THE LIPID BILAYER: COMPOSITION AND STRUCTURAL ORGANIZATION

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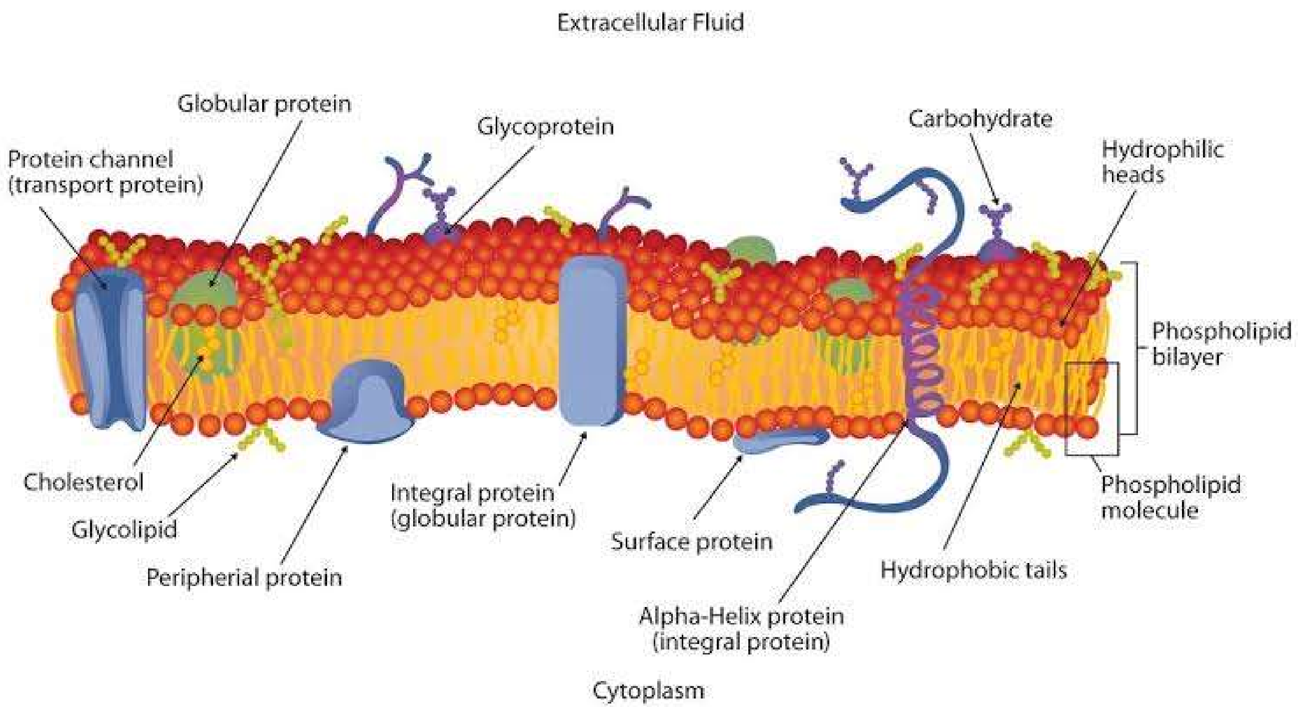
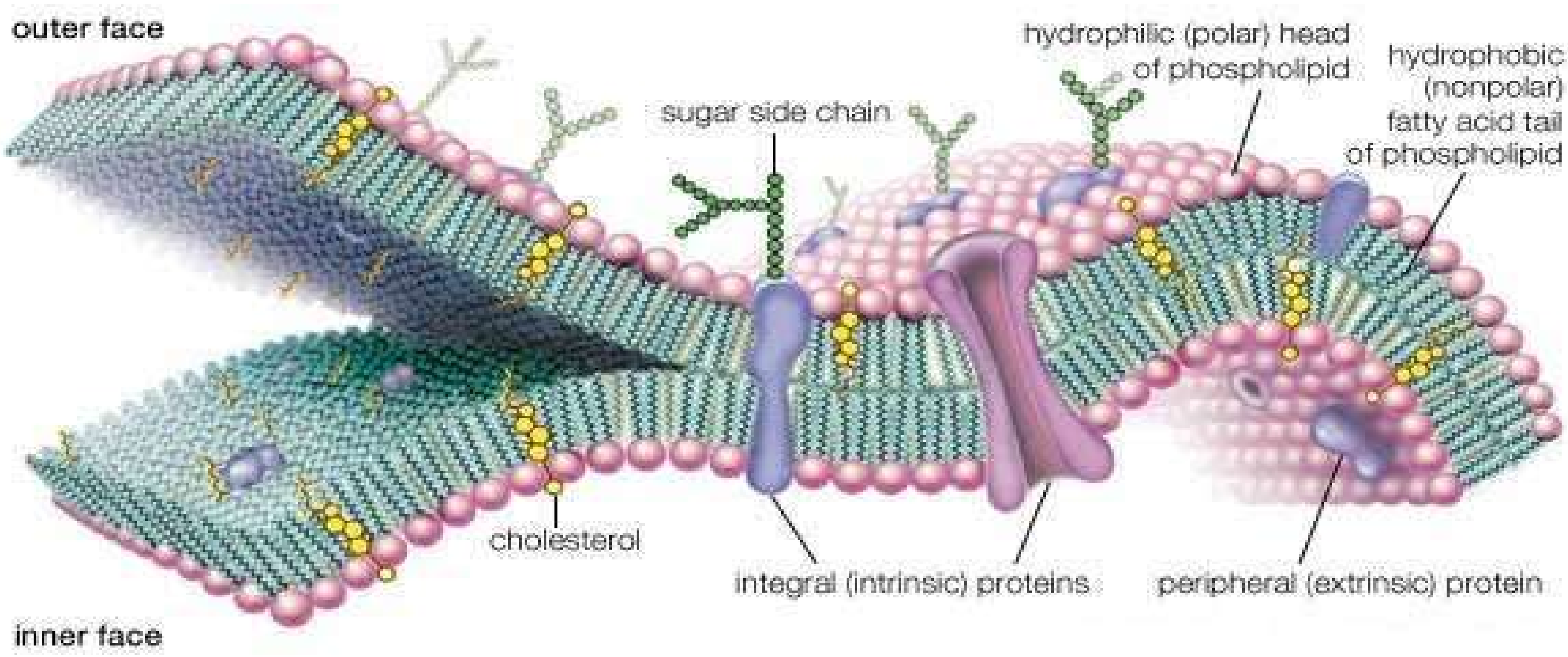


