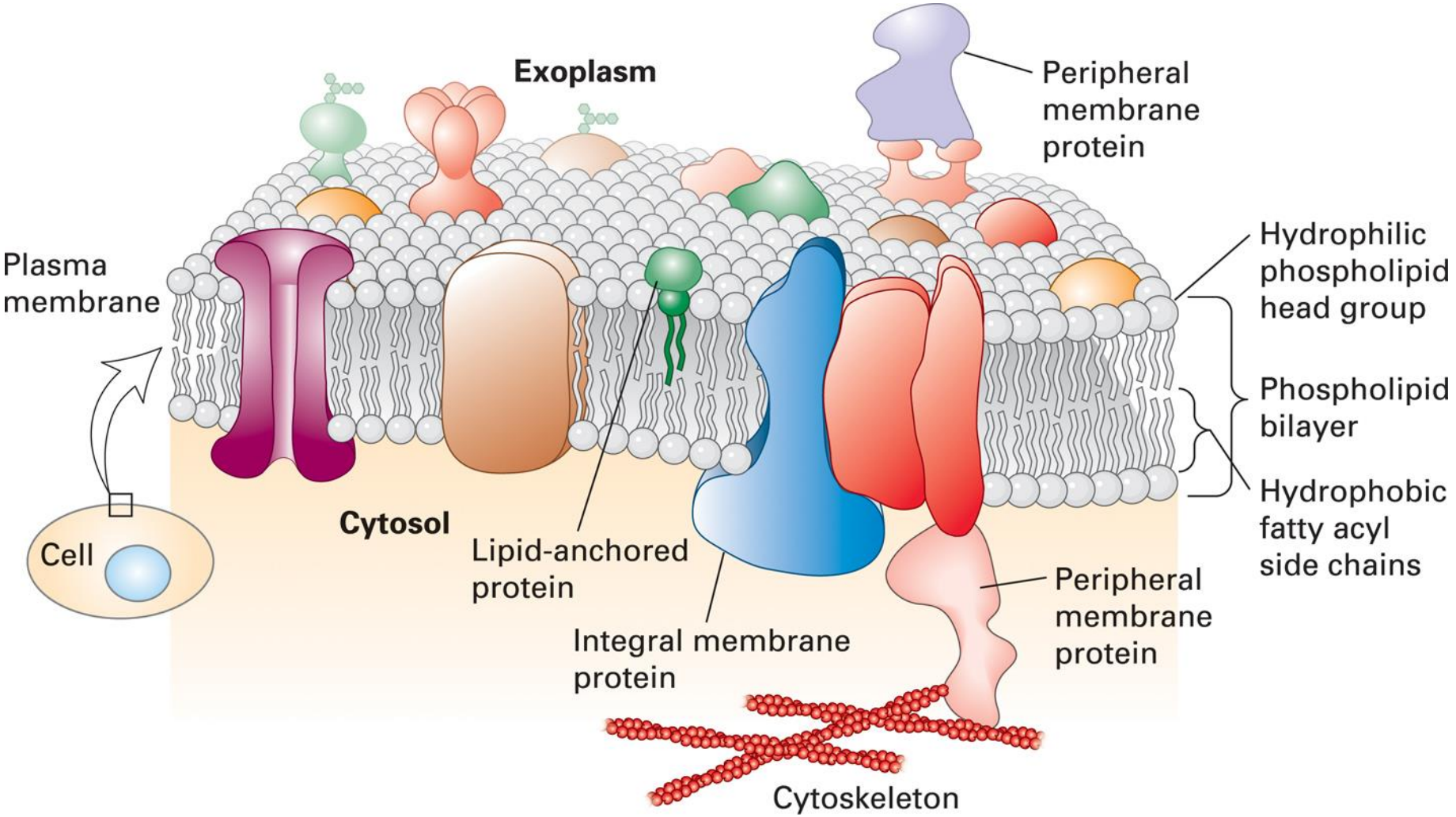
FLUID MOSAIC MODEL OF BIOMEMBRANES



MEMBRANE BILAYER

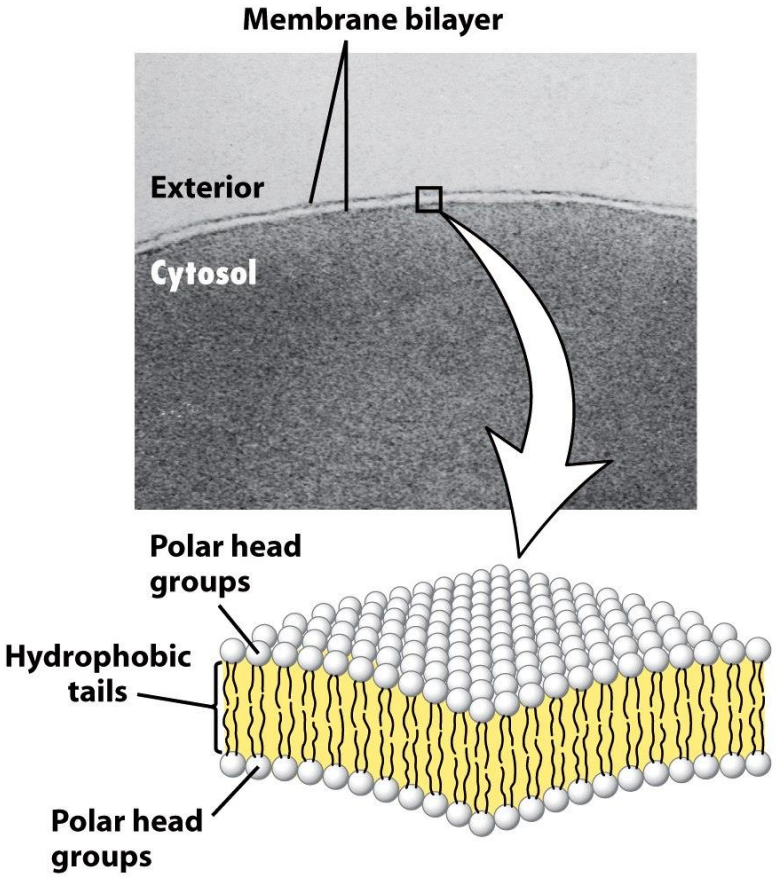
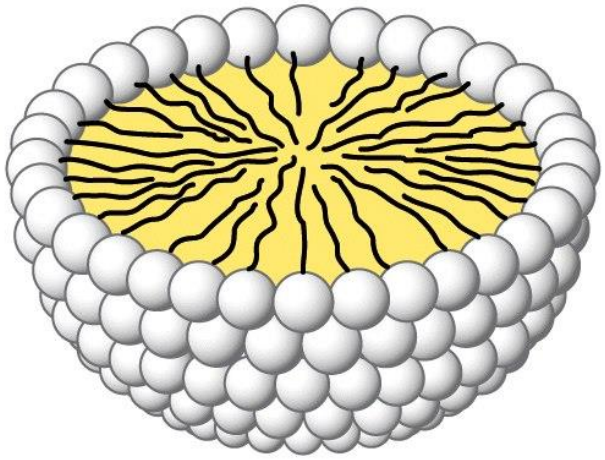


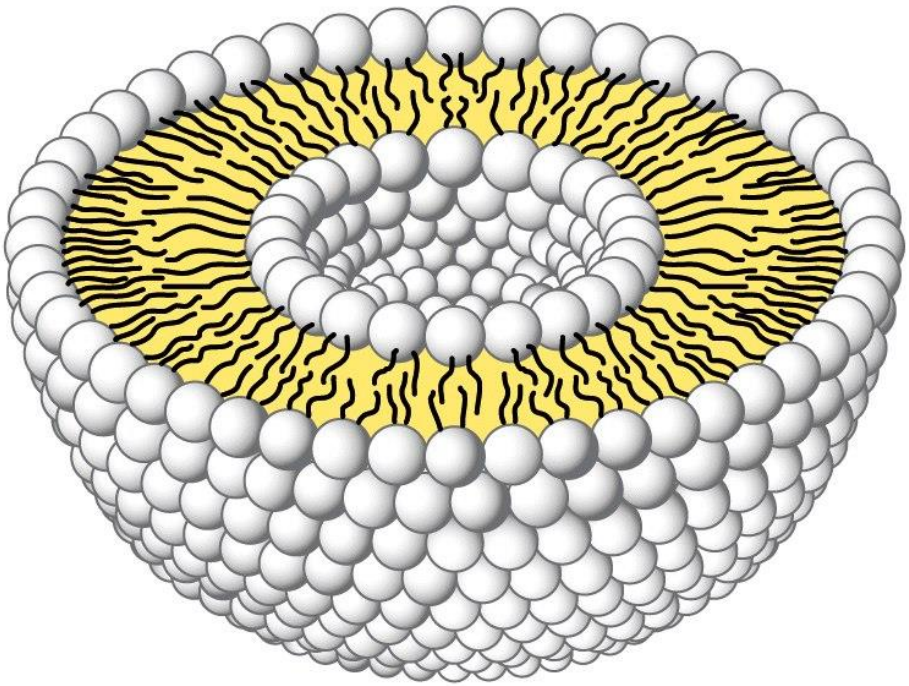
Figure 10-6ab
Molecular Cell Biology, Sixth Edition

Phospholipids are very amphipathic molecules They have a hydrophobic and a hydrophilic region. When phospholipids are mechanically dispersed in solution, they form one of three structures - micelles, liposomes and phospholipid bilayers.

