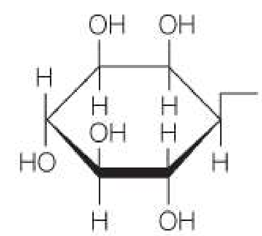
Glycerophospholipids

- are the major class of naturally occurring phospholipids, that is, lipids with phosphate containing head groups



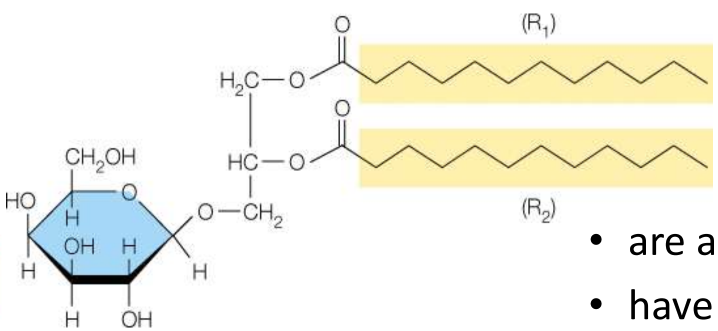
(a) Stereochemical view of a generalized glycerophospholipid.

TABLE 10.3 The hydrophilic groups[a] that distinguish common glycerophospholipids

Name of Glycerophospholipid	R_3 (in Figure 10.6)
Phosphatidic acid	H— (ionized at neutral pH)
Phosphatidylethanolamine (PE)	$H_3\overset{+}{N}—CH_2—CH_2—$
Phosphatidylcholine (PC)	$(CH_3)_3\overset{+}{N}—CH_2—CH_2—$
Phosphatidylserine (PS)	$H_3\overset{+}{N}—C(H)(COO^-)—CH_2—$
Phosphatidyl inositol (PI)	

[a] These are the R_3 groups in Figure 10.6. In addition to this variation, there is also a great deal of variation in the hydrocarbon tails (R_1 and R_2 groups).

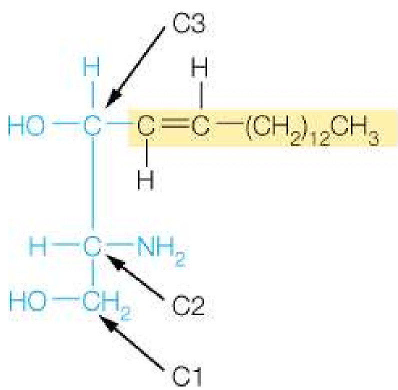
Glycoglycerolipids



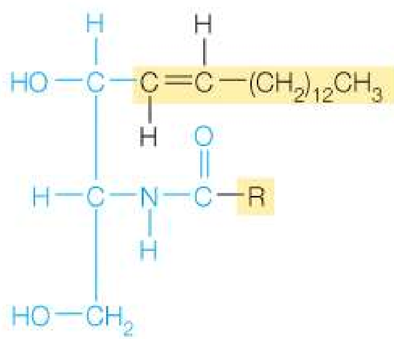
- are a second class of membrane lipids
- have a carbohydrate linked to their head group

Sphingolipids and Glycospingolipids

- are a third class of membrane constituents, in which a fatty acid is linked to the amino alcohol sphingosine via an amide bond