The Fluid Mosaic Model of Biomembrane



Plasma membrane

- 1. Affect shape and function
- 2. Anchor protein to the membrane
- 3. Modify membrane protein activities
- 4. Transducing signals to the cytoplasm

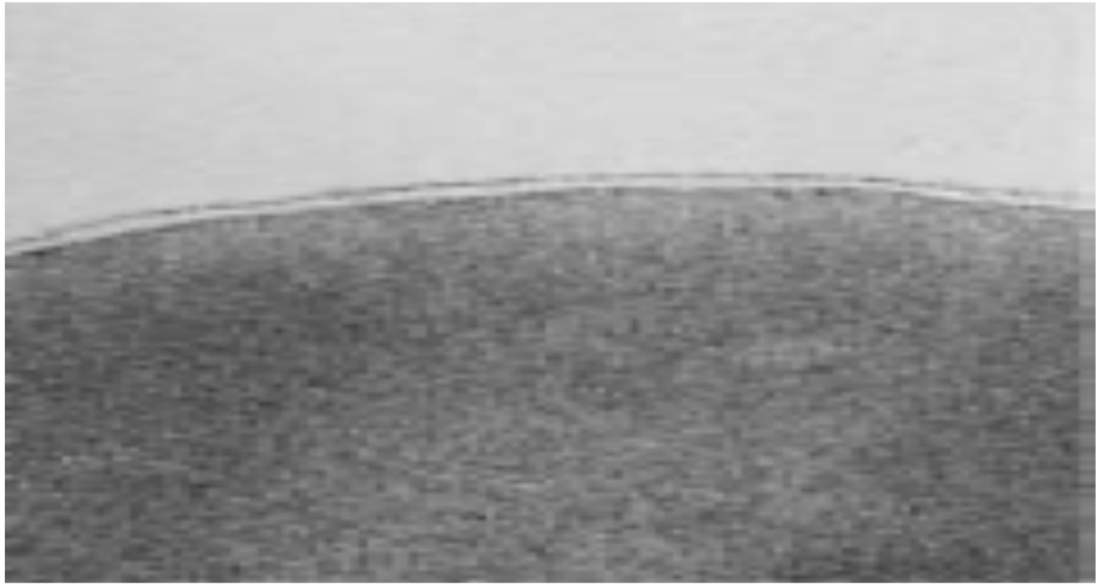
"A living cell is a self-reproducing system of molecules held inside a container - the plasma membrane"

Membrane comprised of lipid sheet (5 nm thick)

- Primary purpose - barrier to prevent cell contents spilling out BUT, must be selective barrier

LIPID COMPOSITION AND STRUCTURAL ORGANIZATION

- Phospholipids of the composition present in cells spontaneously form sheet like phospholipid bilayers, which are two molecules thick.
- The hydrocarbon chains of the phospholipids in each layer, or leaflet, form a hydrophobic core that is 3–4 nm thick in most biomembranes.
- Approx 10^6 lipid molecule in 1µm×1µm area of lipid bilayer.
- Electron microscopy of thin membrane sections stained with osmium tetroxide, which binds strongly to the polar head groups of phospholipids, reveals the bilayer structure.
- A cross section of all single membranes stained with osmium tetroxide looks like a railroad track: two thin dark lines (the stain–head group complexes) with a uniform light space of about 2nm (the hydrophobic tails) between them.



PROPERTIES

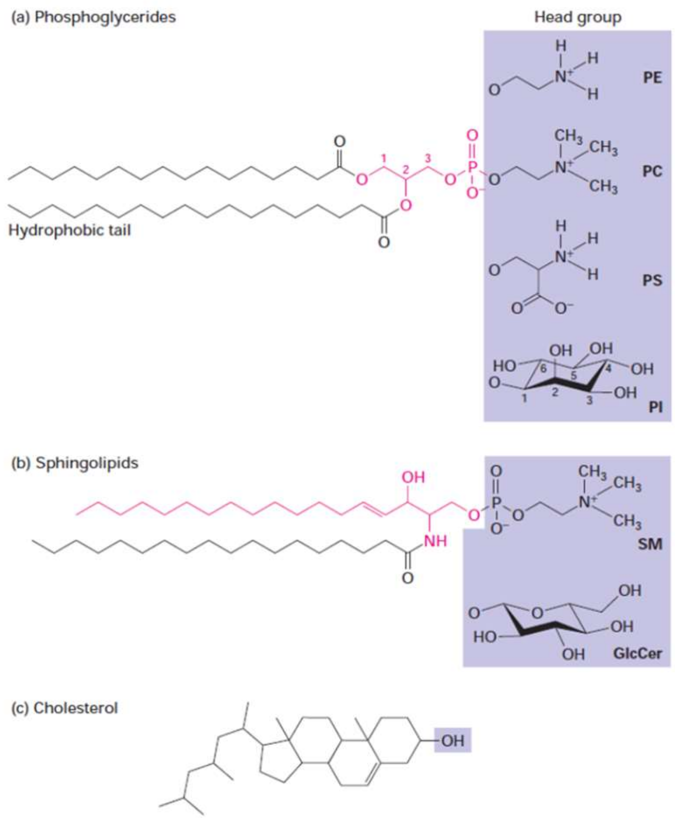
- PERMIABILITY: The hydrophobic core is an impermeable barrier that prevents the diffusion of water-soluble (hydrophilic) solutes across the membrane.
- STABILITY: The bilayer structure is maintained by hydrophobic and van der Waals interactions between the lipid chains. Even though the exterior aqueous environment can vary widely in ionic strength and pH, the bilayer has the strength to retain its characteristic architecture.

Three Classes of Lipids Are Found in Biomembranes

1.Phosphoglycerides ;most abundant

2. Sphingolipids

3. Steroid: stable lipid bilayer



◀ **FIGURE 5-5 Three classes of membrane lipids.** (a) Most phosphoglycerides are derivatives of glycerol 3-phosphate (red) containing two esterified fatty acyl chains, constituting the hydrophobic "tail" and a polar "head group" esterified to the phosphate. The fatty acids can vary in length and be saturated (no double bonds) or unsaturated (one, two, or three double bonds). In phosphatidylcholine (PC), the head group is choline. Also shown are the molecules attached to the phosphate group in three other common phosphoglycerides: phosphatidylethanolamine (PE), phosphatidylserine (PS), and phosphatidylinositol (PI). (b) Sphingolipids are derivatives of sphingosine (red), an amino alcohol with a long hydrocarbon chain. Various fatty acyl chains are connected to sphingosine by an amide bond. The sphingomyelins (SM), which contain a phosphocholine head group, are phospholipids. Other sphingolipids are glycolipids in which a single sugar residue or branched oligosaccharide is attached to the sphingosine backbone. For instance, the simple glycolipid glucosylcerebroside (GlcCer) has a glucose head group. (c) Like other membrane lipids, the steroid cholesterol is amphipathic. Its single hydroxyl group is equivalent to the polar head group in other lipids; the conjugated ring and short hydrocarbon chain form the hydrophobic tail. [See H. Sprong et al., 2001, *Nature Rev. Mol. Cell Biol.* **2**:504.]

