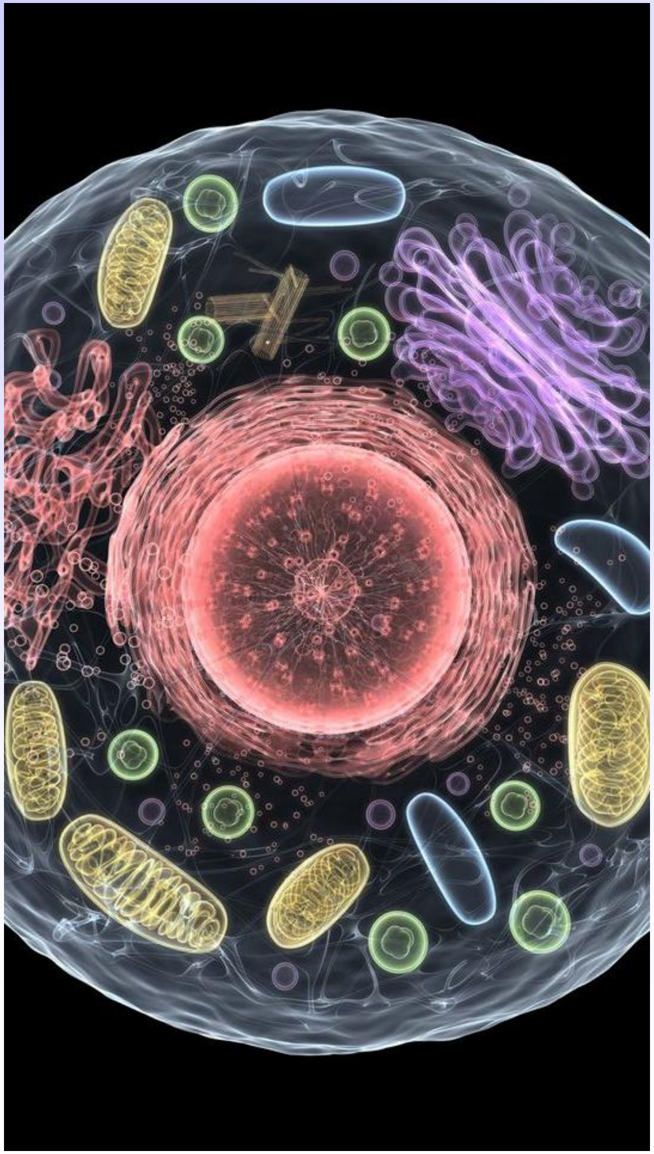
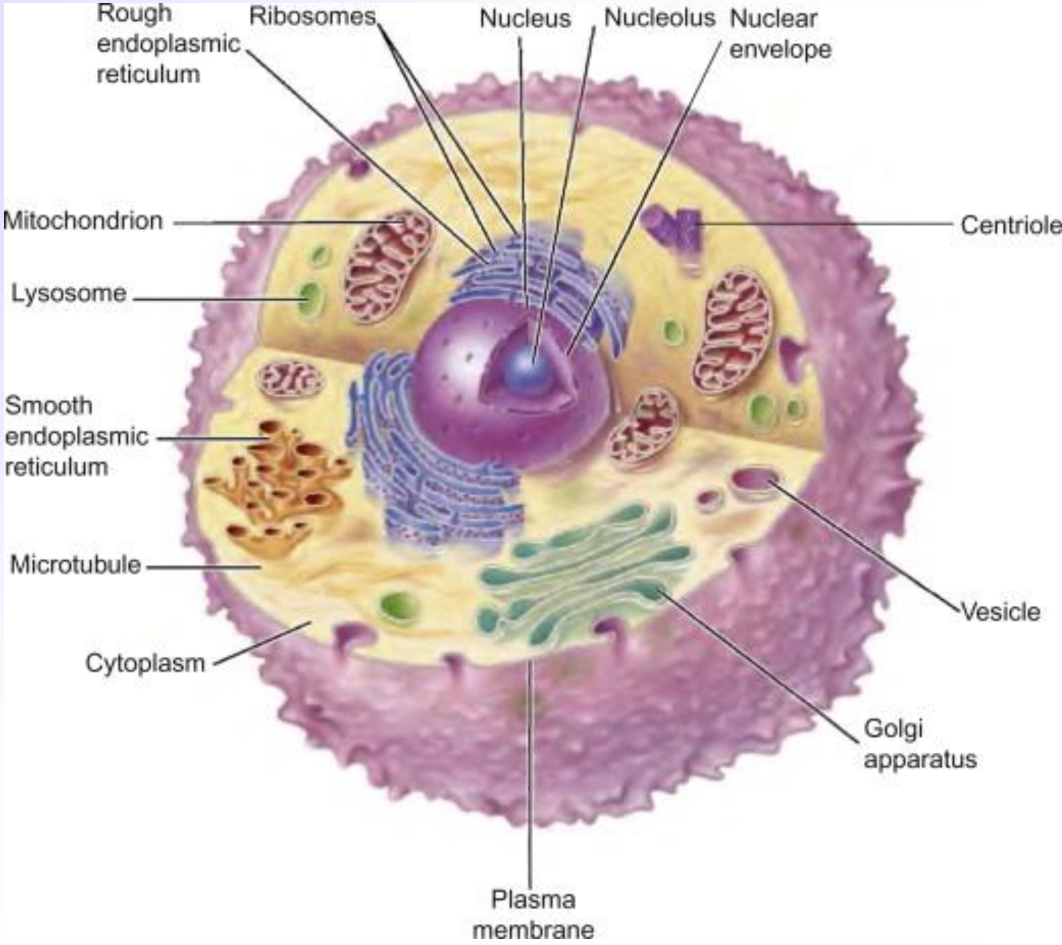
University of Teramo