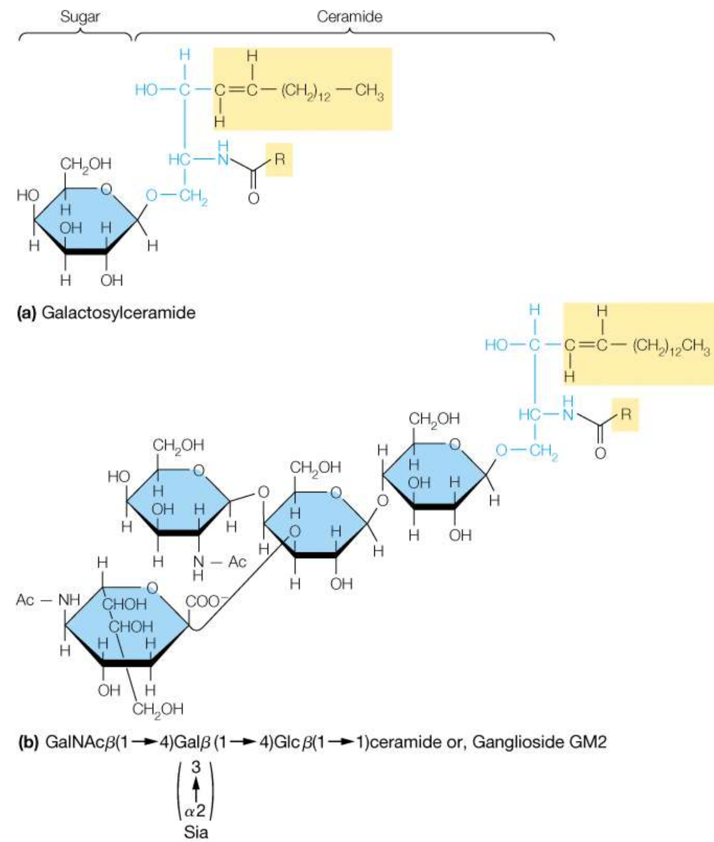


Sphingosine = (2S,3R)-2-aminooctadec-4-ene-1,3-diol



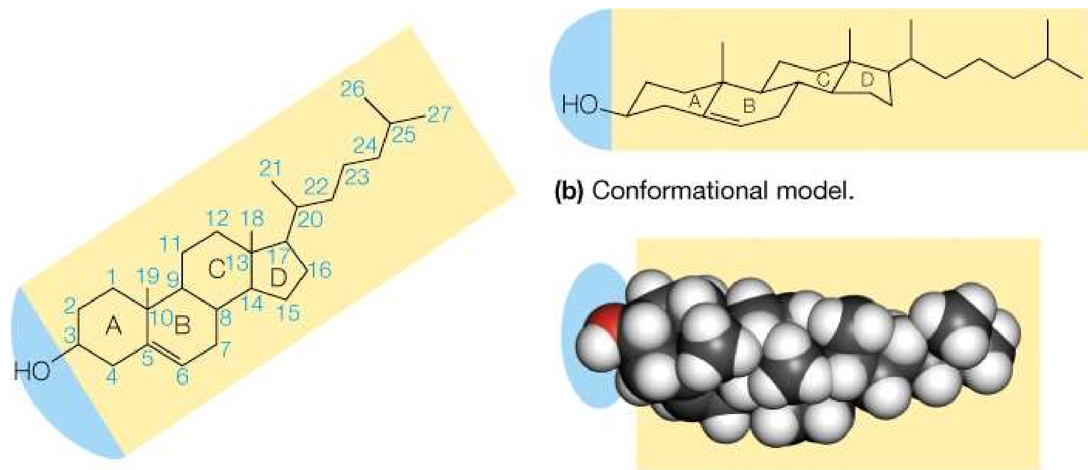
General structure of a ceramide (R = hydrocarbon)

- constitute a fourth class of membrane lipids
- are sphingolipids with sugars attached to their head groups



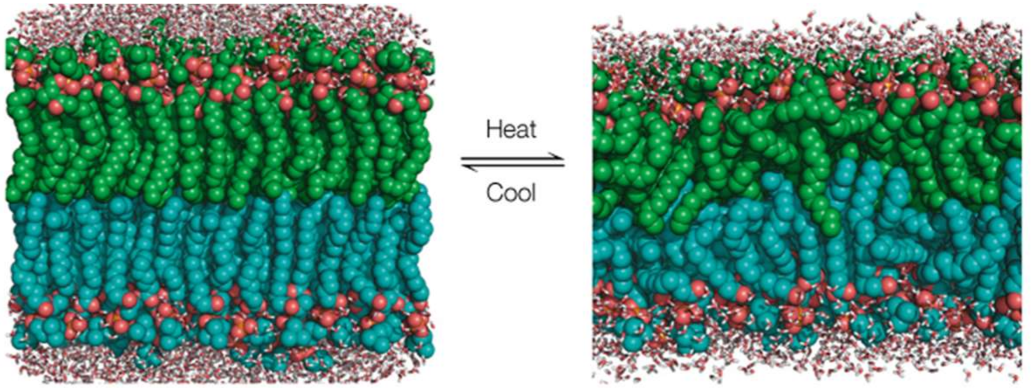
Cholesterol

- are a fifth class of membrane lipids that is based on a tetracyclic hydrocarbon structure and thus is significantly different from the other four classes
- is only weakly amphipathic because of its hydroxyl group
- The bulky, rigid cholesterol structure disrupts regular fatty acid chain packing in membranes
- is the precursor to all steroids
- We make it ourselves!



(a) Structural formula. (b) Conformational model. (c) Space-filling model.