BILAYER STRUCTURE OF BIOMEMBRANES



Micelle



Liposome

Figure 10-6c
Molecular Cell Biology, Sixth Edition

Liposomes are used in drug delivery.
Remember – core is hydrophilic

FORMATION OF PURE PHOSPHOLIPID BILAYERS

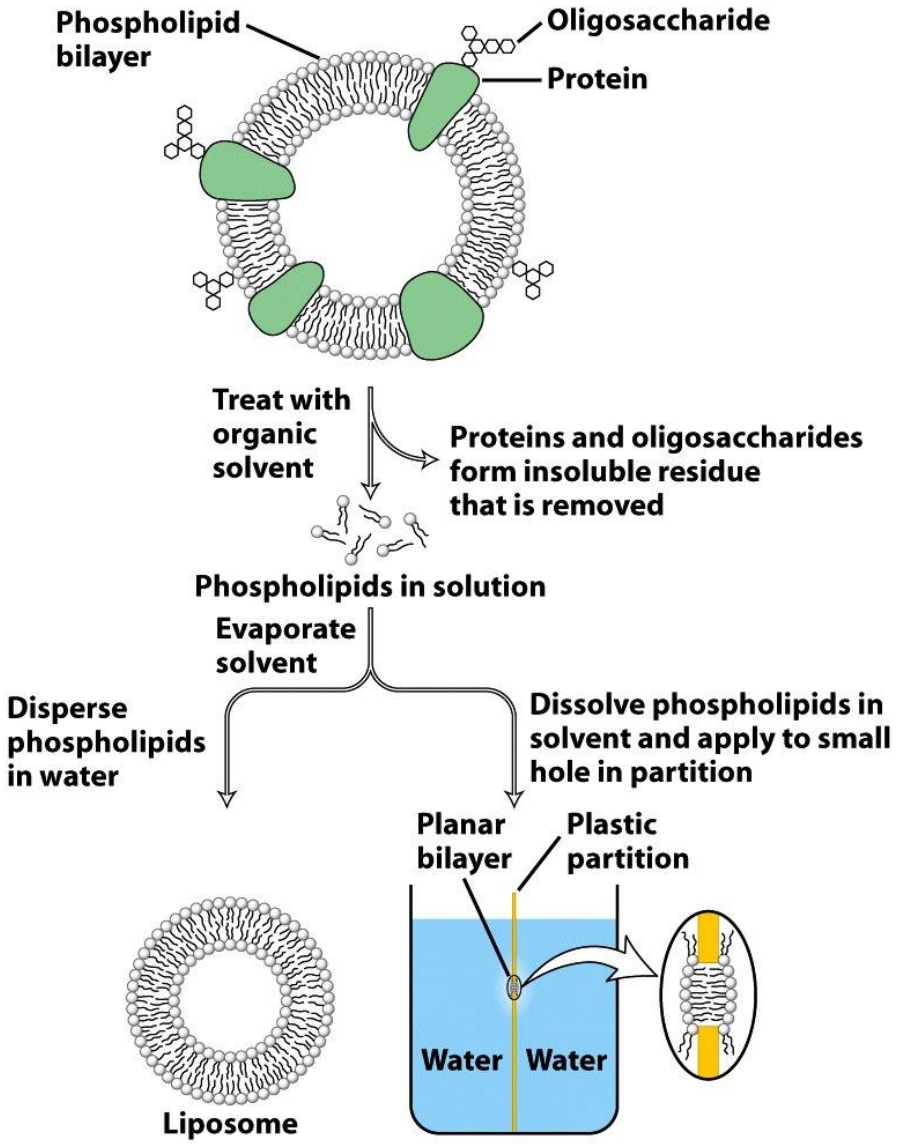


Figure 10-7
Molecular Cell Biology, Sixth Edition

LIPID CLASSIFICATION

Three classes of Membrane lipids:

- PHOSPHOGLYCERIDES
- SPHINGOLIPIDS
- STEROIDS

PHOSPHOGLYCERIDES

Phosphoglycerides are derivatives of glycerol 3-phosphate.

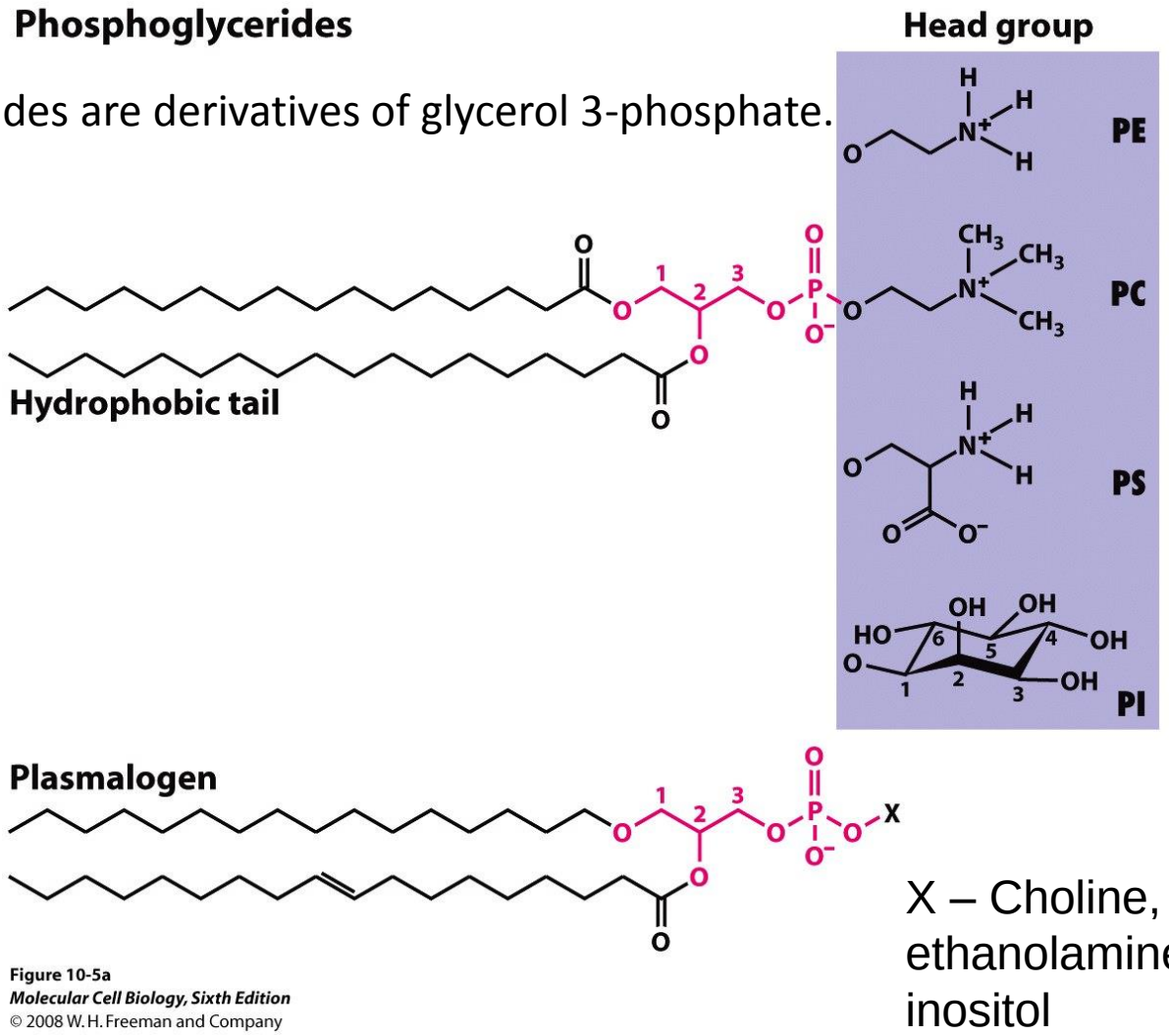


Figure 10-5a
Molecular Cell Biology, Sixth Edition

Phosphatidyl ethanolamine

Phosphatidyl choline

Phosphatidyl serine

Phosphatidyl inositol

X – Choline, ethanolamine, serine or inositol

The amount of plasmalogens is high in brain and heart tissue

SPHINGOLIPIDS

These are derived from sphingosine, an amino alcohol with a long hydrocarbon chain. Glycolipids most abundant in nervous tissue.