PHOSPHOGLYCERIDES

- The most abundant class of lipids in most membranes.
- Derivatives of glycerol 3-phosphate.
- A typical phosphoglyceride molecule consists of a hydrophobic tail composed of two fatty acyl chains esterified to the two hydroxyl groups in glycerol phosphate and a polar head group attached to the phosphate group.
- The two fatty acyl chains may differ in the number of carbons that they contain (commonly 16 or 18) and their degree of saturation (0, 1, or 2 double bonds).

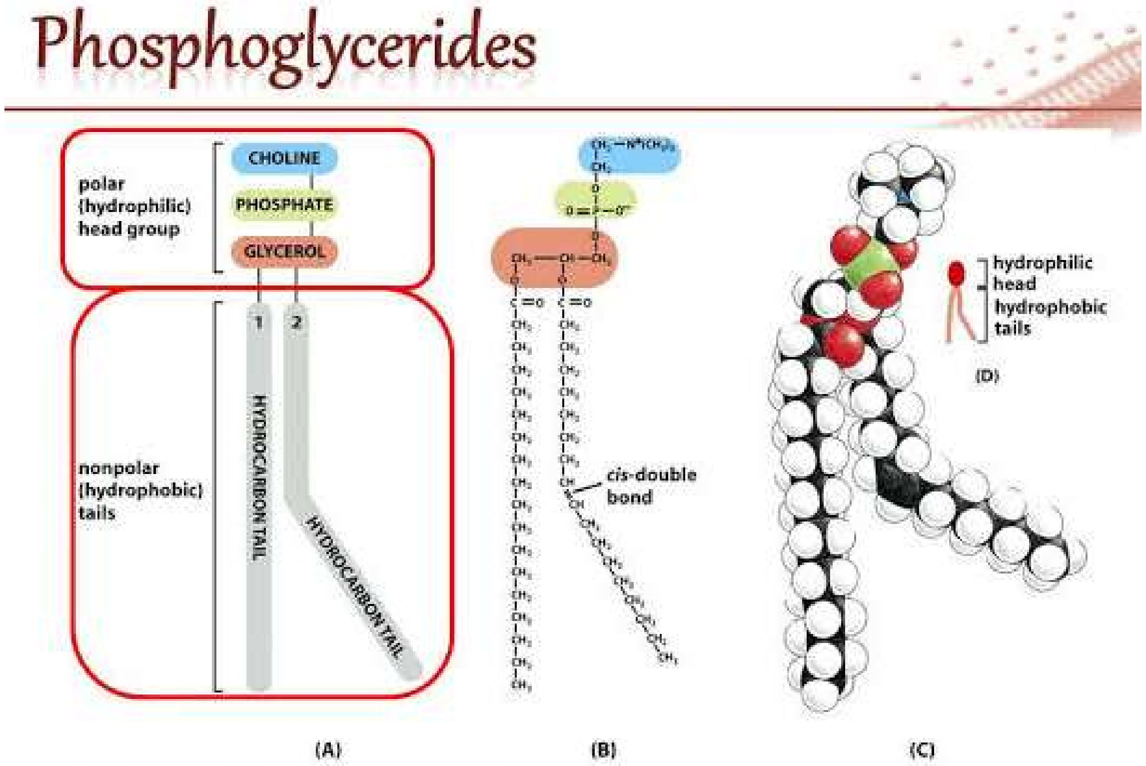
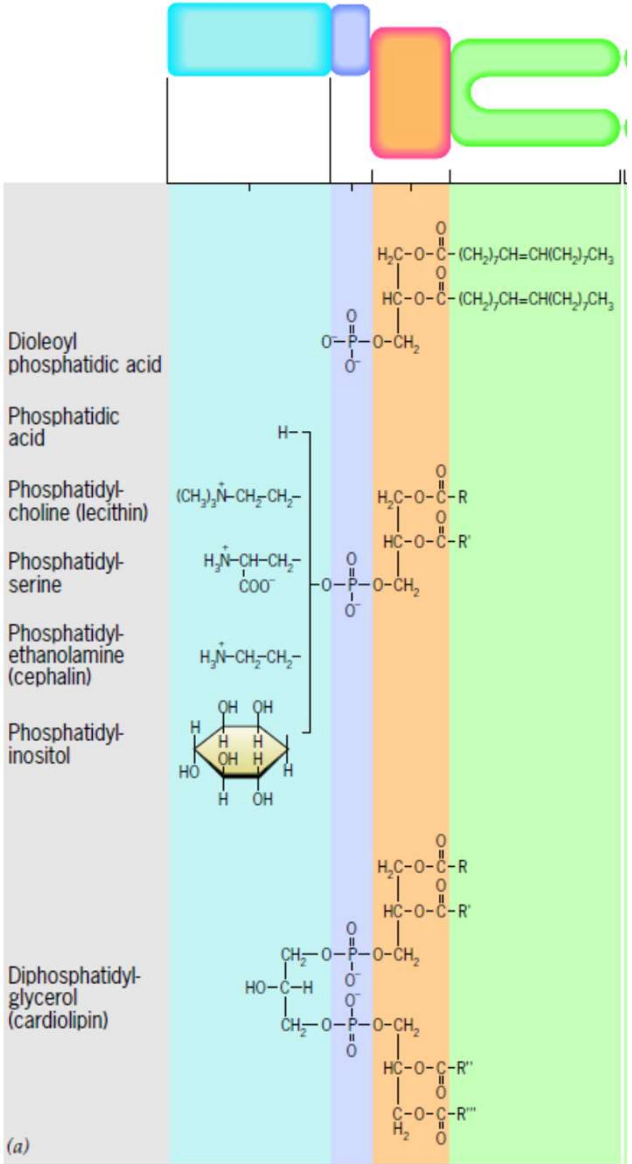


Figure 10-3 Molecular Biology of the Cell 5/e (© Garland Science 2008)