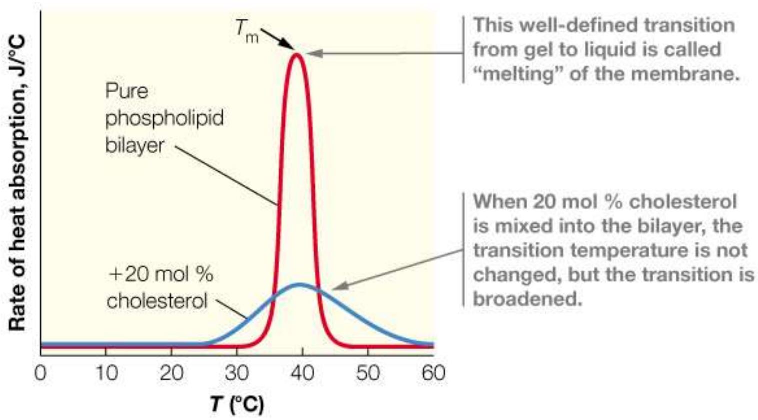
FIGURE 10.8 Cholesterol.



Gel state (below T_m). Hydrocarbon tails are packed together in a highly ordered gel state.

Liquid crystal state (above T_m). Movement of the chains becomes more dynamic, and the interior of the membrane resembles a liquid hydrocarbon.

(a) Transition from gel to liquid crystal states. A computational model of the change in bilayer structure at the transition temperature (T_m). Lipids are shown as green or cyan spheres, and water molecules (above and below the lipid bilayer) are shown as sticks.



(b) Transition with and without cholesterol. Measurement of the heat absorbed by a membrane as they temperature is raised each degree shows a sharp spike at the T_m for a pure dipalmitoylphosphatidylcholine bilayer.

Lipids can melt but are stabilized by cholesterol

- At the melting temperature (T_m) lipids change from the gel state to a liquid crystal state
- This change is quite sharp in the absence of cholesterol.
- When cholesterol is present, the transition is more gentle as suited to biological systems.

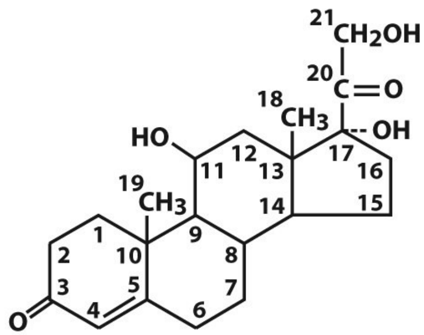
Biological Membranes have different Lipid Compositions

TABLE 10.4 Lipid composition of some biological membranes

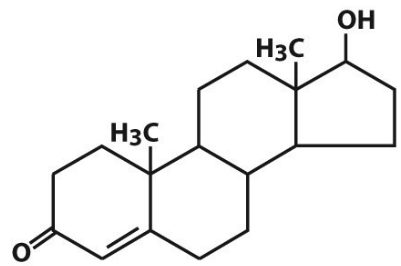
	Percentage of Total Composition in			
Lipid	Human Erythrocyte Plasma Membrane	Human Myelin	Bovine Heart Mitochondria	*E. coli* Cell Membrane
Phosphatidic acid	1.5	0.5	0	0
Phosphatidylcholine	19	10	39	0
Phosphatidylethanolamine	18	20	27	65
Phosphatidylglycerol	0	0	0	18
Phosphatidylinositol	1	1	7	0
Phosphatidylserine	8.0	8.0	0.5	0
Sphingomyelin	17.5	8.5	0	0
Glycolipids	10	26	0	0
Cholesterol	25	26	3	0
Others	0	0	23.5	17

Data from C. Tanford (1973) *The Hydrophobic Effect.* Wiley, New York.

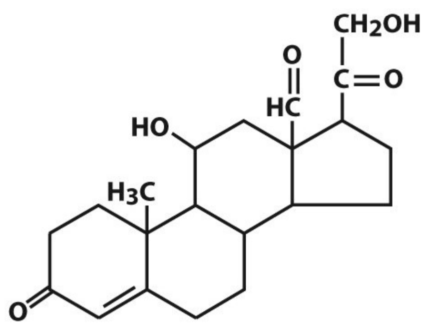
Sterols form Steroid Hormones



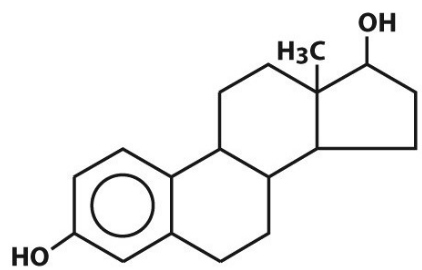
Cortisol (hydrocortisone)
(a glucocorticoid)



Testosterone
(an androgen)