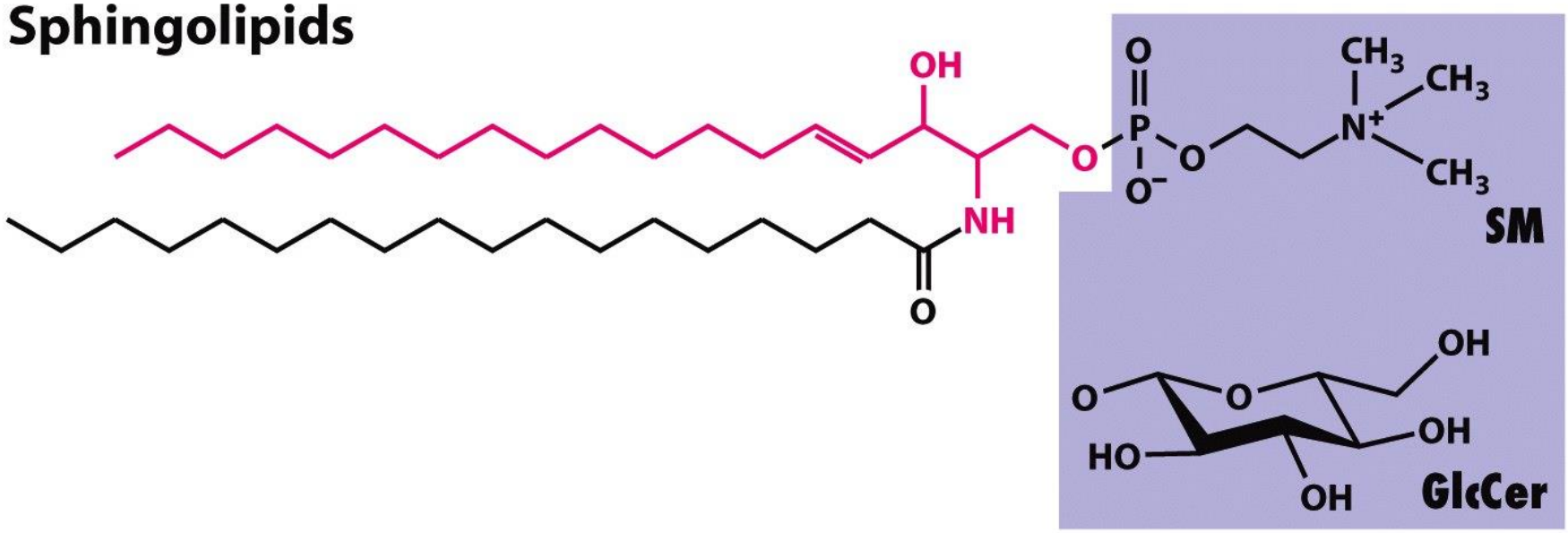


Figure 10-5b
Molecular Cell Biology, Sixth Edition

STEROIDS

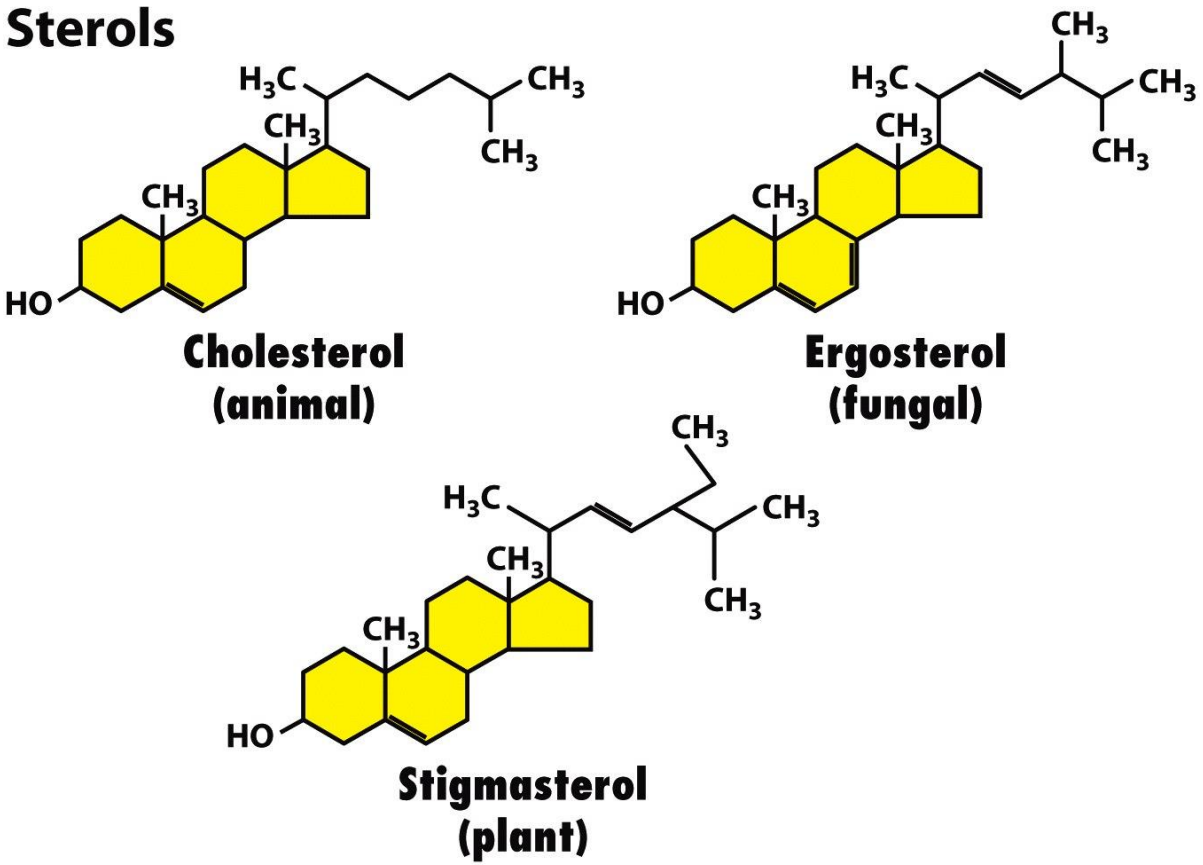


Figure 10-5c
Molecular Cell Biology, Sixth Edition

Cholesterol is a precursor for bile acids, steroid hormones and Vitamin D(produced in the skin and kidneys).

PROPERTIES OF MEMBRANES

- HYDROPHOBIC CORE IS AN IMPERMEABLE BARRIER
- STABILITY – Vander Waals interaction, and hydrophobic interaction stabilize the fatty acyl groups whereas ionic and hydrogen bonds stabilize the polar head groups
- PHOSPHOLIPID BILAYERS SPONTANEOUSLY FORM CLOSED SEALED COMPARTMENTS