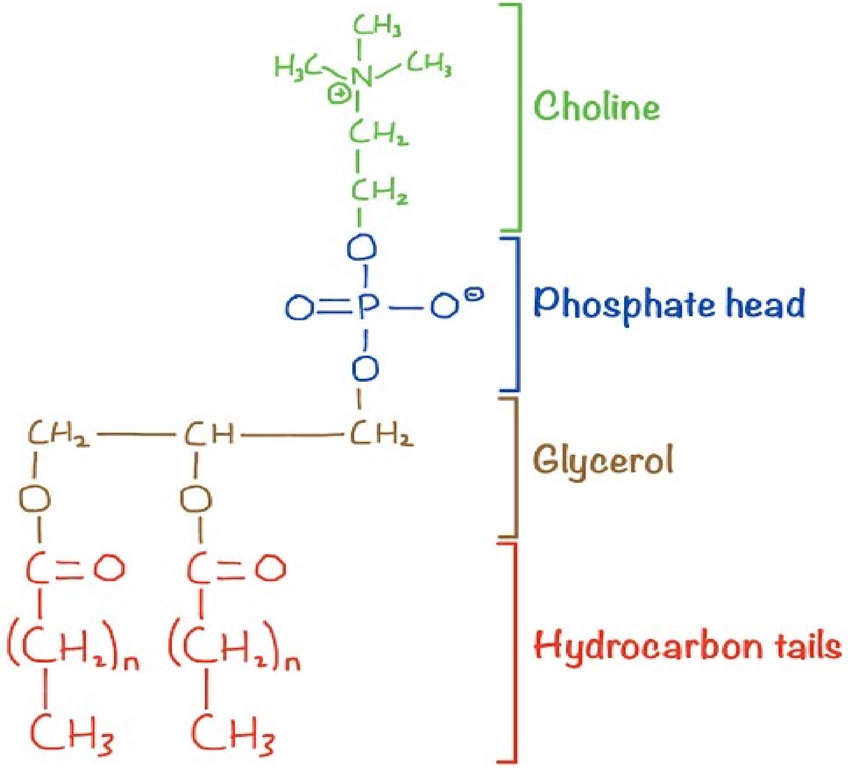


Dioleoyl phosphatidic acid
Phosphatidic acid
Phosphatidyl-choline (lecithin)
Phosphatidyl-serine
Phosphatidyl-ethanolamine (cephalin)
Phosphatidyl-inositol
Diphosphatidyl-glycerol (cardiolipin)
(a)

A phosphoglycerides is classisfied on the basis of the nature of head group

Phosphatidylcholines

The most abundant phospholipids in the plasma membrane, the head group consists of choline, a positively charged alcohol, esterified to the negatively charged phosphate.



Phosohatidylethanolamin

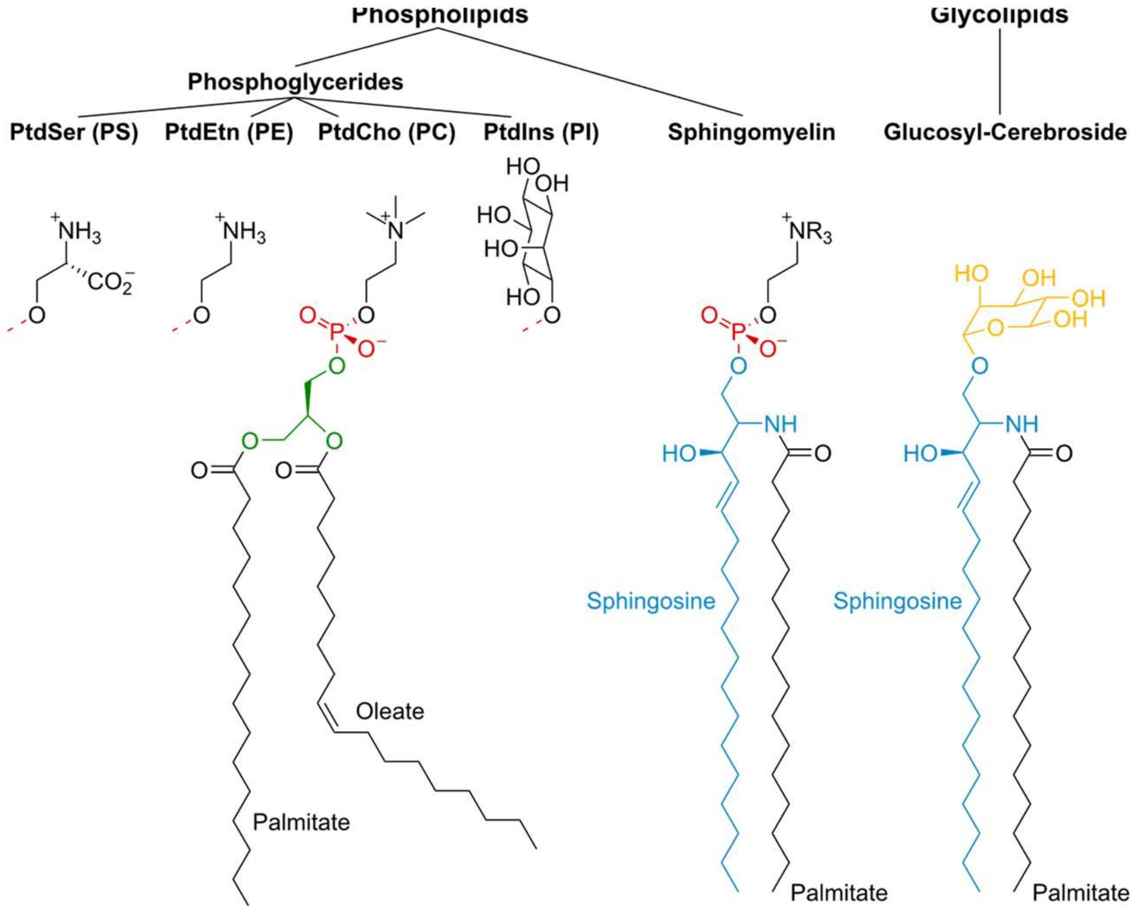
Phosphatidylethanolamines are a class of phospholipids found in biological membranes.

They are synthesized by the addition of cytidine diphosphate-ethanolamine to diglycerides, releasing cytidine monophosphate.

Phosphatidylethanolamines play a role in membrane fusion and in disassembly of the contractile ring during cytokinesis in cell division.

Phosphatidylethanolamine is an important precursor, substrate, or donor in several biological pathways.