Aldosterone
(a mineralocorticoid)



β-Estradiol
(an estrogen)

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Figure 9-11

Membrane composition

- Membranes consist of both lipid and **proteins**
- Two classes of membrane proteins
  - Integral
    - A section of the protein is embedded within or spans the membrane
    - Important for transporting water, ions and molecules across the membrane and for signalling
  - Peripheral or membrane-anchored
    - Only associates with the polar head groups or has a covalently attached lipid anchor, e.g. fatty acid or other hydrophobic group such as farnesol
    - Can move on the membrane surface ("surfing")

Besides Lipids, there are mainly Proteins in Biological Membranes

TABLE 10.5 Protein, lipid, and carbohydrate content of some membranes

	Percent by Weight		
Membrane	**Protein**	**Lipid**	**Carbohydrate**
Myelin	18	79	3
Human erythrocyte (plasma membrane)	49	43	8
Mitochondria (outer membrane)	52	48	0
Sarcoplasmic reticulum (muscle cells)	67	33	0
Chloroplast lamellae	70	30	0
Gram-positive bacteria	75	25	0
Mitochondria (inner membrane)	76	24	0

Adapted from *Annual Review of Biochemistry* 41:731, G. Guidotti, Membrane proteins.

Membrane structure

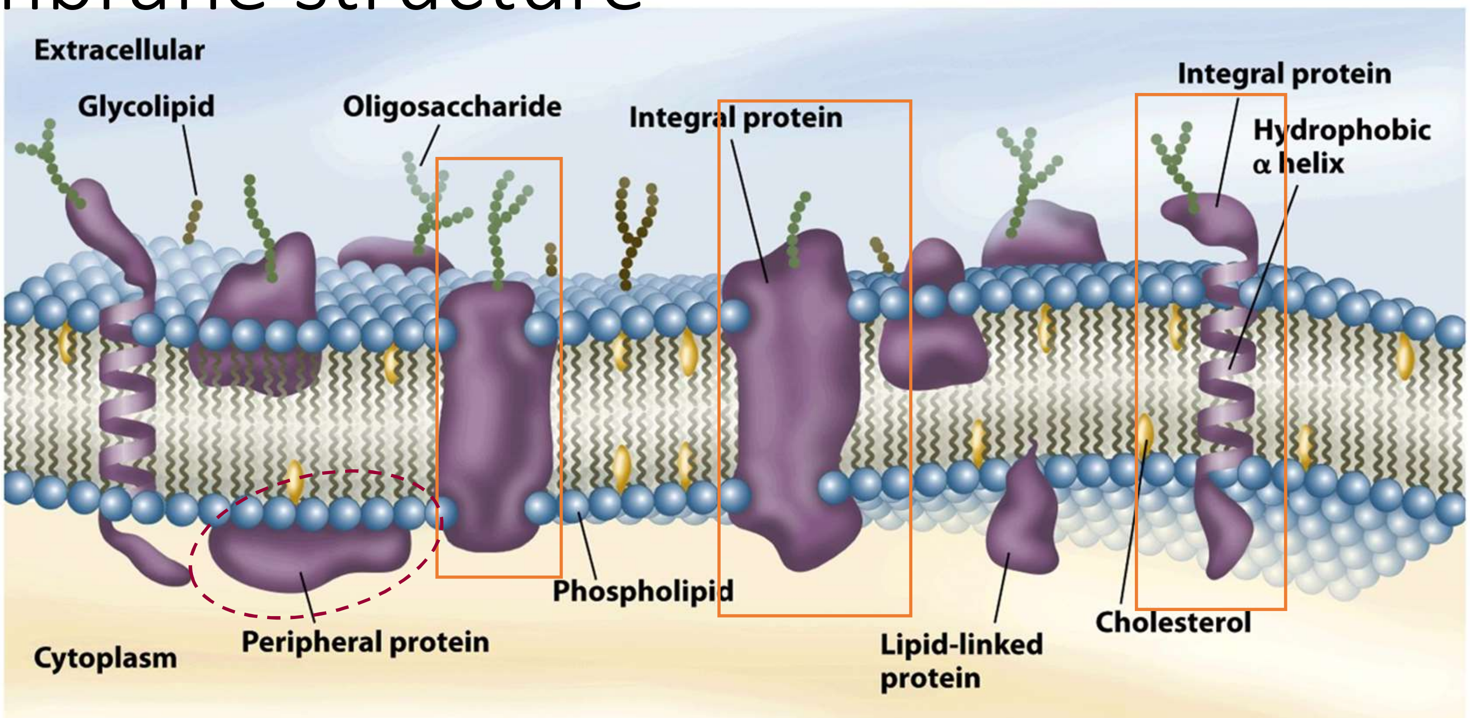
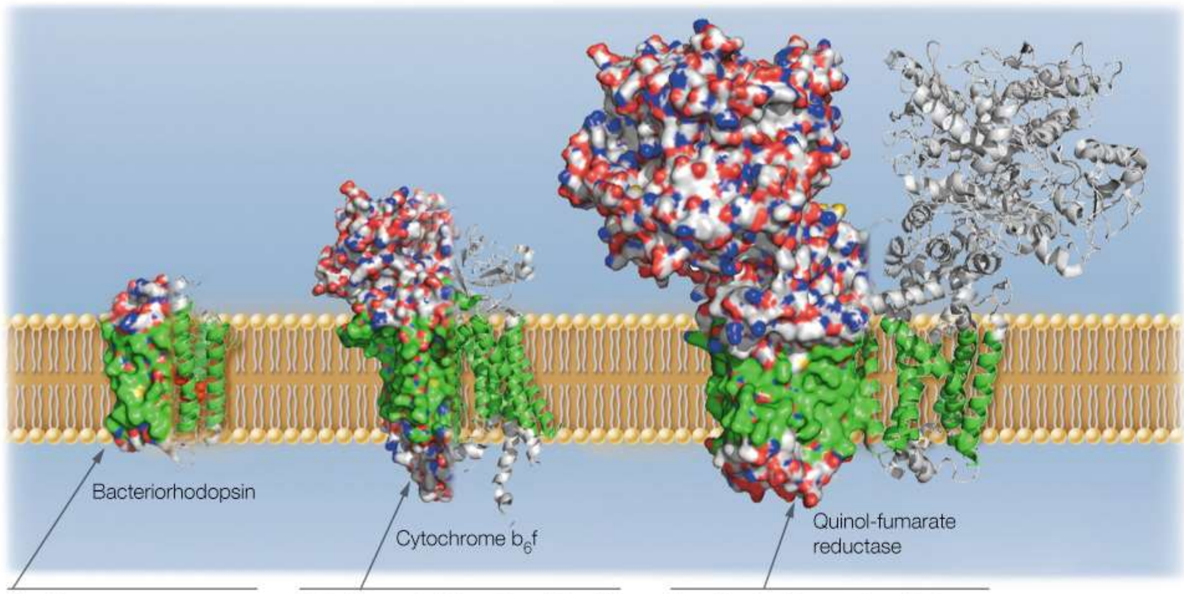