MEMBRANE BUDDING AND FUSION

Faces of cellular membranes are conserved

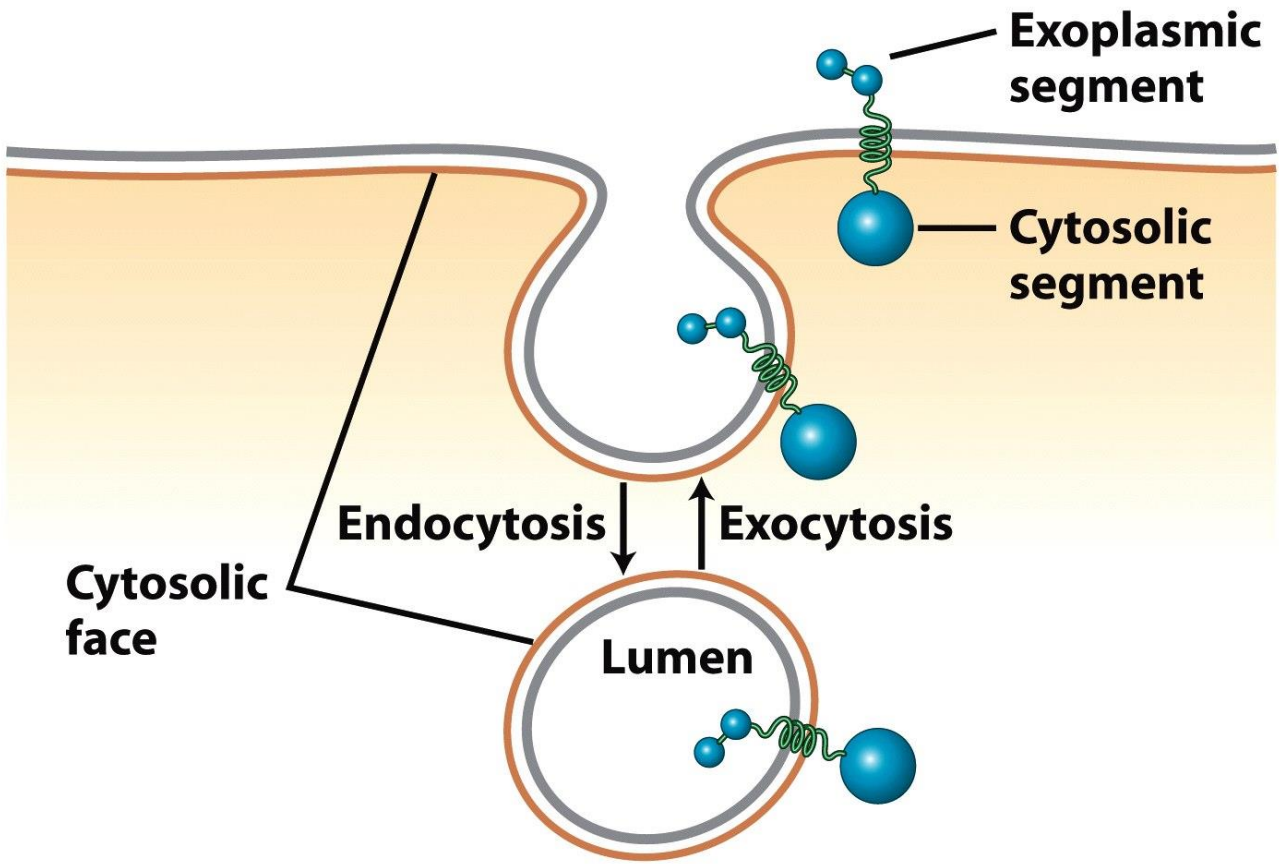


Figure 10-9
Molecular Cell Biology, Sixth Edition

CYTOSOLIC AND EXOPLASMIC FACES ARE CONSERVED

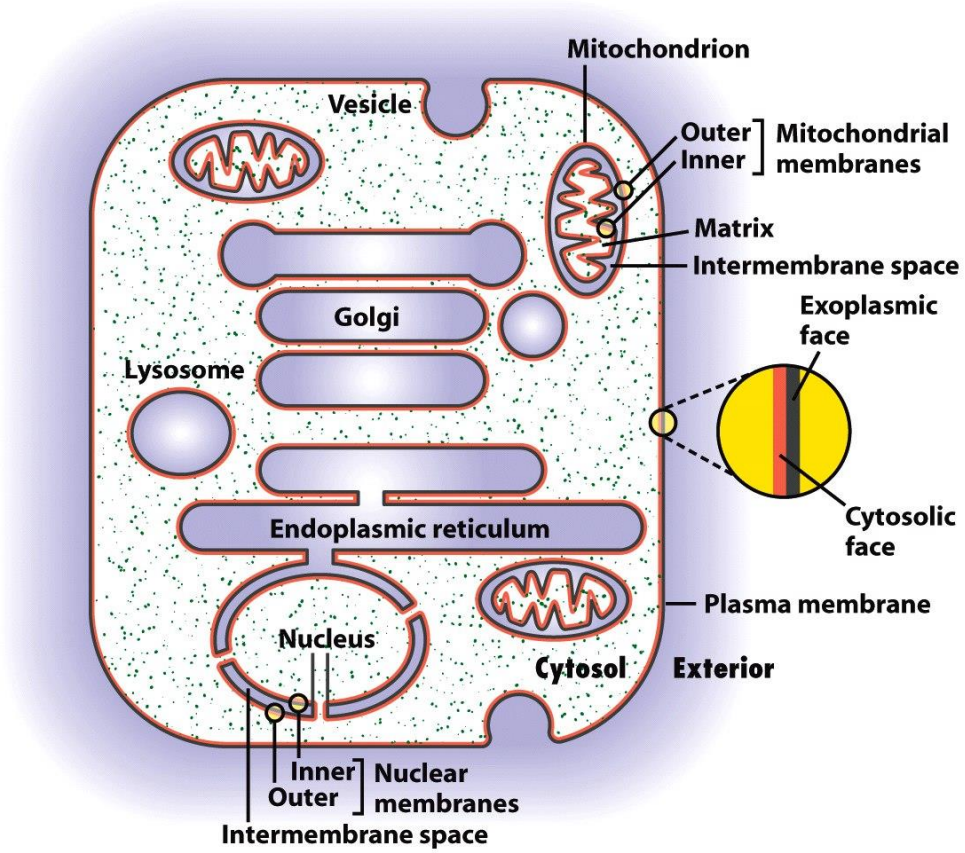


Figure 10-8
Molecular Cell Biology, Sixth Edition

LIPID COMPOSITION IN THE EXOPLASMIC AND CYTOSOLIC FACES OF THE MEMBRANES

ER – Phospholipid synthesis

Golgi - Sphingolipids are synthesized

TABLE 10-1 Major Lipid Components of Selected Biomembranes

	COMPOSITION (MOL %)			
SOURCE/LOCATION	PC	PE + PS	SM	CHOLESTEROL
Plasma membrane (human erythrocytes)	21	29	21	26
Myelin membrane (human neurons)	16	37	13	34
Plasma membrane (*E. coli*)	0	85	0	0
Endoplasmic reticulum membrane (rat)	54	26	5	7
Golgi membrane (rat)	45	20	13	13
Inner mitochondrial membrane (rat)	45	45	2	7
Outer mitochondrial membrane (rat)	34	46	2	11
Primary leaflet location	Exoplasmic	Cytosolic	Exoplasmic	Both

PC = phosphatidylcholine; PE = phosphatidylethanolamine; PS = phosphatidylserine; SM = sphingomyelin.
SOURCE: W. Dowhan and M. Bogdanov, 2002, in D. E. Vance and J. E. Vance, eds., *Biochemistry of Lipids, Lipoproteins, and Membranes*, Elsevier.

Table 10-1
Molecular Cell Biology, Sixth Edition

Lipid composition is different in the two leaflets

- Phosphatidyl choline and sphigomyelin form less fluid layers and are found in the exoplasmic leaflet
- PE, PS and PI which form more fluid bilayers are located in the cytosolic leaflet.
- Cholesterol is evenly distributed in both leaflets
- Asymmetric distribution occurs is not clear
- Enzymes called flipases powered by ATP
- Lipid rafts – more ordered less fluid bilayers that contain cholesterol and sphingomyelin. Lipid rafts are microdomains surrounded by the more fluid phosphoglycerides. These are about 50nm in diameter.

Membrane fluidity

Membrane fluidity depends on:

- Lipid composition
- Structure of the hydrophobic tails – saturated fatty acids aggregate forming a gel-like state whereas short fatty acyl chains and cis-unsaturated fatty acyl chains result in less stable interactions and hence have more fluidity
- Temperature

- Cholesterol content can decrease membrane fluidity – interaction of the steroid ring with the long hydrophobic tails tends to immoblize these lipids (refer to Lipid rafts in previous slide). On the other hand at lower concentrations, the steroid ring separates and causes the inner region of the phospholipid to become more fluid

- Cholesterol increases membrane thickness in phosphoglyceride bilayers but not in sphingomyelin bilayers.

HOW LIPIDS AFFECT CURVATURE AND BILAYER THICKNESS OF MEMBRANES

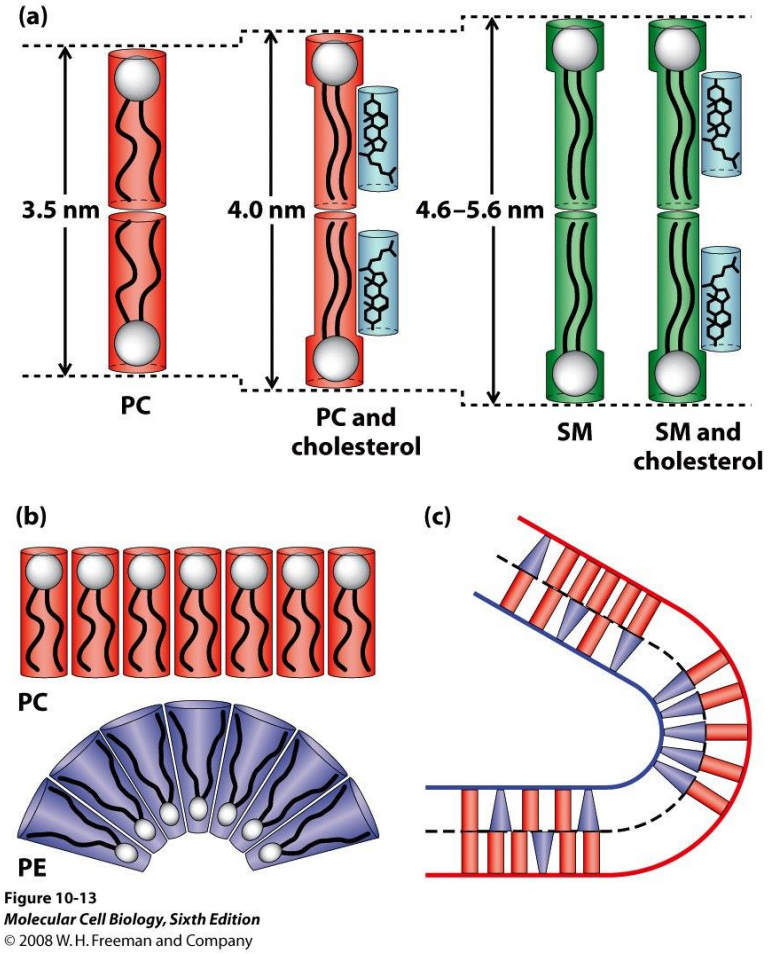


Figure 10-13
Molecular Cell Biology, Sixth Edition

PHOSPHOLIPID BILAYER- lateral and rotational movement

A typical lipid molecule exchanges places about 10^7 times per second and also diffuses several micrometes per second at 37°C.