As a polar head group, phosphatidylethanolamine creates a more viscous lipid membrane compared to phosphatidylcholine.



Phosphatidylserine

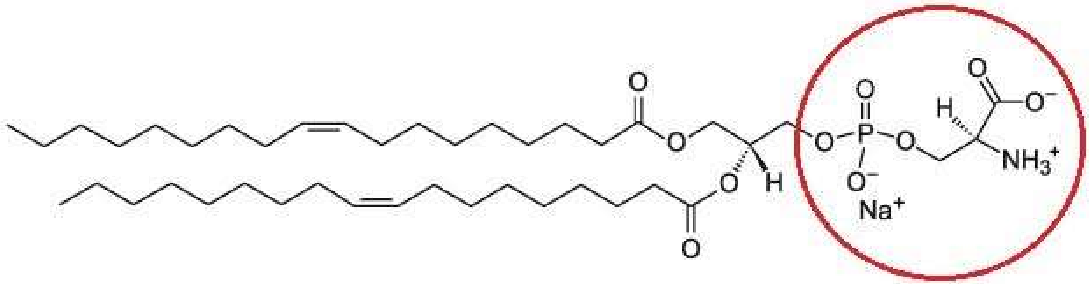
- It consists of two fatty acids attached in ester linkage to the first and second carbon of glycerol and serine attached through a phosphodiester linkage to the third carbon of the glycerol.

CELL SIGNALING

Phosphatidylserine are actively held facing the cytosolic side of the cell membrane by the enzyme flippase. When a cell undergoes apoptosis , phosphatidylserines flip to the extracellular surface of the cell, they act as a signal for macrophages to engulf the cells.

COAGULATION

When circulating platelets encounter the site of an injury, collagen and thrombin-mediated activation causes externalization of phosphatidylserine (PS) from the inner membrane layer, where it serves as a pro-coagulant surface

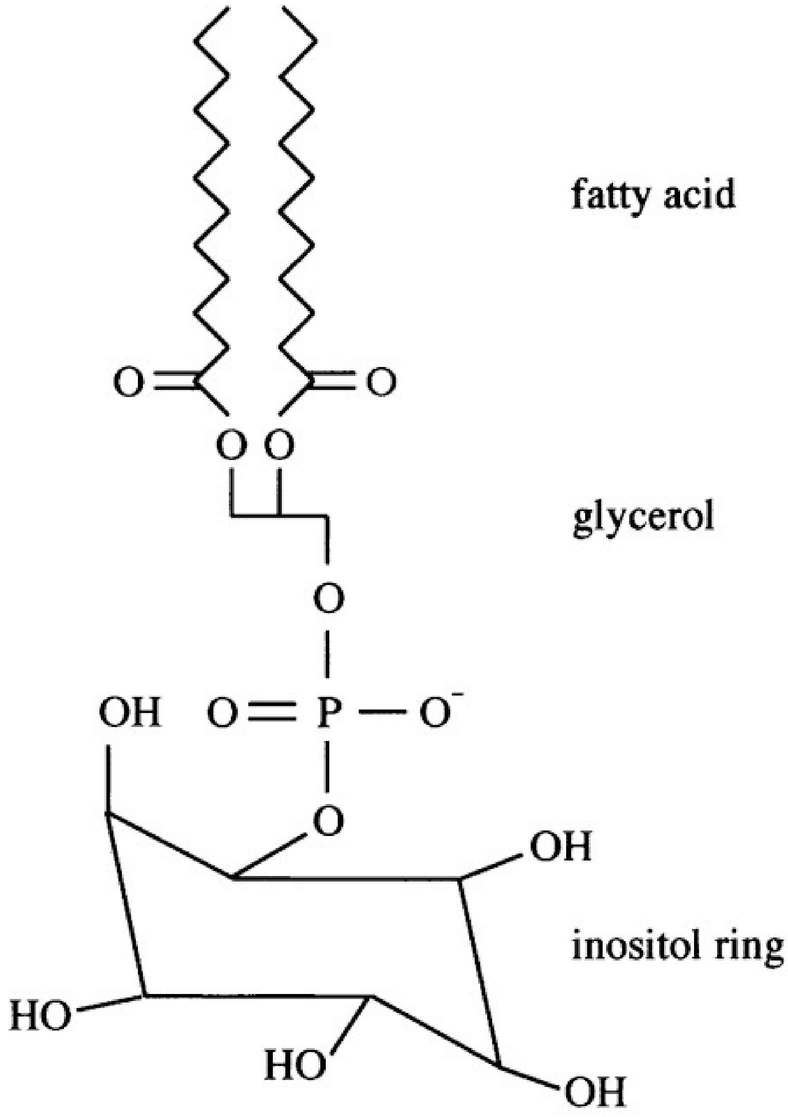


Phosphatidylinositol

Phosphoinositides are phospholipids comprising a water-soluble head group (myo-inositol) linked by a glycerol moiety to two fatty acid chains, usually a saturated C18 residue (stearoyl) in the 1-position and a tetra-unsaturated C20 residue (arachidonoyl) in the 2-position.

It functions as substrate for lipid kinases and phospholipases to generate second messengers, regulators of the cytoskeleton, of enzymes and of ion channels, and docking sites for reversible recruitment of proteins to membranes.

Also play important roles in lipid signaling, cell signaling and membrane trafficking.



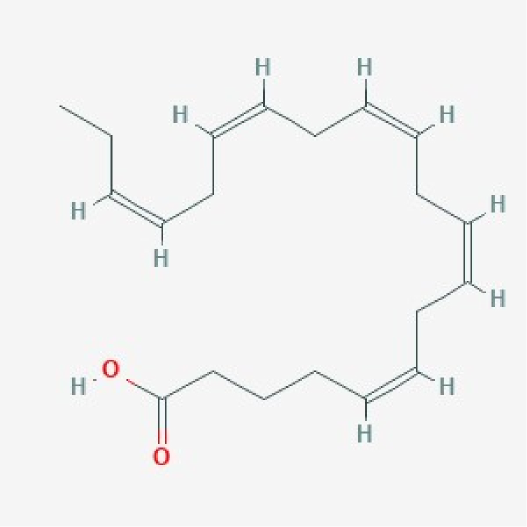
Phosphatidylinositol (PtdIns)