Figure 9-25

Membrane Proteins are mainly integral

Examples of α-helical transmembrane proteins.



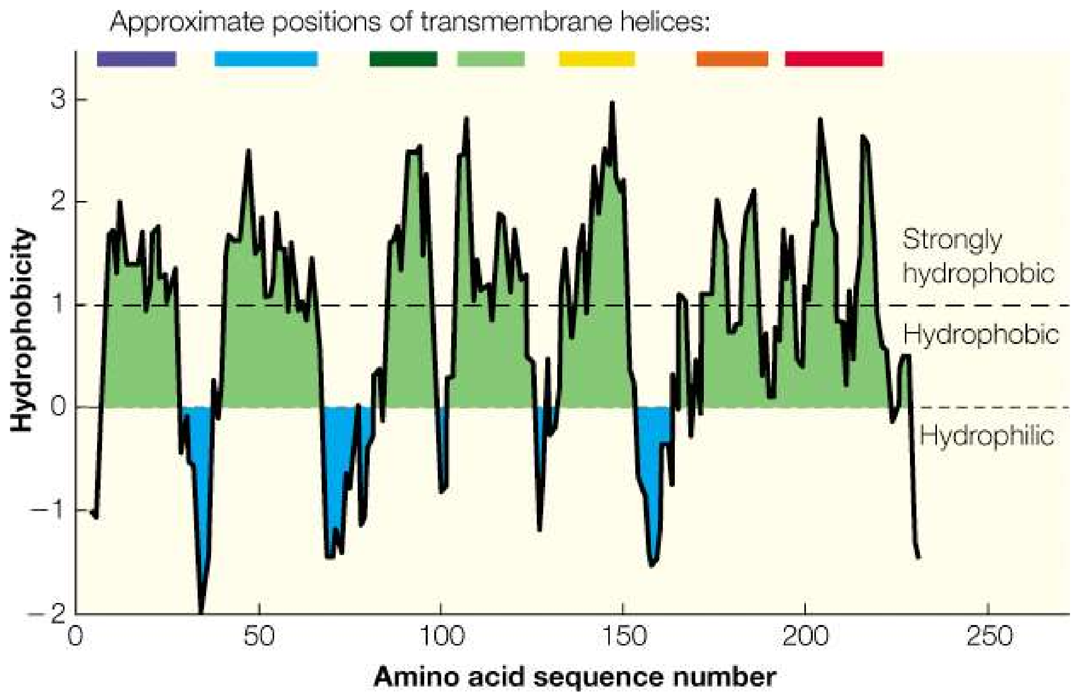
H. salinarum bacteriorhodopsin (PDB ID: 1c3w) is a proton pump in photosynthetic bacteria.