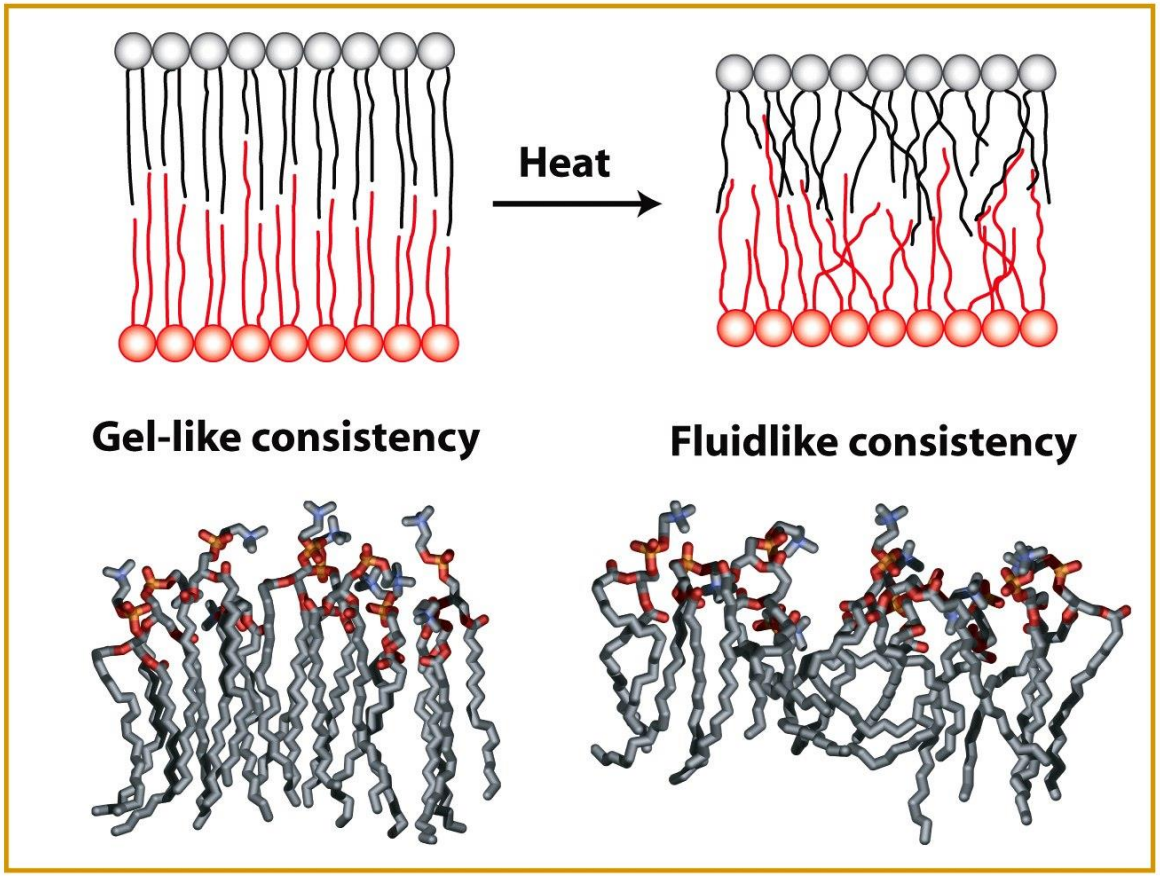


Figure 10-11
Molecular Cell Biology, Sixth Edition

Phase transition from a gel-like to a fluid-like consistency.

LIPID DROPLETS FORMATION

Stores excess lipids

Also known to store proteins targeted for degradation

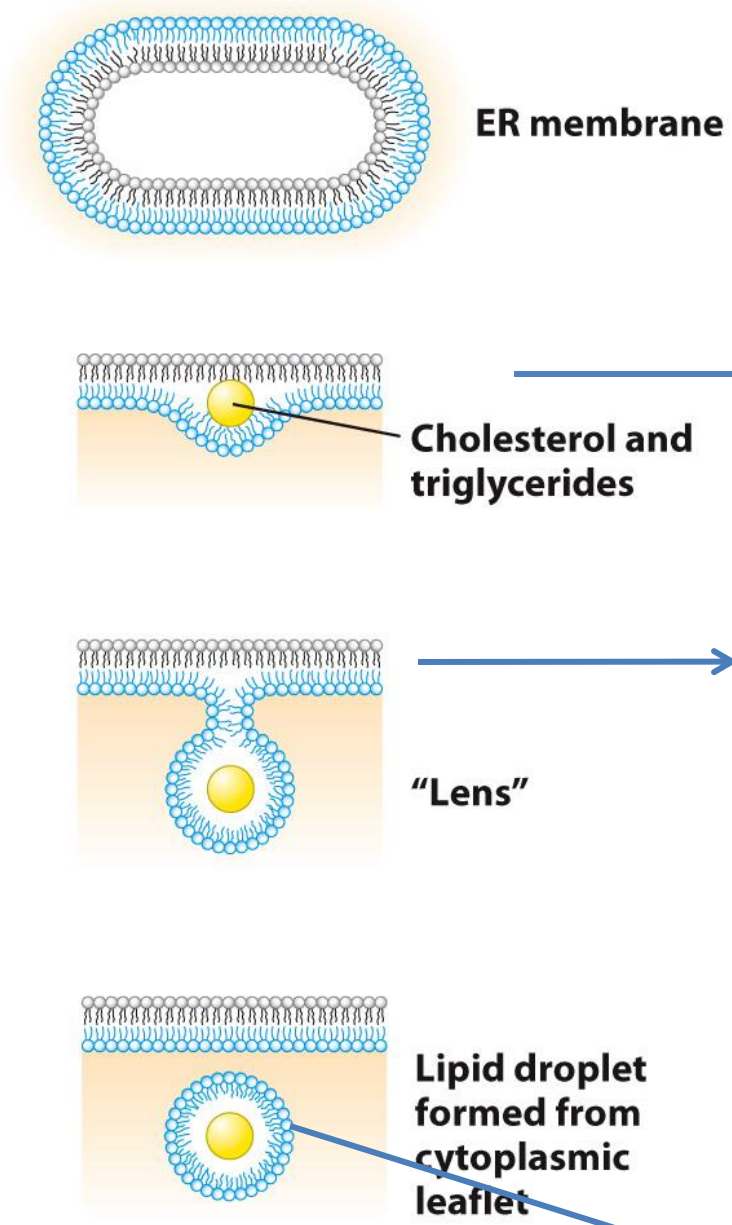


Figure 7-13
Molecular Cell Biology, Eighth Edition

FRAP EXPERIMENTS

To detect the lateral movement of proteins and lipids within the plasma membranes

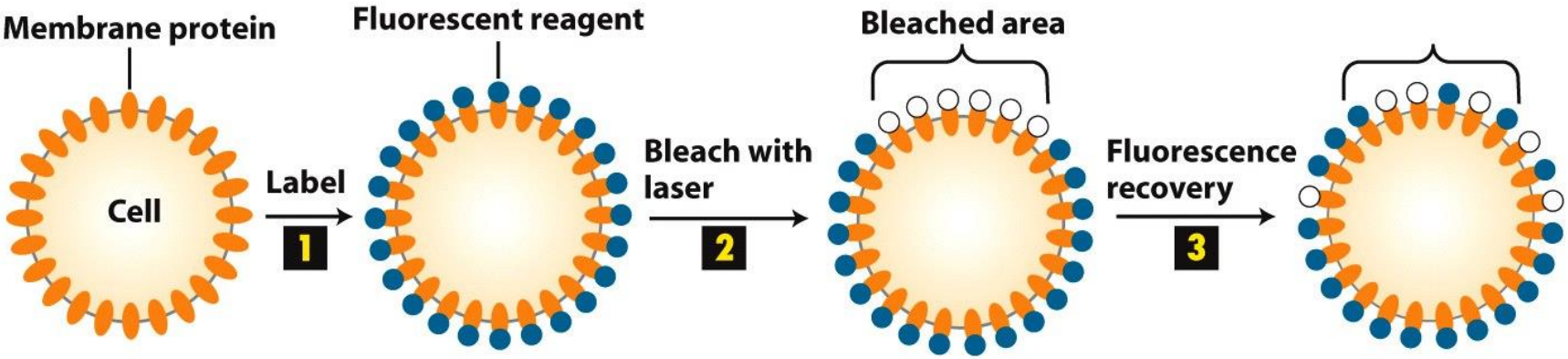


Figure 10-12a
Molecular Cell Biology, Sixth Edition

FRAP EXPERIMENT (cont'd)