Plasmalogens

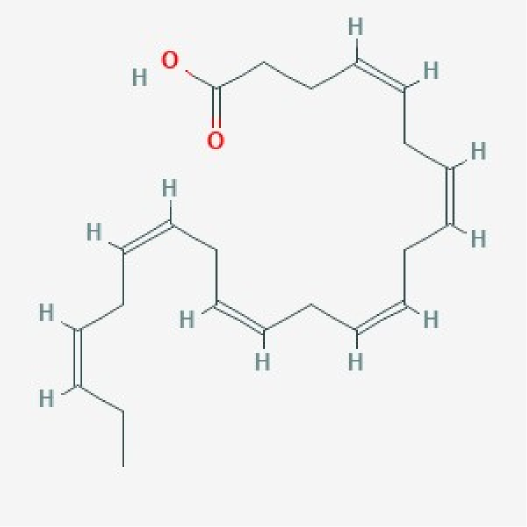
- The plasmalogens are a group of phosphoglycerides that contain one fatty acyl chain, attached to glycerol by an ester linkage, and one long hydrocarbon chain, attached to glycerol by an ether linkage.
- These molecules constitute about 20 percent of the total phosphoglyceride content in humans. Their abundance varies among tissues and species but is especially high in human brain and heart tissue.
- The additional chemical stability of the ether linkage in plasmalogens or the subtle differences in their three dimensional structure compared with that of other phosphoglycerides may have as-yet unrecognized physiologic significance.

Recent interest has focused on the apparent health benefits of two highly unsaturated fatty acids (EPA and DHA) found at high concentration in fish oil. EPA and DHA contain five and six double bonds, respectively, and are incorporated primarily into PE and PC molecules of certain membranes, most notably in the brain and retina.
EPA and DHA are described as omega-3 fatty acids because their last double bond is situated 3 carbons from the omega (CH3) end of the fatty acyl chain.
With fatty acid chains at one end of the molecule and a polar head group at the other end, all of the phosphoglycerides exhibit a distinct amphipathic character.

EPA(eicosapentaenoic acid)



DHA(docosahexaenoic acid)



Sphingolipids

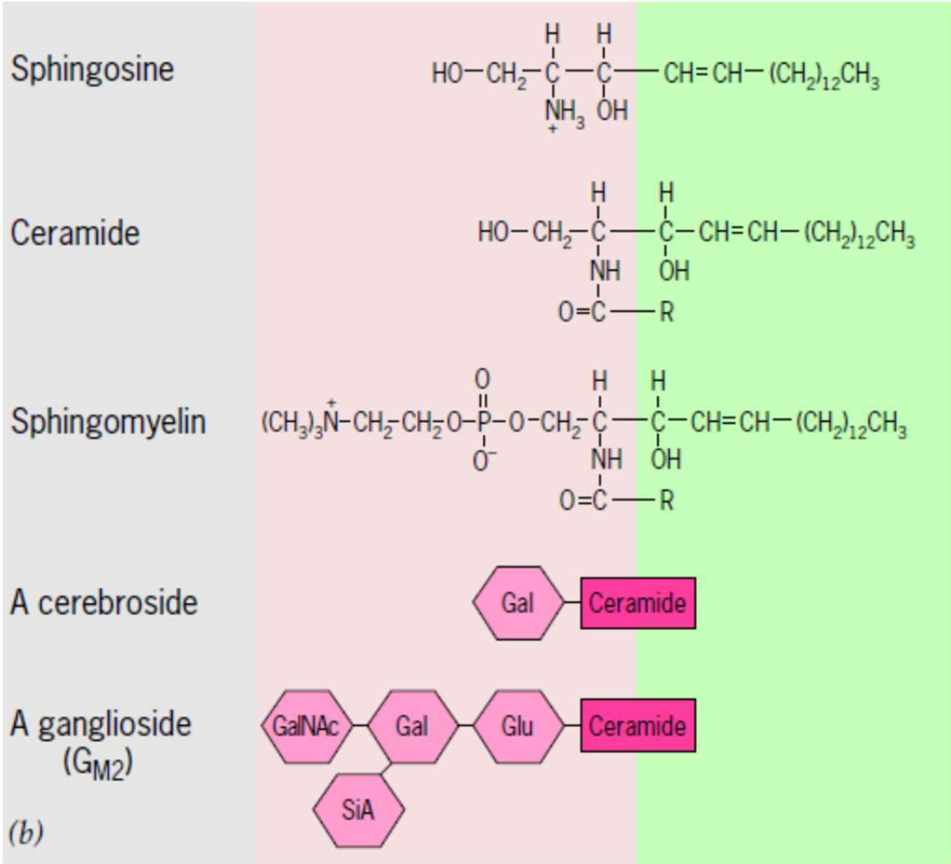
All of these compounds are derived from sphingosine, an amino alcohol with a long hydrocarbon chain, and contain a long-chain fatty acid attached to the sphingosine amino group.

Protect the cell surface against harmful environmental factors by forming a mechanically stable and chemically resistant outer leaflet of the plasma membrane lipid bilayer.

Some glycosphingolipids were found to be involved in specific functions, such as cell recognition and signaling.

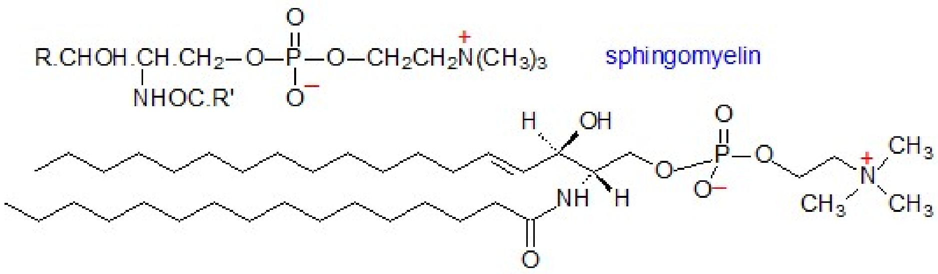
Sphingolipid-based microdomains, or "lipid rafts" were originally proposed to sort membrane proteins along the cellular pathways of membrane transport.