Cytochrome b_6f from *C. reinhardtii* (PDB ID: 1q90) is a photosynthetic proton pump and electron transporter.

E. coli quinol-fumarate reductase (PDB ID: 1l0v) is an electron transport protein that catalyzes the reduction of fumarate to succinate.

Membrane-spanning regions may also be α-helices, embedded in the membrane lipid bilayer (shown in green)

Bacteriorhodopsin is an integral membrane protein with 7 transmembrane (7TM) segments



Amino acid hydrophobicity plot for bacteriorhodopsin, showing that the membrane-spanning helical regions are highly hydrophobic. This pattern of side chain hydrophobicity is typical of membrane-spanning proteins

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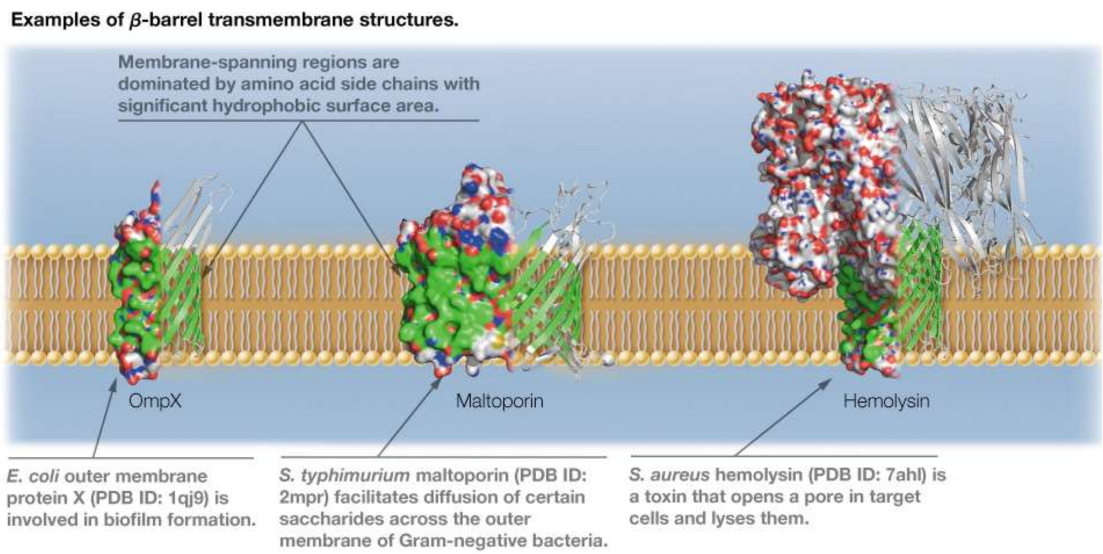
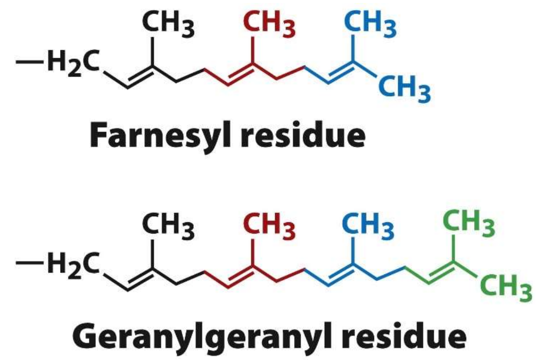
Bacterial Membrane Proteins



Membrane-spanning regions may be β-barrels. The intermembrane region of membrane proteins presents apolar amino acids (shown in green) toward the fatty acyl tails of phospholipids