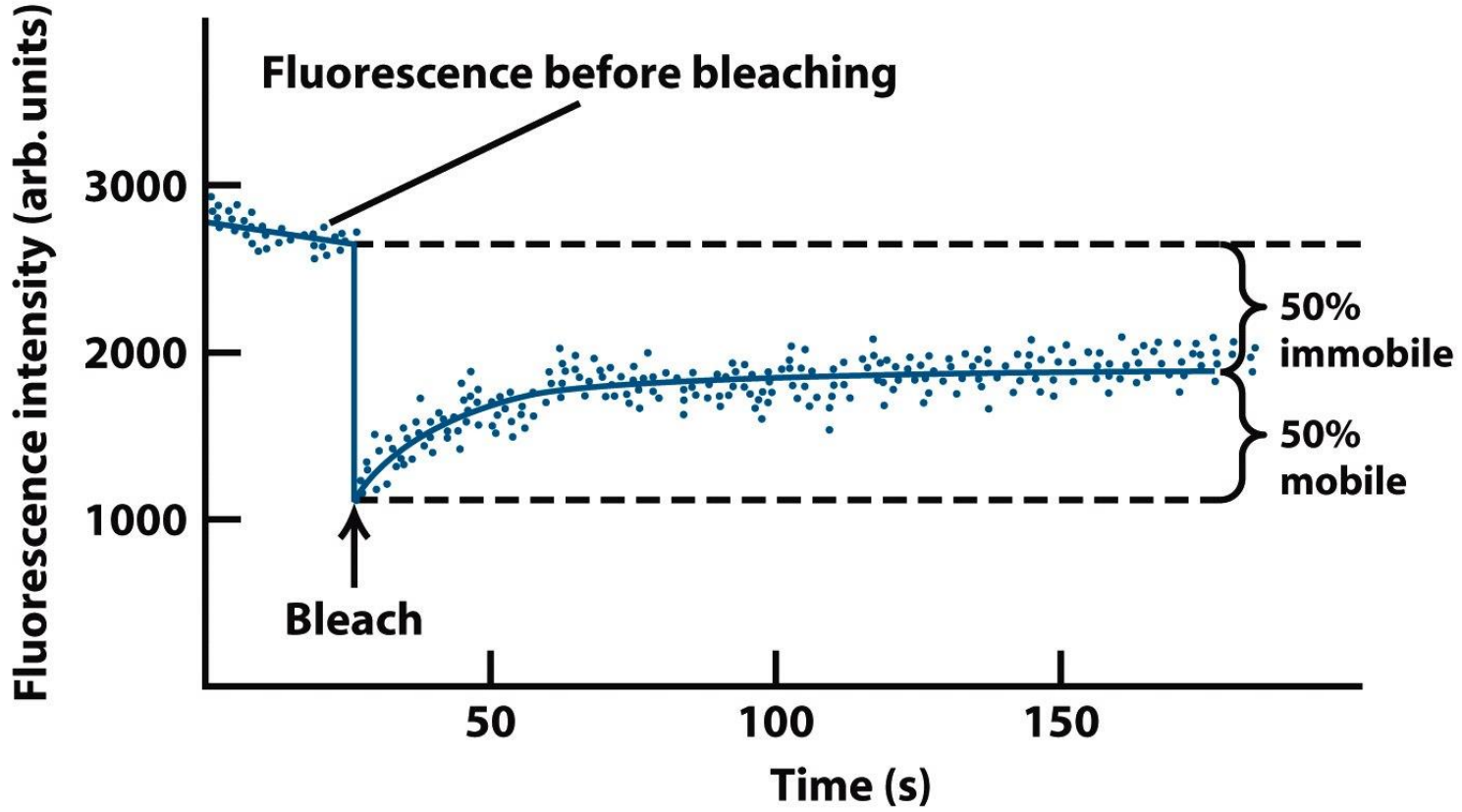


Figure 10-12b
Molecular Cell Biology, Sixth Edition

MEMBRANE PROTEINS

- INTEGRAL or TRANS – MEMBRANE PROTEINS
- LIPID-ANCHORED MEMBRANE PROTEINS
- PERIPHERAL MEMBRANE PROTEINS

Integral membrane proteins

- Contain membrane spanning α- helices
- 20-25 hydrophobic uncharged amino acids (3.75 nm)
- Segment is perpendicular to the membrane or is at an oblique angle
- Hydrophilic amide peptide bonds in the interior of the α-helix
- Hydrophobic side chains interact with fatty acyl groups by hydrophobic and van derWaals interaction
- Ionic interactions between the hydrophilic amino acids and the phospholipid polar head groups