- **Sphingolipids consist of sphingosine linked to a fatty acid by its amino group - ceramide.**
- **If the substitution is phosphorylcholine-sphingomyelin**
- **If the substitution is a carbohydrate-glycolipid**
- **If the carbohydrate is a simple sugar, the glycolipid is called a cerebroside**
- **if it is a small cluster of sugars that includes sialic acid, the glycolipid is called a ganglioside.**

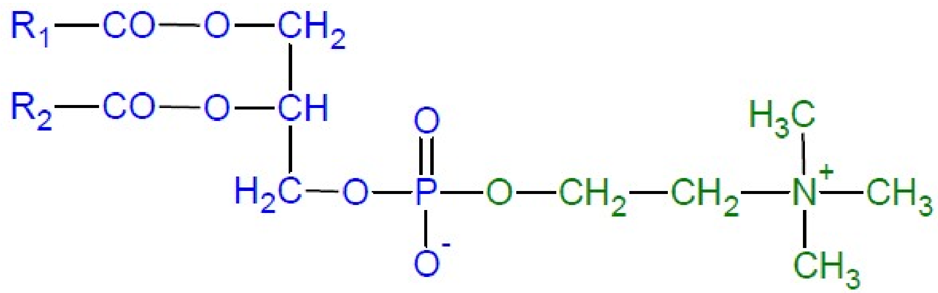


- **Sphingomyelin** is a type of sphingolipid found in animal cell membranes, especially in the membranous myelin sheath that surrounds some nerve cell axons.
  It usually consists of phosphocholine and ceramide, or a phosphoethanolamine head group; therefore, sphingomyelins can also be classified as sphingophospholipids.

  Functions:
  1. Membrane
  2. Apoptosis
  3. Signal transduction



N-(hexadecanoyl)-sphing-4-enine-1-phosphocholine



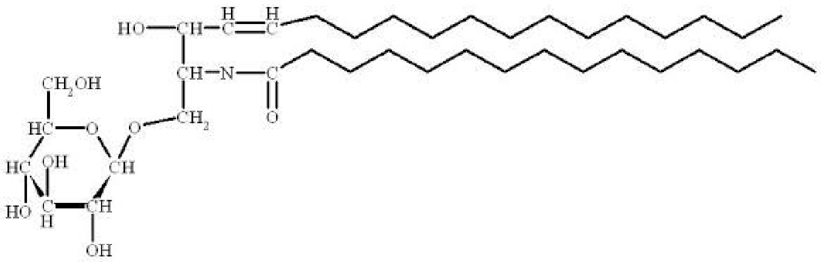
Phosphatidylcholine

- Another sphingolipids are amphipathic glycolipids whose polar head groups are sugars. **Glucosylcerebroside**,the simplest glycosphingolipid, contains a single glucose unit attached to sphingosine.

  In the complex glycosphingolipids called **gangliosides**, one or two branched sugar chains containing sialic acid groups are attached to sphingosine.

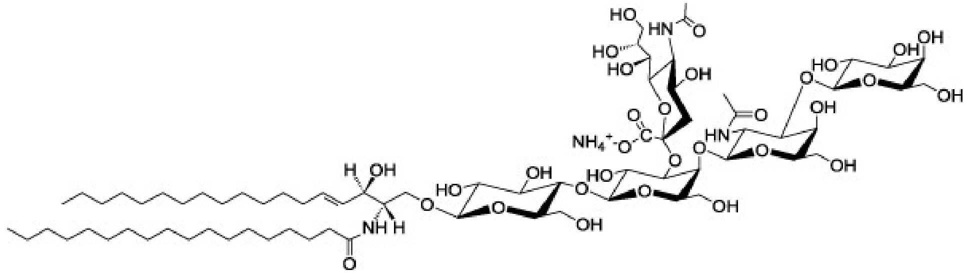
  Glycolipids constitute 2–10 percent of the total lipid in plasma membranes; they are most abundant in nervous tissue.

glucosylcerebroside



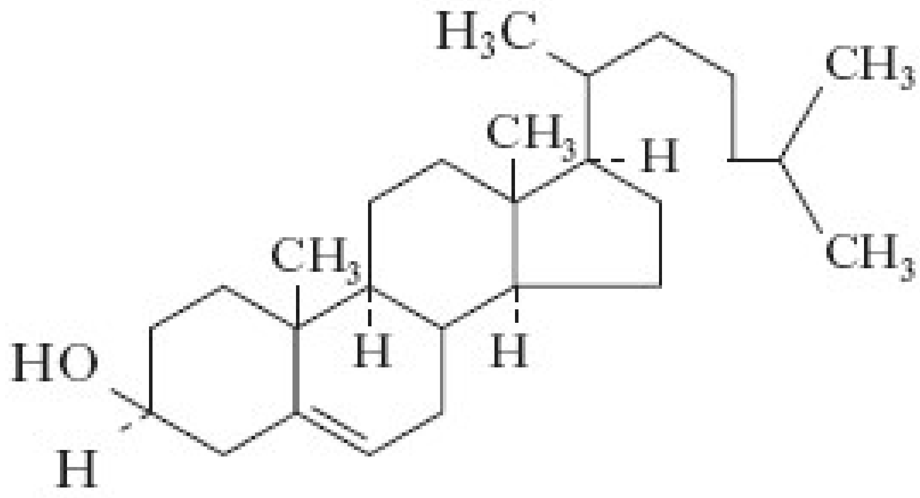
Tro, Chemistry: A Molecular Approach 27

ganglioside



Cholesterol

- Cholesterol and its derivatives constitute the third important class of membrane lipids, the steroids.
- Although cholesterol is almost entirely hydrocarbon in composition, it is amphipathic because its hydroxyl group can interact with water.
- Cholesterol is especially abundant in the plasma membranes of mammalian cells but is absent from most prokaryotic cells. As much as 30–50 percent of the lipids in plant plasma membranes consist of certain steroids unique to plants.



- Cholesterol restricts the random movement of phospholipid head groups at the outer surfaces of the leaflets, but its effect on the movement of long phospholipid tails depends on concentration.
- At the usual cholesterol concentrations, the interaction of the steroid ring with the long hydrophobic tails of phospholipids tends to immobilize these lipids and thus decrease biomembrane fluidity
- At lower cholesterol concentrations, however, the steroid ring separates and disperses phospholipid tails, causing the inner regions of the membrane to become slightly more fluid.