Lipid Modifications Link Proteins to Bilayer

1. Short HC extensions



2. Long GPI "anchor"

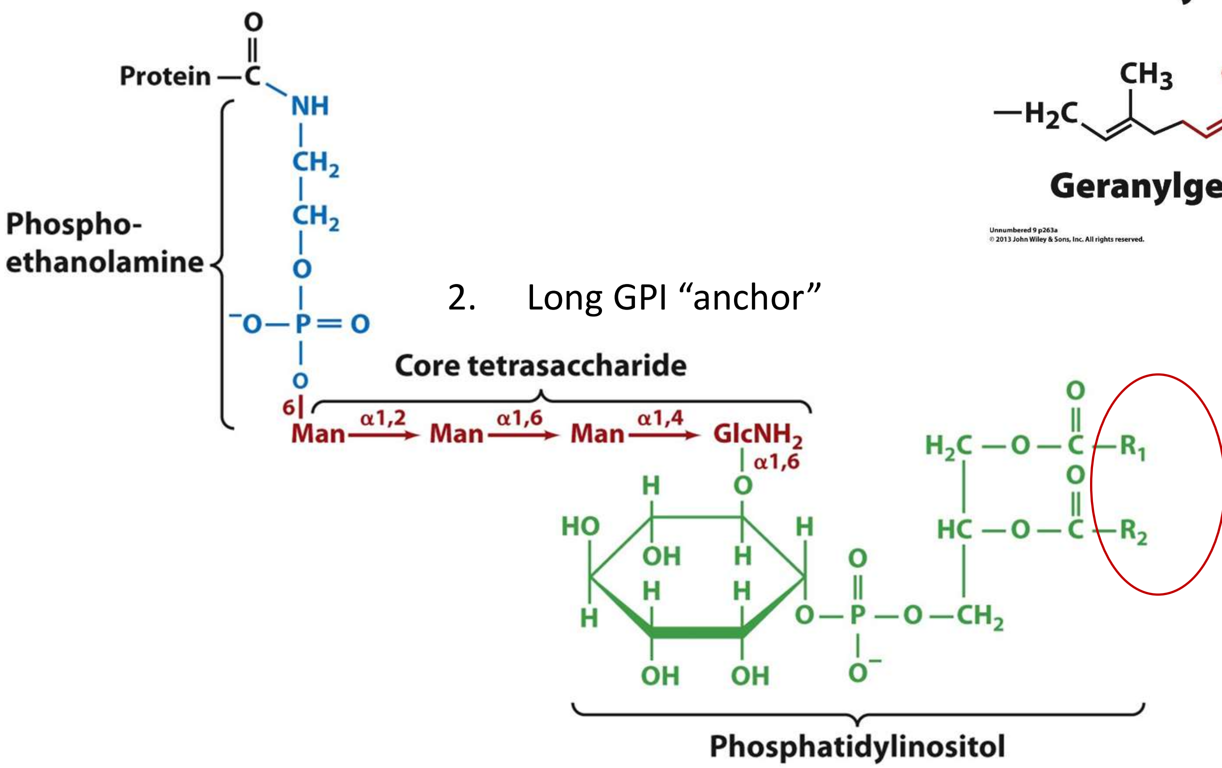


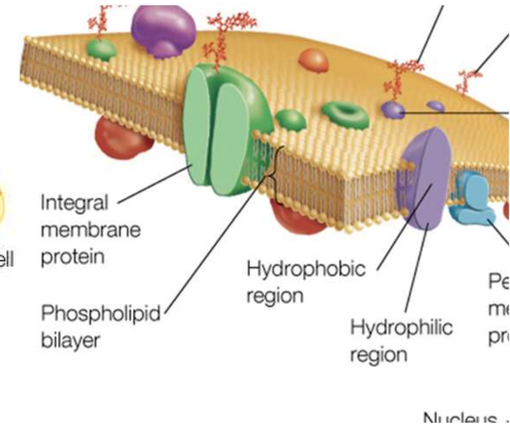
Figure 9-24

Membrane Proteins

- Unlike lipids, membrane proteins have a fixed orientation.
- Integral membrane proteins contain a transmembrane structure consisting of α helices or a β barrel with a hydrophobic surface.
- Peripheral membrane proteins interact non-covalently with proteins or lipids at the membrane surface.
- Lipid-linked proteins have a covalently attached hydrocarbon, fatty acid, or glycosylphosphatidylinositol (GPI-) group.