GLYCOPHORIN A – single pass integral membrane protein

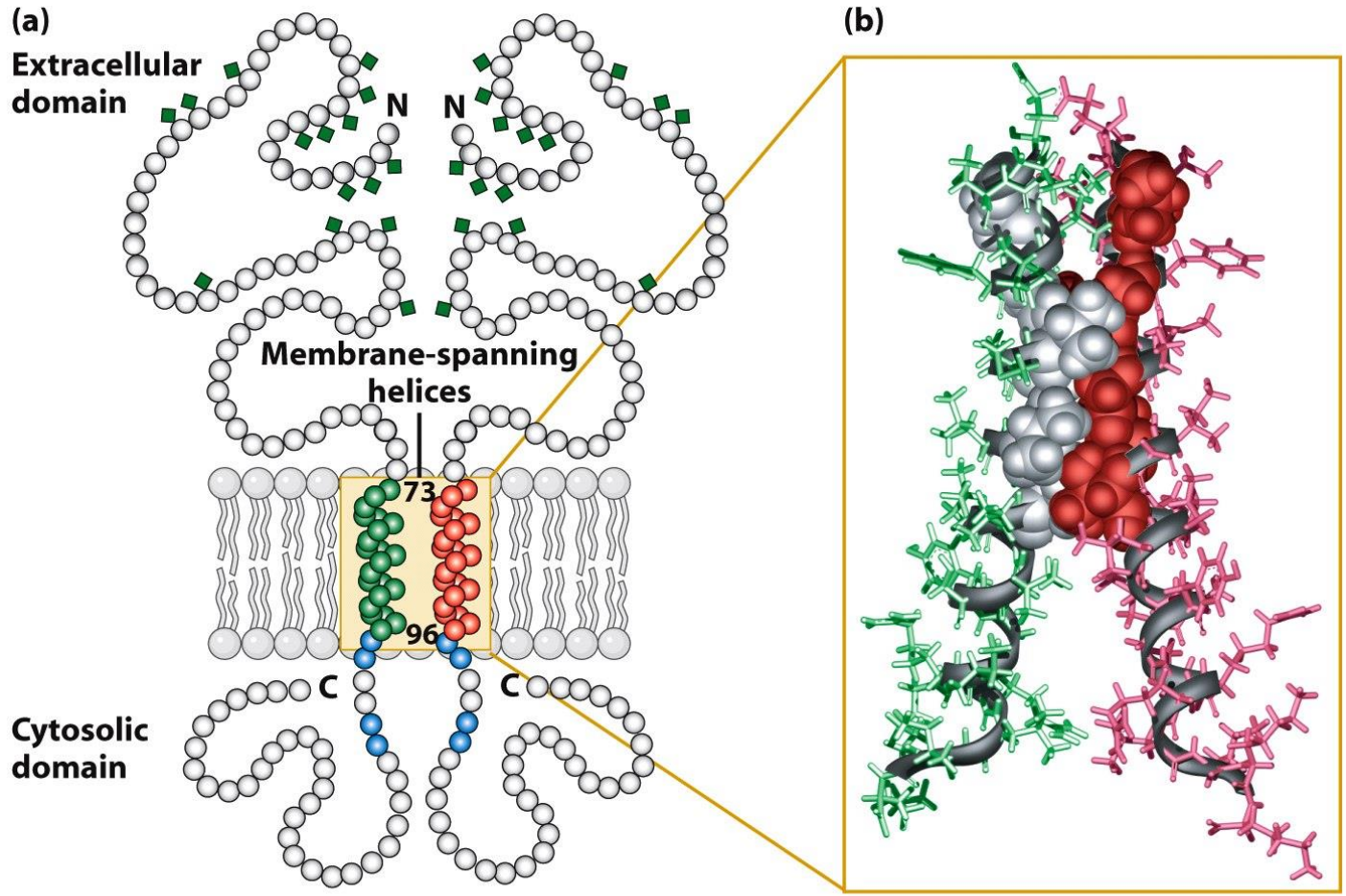


Figure 10-15
Molecular Cell Biology, Sixth Edition

Multipass Transmembrane Protein

(a) Rhodopsin – Bacterial protein has 7 membrane spanning helices

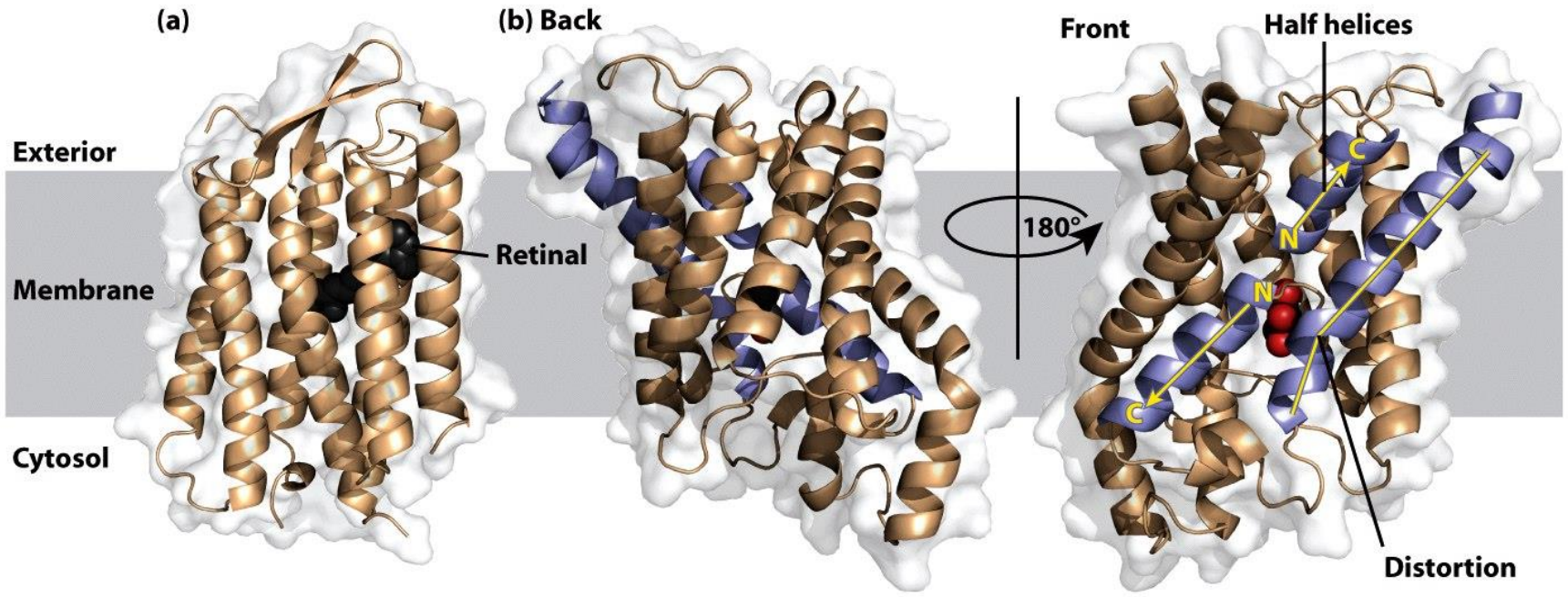


Figure 10-16
Molecular Cell Biology, Sixth Edition

(b) – Glycerol channel protein, Glpf belongs to the aquaporin family

The channel is lined by side groups of hydrophilic amino acids present in the alpha helix

Multiple membrane spanning β strands

- Porins
- Found in the outer membrane of Gram-negative bacteria, outer membrane of mitochondria and chloroplasts
- Porins provide channels for the movement of disaccharides, water-soluble molecules and ions
- Trimers of identical subunits
- Each subunit – 16 beta strands that twist to form a barrel-shaped structure
- Barrel - Hydrophilic interior and hydrophobic exterior

Single subunit of outer membrane Porin from E.coli

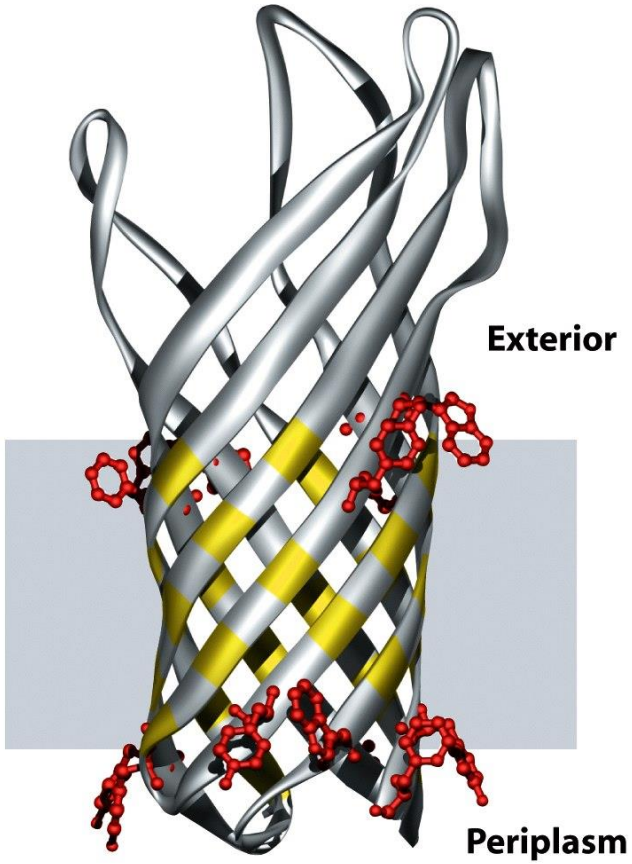


Figure 10-18
Molecular Cell Biology, Sixth Edition

LIPID-ANCHORED PROTEINS

Cytosolic anchors are different from exoplasmic anchors

Cytosolic anchors:

Acylation - Fatty acyl groups (myristate or palmitate) attached to the glycine residue in the N-terminus example: v-src

Prenylation – Hydrocarbon chains attached to a cysteine residue near the C-terminus. These hydrocarbon chains are made from 5-carbon isoprene units. These are 15-carbon farnesyl or 20-carbon geranylgeranyl.

In some case a second geranylgeranyl group or plamitate is attached to a second cysteine example: Ras

Exoplasmic anchors:

GPI anchors (Glycosylphosphatidyl inositol): Red- phosphatidyl Inositol

Purple – phosphoethanolamine

Grenn – sugar residues

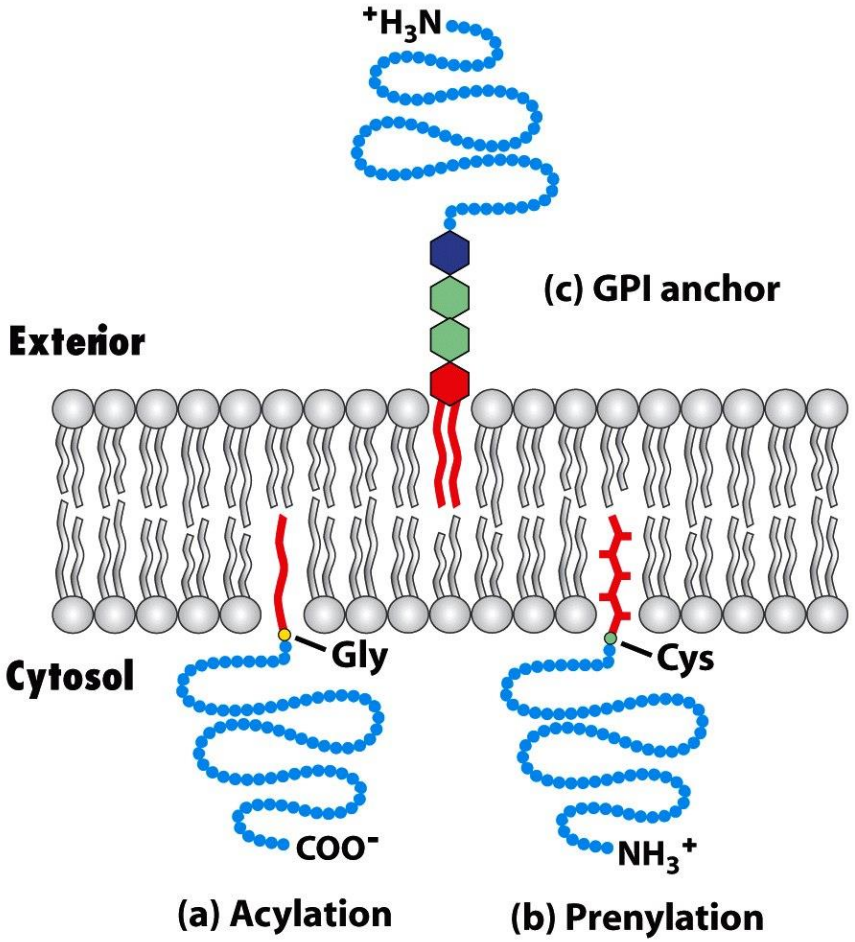


Figure 10-19
Molecular Cell Biology, Sixth Edition

PERIPHERAL PROTEINS - Mechanism of action of Phospholipase A_2

This enzyme has a calcium containing active site buried in a channel hydrophobic amino acids.
The enzyme contains a rim of positively charged amino acids that bind to the negatively charged phospholipids. (eg. PS)
This binding induces a conformational change in the enzyme and it opens its hydrophobic channel.
A phospholipid molecule moves from the bilayer to the channel.
The enzyme bound calcium binds to the phosphate in the head group and positions the ester bond to be cleaved.