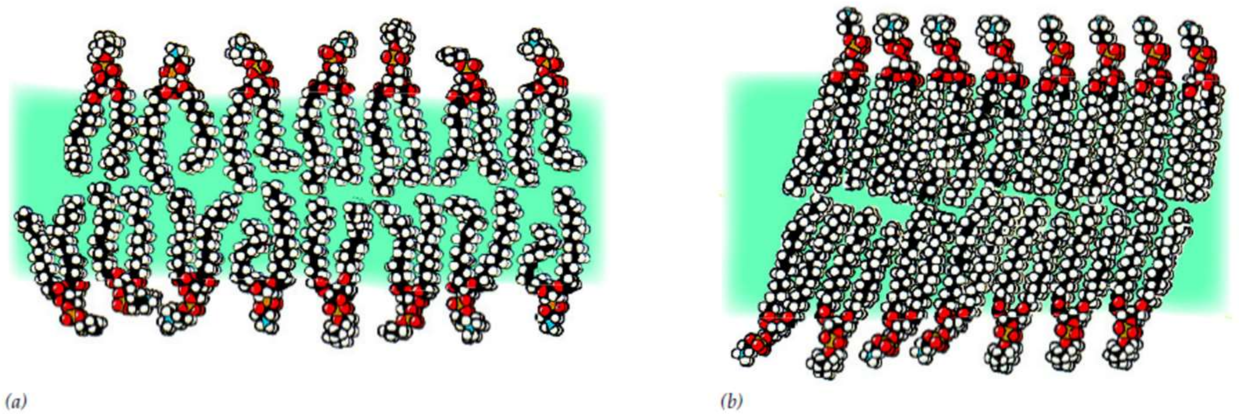


Figure 4.23 **The structure of the lipid bilayer depends on the temperature.** The bilayer shown here is composed of two phospholipids: phosphatidylcholine and phosphatidylethanolamine. (*a*) Above the transition temperature, the lipid molecules and their hydrophobic tails are free to move in certain directions, even though they retain a considerable degree of order. (*b*) Below the transition temperature, the movement of the molecules is greatly restricted, and the entire bilayer can be described as a crystalline gel. (A–B: R. N. ROBERTSON, THE LIVELY MEMBRANES, CAMBRIDGE UNIV. PRESS; 1983, REPRINTED WITH PERMISSION OF CAMBRIDGE UNIV. PRESS.)

Table 4.1 Lipid Compositions of Some Biological Membranes*

Lipid	Human erythrocyte	Human myelin	Beef heart mitochondria	*E. coli*
Phosphatidic acid	1.5	0.5	0	0
Phosphatidylcholine	19	10	39	0
Phosphatidyl-ethanolamine	18	20	27	65
Phosphatidylgycerol	0	0	0	18
Phosphatidylserine	8.5	8.5	0.5	0
Cardiolipin	0	0	22.5	12
Sphingomyelin	17.5	8.5	0	0
Glycolipids	10	26	0	0
Cholesterol	25	26	3	0

*The values given are weight percent of total lipid.
Source: C. Tanford, *The Hydrophobic Effect*, p. 109, copyright 1980, John Wiley & Sons, Inc. Reprinted by permission of John Wiley & Sons, Inc.

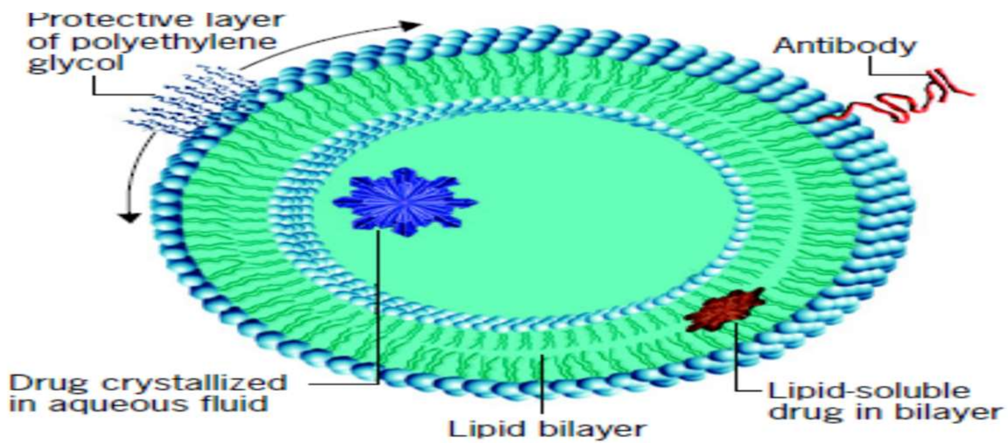
TABLE 5-1 Major Lipid Components of Selected Biomembranes

	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.

NATURE AND IMPORTANCE OF LIPID BILAYER

- Lipid composition can determine the physical state of the membrane and influence the activity of particular membrane proteins.
- Membrane lipids also provide the precursors for highly active chemical messengers that regulate cellular function.
- Due to the flexibility of the lipid bilayer, membranes are deformable and their overall shape can change, as occurs during locomotion or cell division.
- Help in maintaining the proper internal composition of a cell, in separating electric charges across the plasma membrane.
- Ability to self-assemble; Liposome.



The asymmetry of membrane lipid

N.B:If intact human red blood cells are treated with a lipid-digesting phospholipase, approximately 80 percent of the (PC) of the membrane is hydrolyzed, but only about 20 percent of the membrane's (PE) and less than 10 percent of its (PS) are attacked.

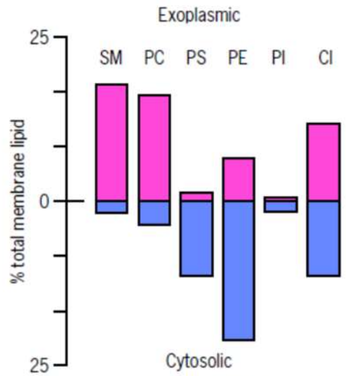


Figure 4.10 **The asymmetric distribution of phospholipids (and cholesterol) in the plasma membrane of human erythrocytes.** (SM, sphingomyelin; PC, phosphatidylcholine; PS, phosphatidylserine; PE, phosphatidylethanolamine; PI, phosphatidylinositol; Cl, cholesterol.)

- All the glycolipids of the plasma membrane are in the outer leaflet often serve as receptors for extracellular ligands.
- Phosphatidylethanolamine(inner leaflet) tends to promote the curvature of the membrane.
- Phosphatidylserine(inner leaflet) has a net negative charge at physiologic pH, which makes it a candidate for binding positively charged lysine and arginine residues.
- PS on the outer surface of aging lymphocytes marks the cells for destruction by macrophages, whereas its appearance on the outer surface of platelets leads to blood coagulation.
- Phosphatidylinositol (PI) (inner leaflet) can be phosphorylated at different sites on the inositol ring, which converts the lipid into a phosphoinositide which play a key role in the transfer of stimuli from the plasma membrane to the cytoplasm and the recruitment of proteins to the cytosolic face of the plasma membrane.

Thank you

REFERENCE: 1. CELL BIOLOGY (B. ALBERTS)

2. CELL BIOLOGY (KARP)