Membrane Structure
- the Fluid Mosaic Model

- Biological membranes consist of lipid bilayers, in which membrane proteins are embedded
- Biological membranes can be considered as oriented two-dimensional liquids, in which lipids and proteins diffuse more or less freely within their plane (fluid mosaic model)
- However, biological membranes also contain some defined structures or domains, such as protein complexes or lipid rafts



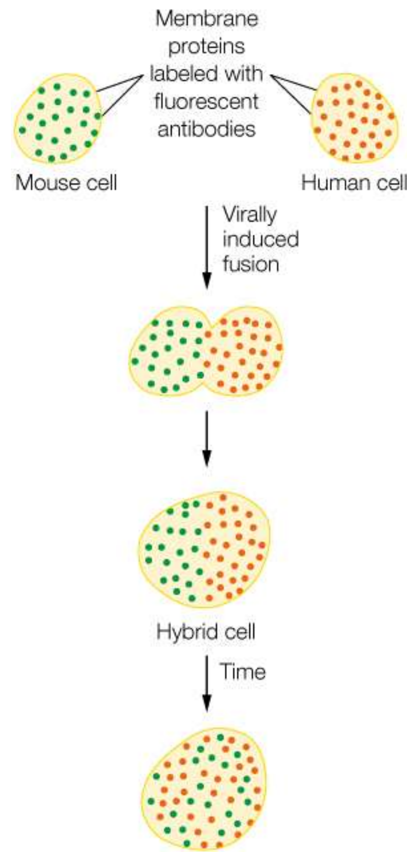
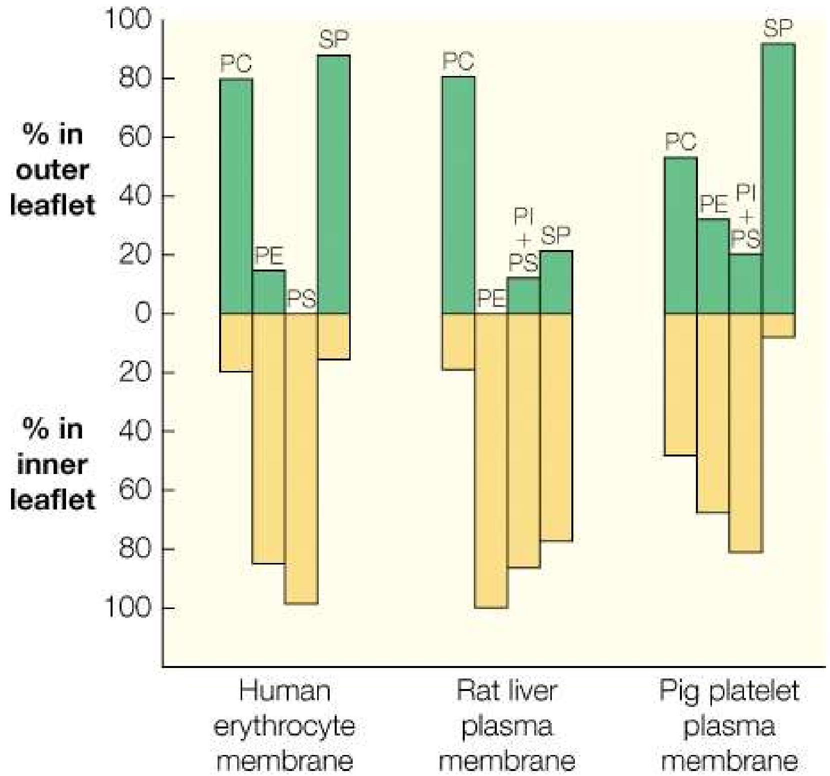


FIGURE 10.10 Experimental demonstration of membrane fluidity.

Membrane Lipid Structure is Asymmetrical



Distribution of the major membrane phospholipids in the inner and outer leaflets of selected membranes

PC: phosphatidylcholine

PE: phosphatidylethanolamine

PS: phosphatidylserine

PI: phosphatidylinositol

SP: sphingomyelin

Membrane Structure Summary

- Biological membranes are asymmetrical
- The lipid and protein content on one side is generally different from that on the other side of the bilayer
- Proteins are oriented in the membrane in a specific way
  - This is very important for protein function e.g. receptors, transporters and enzymes

Biological roles of membranes

1. Form boundaries against infectious agents and toxins
   - around cells (Plasma Membrane)
   - around distinct sub-cellular compartments (e.g. Nucleus, Mitochondria, Lysosomes, Golgi bodies)
2. Compartmentalise and segregate intracellular events, and separate cells from one another
3. Mediate regulation of cellular functions by:
   - allowing inside environment of cells or organelles to differ from outside
   - controlling the transport of substances in and out of the cell
4. Involved in signalling processes:
   - contain specific receptors for external chemical stimuli
   - generate chemical and electrical signals
5. Specific enzyme systems are localized on membranes

Membrane Properties Summary

- Lipids in membrane bilayers are capable of diffusing **within** the layer and **across** layers
- Membranes “melt” with changes in temperatures – stabilized by cholesterol