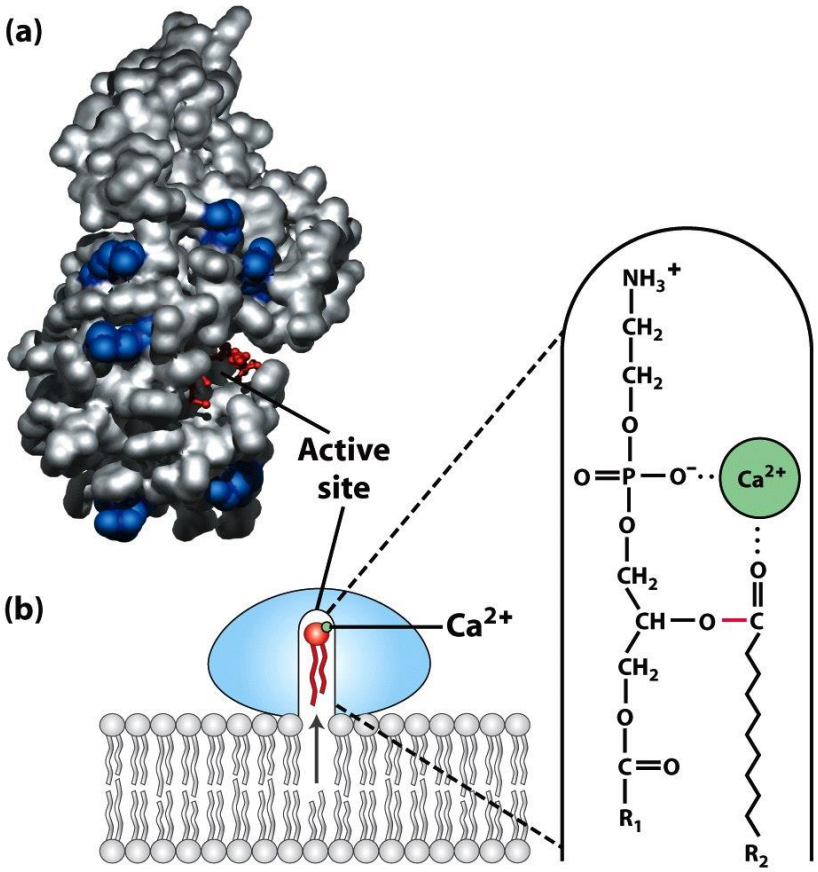


Figure 10-21
Molecular Cell Biology, Sixth Edition

Peripheral proteins - Phospholipase A_2

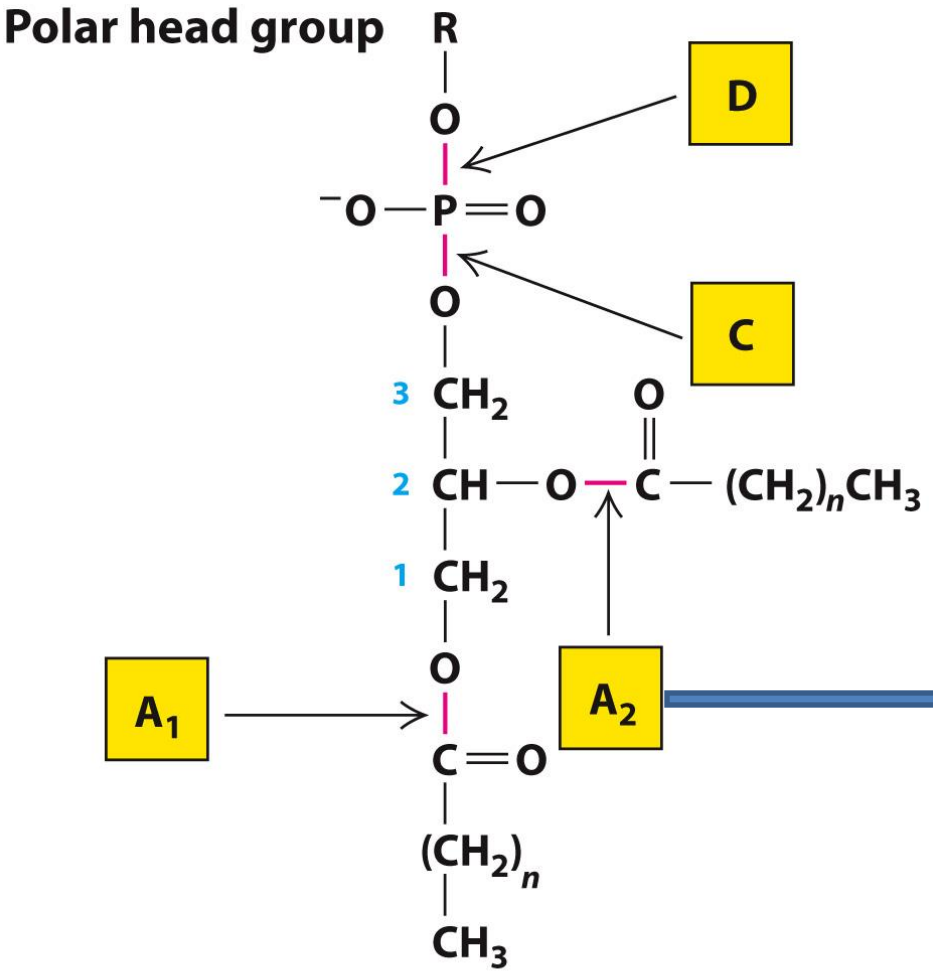


Figure 7-12
Molecular Cell Biology, Eighth Edition

GLYCOPROTEINS AND GLYCOLIPIDS ARE ASYMMETRICALLY ORIENTED IN THE BILAYER

HOW IS BLOOD GROUP DETERMINED?

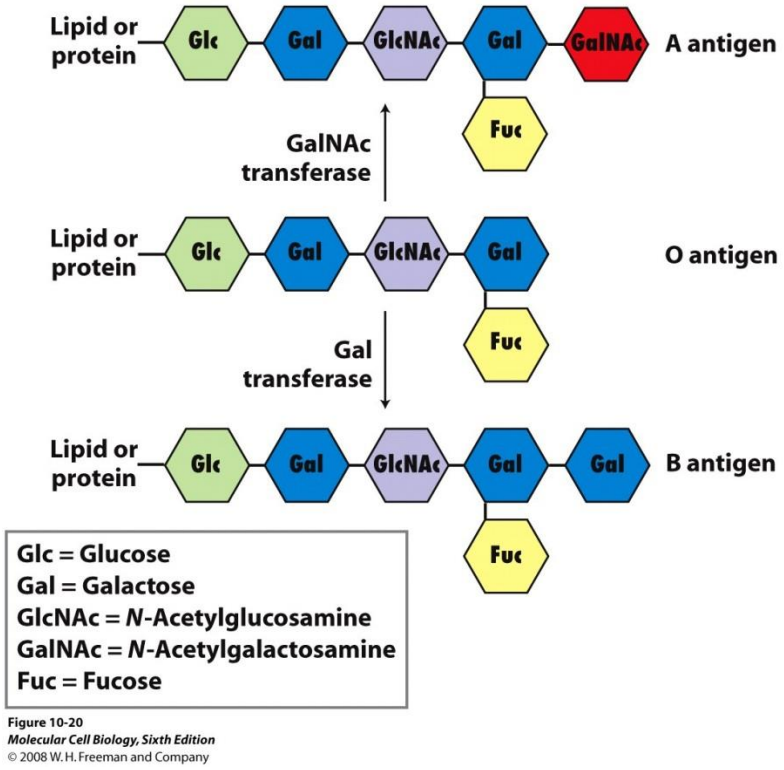


Figure 10-20
Molecular Cell Biology, Sixth Edition

All humans have the enzymes for synthesizing O antigen. In addition persons with A blood group have the enzyme for synthesizing A antigen, B blood group have the enzyme for synthesizing B antigen and AB has enzymes to synthesize A and B antigens.

TABLE 10-2 ABO Blood Groups

BLOOD GROUP	ANTIGENS ON RBCS*	SERUM ANTIBODIES	CAN RECEIVE BLOOD TYPES
A	A	Anti-B	A and O
B	B	Anti-A	B and O
AB	A and B	None	All
O	O	Anti-A and anti-B	O

***See Figure 10-20 for antigen structures.**

Table 10-2
Molecular Cell Biology, Sixth Edition