Degree Program in Biotechnology

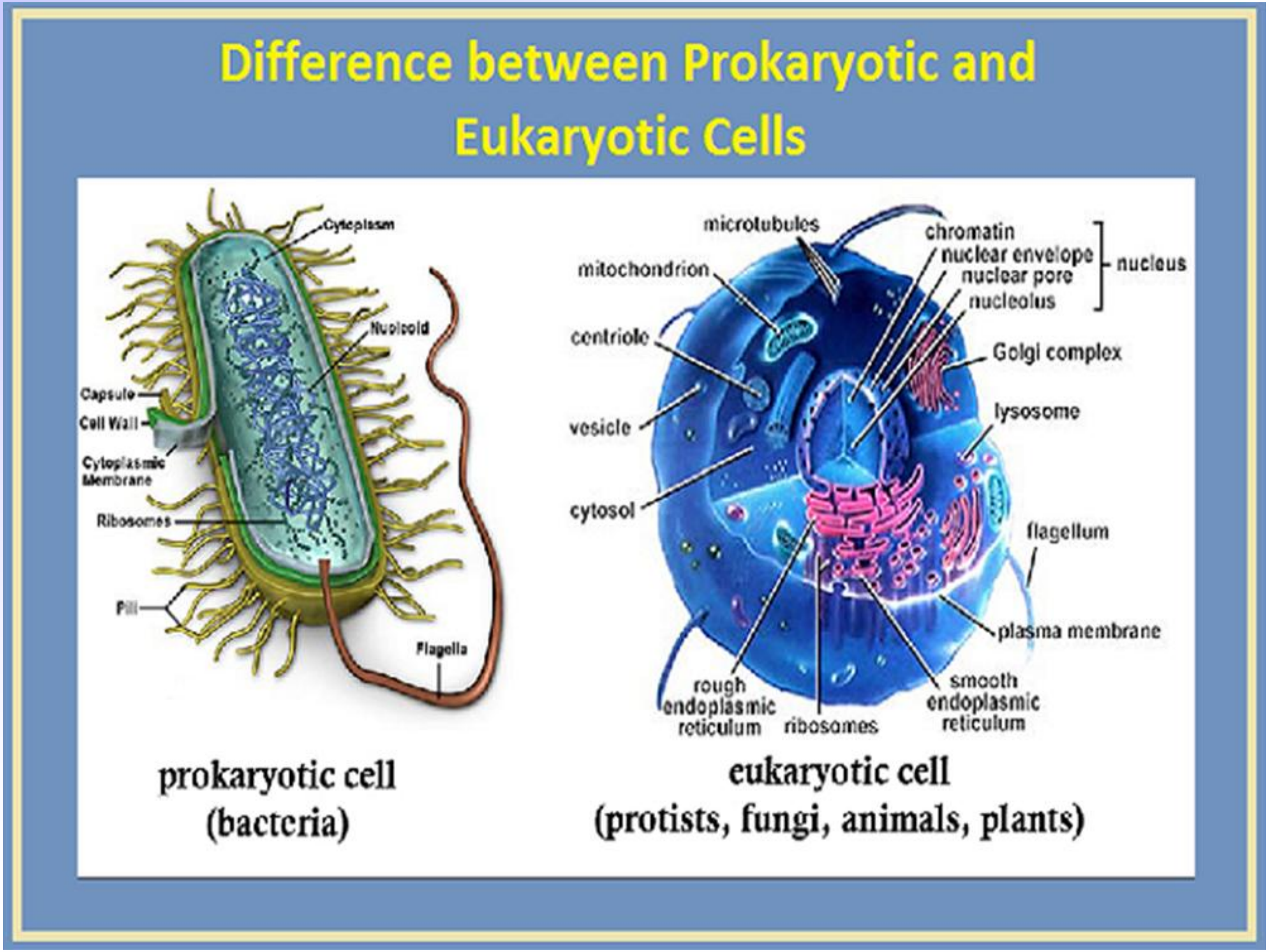
COURSE OF CYTOLOGY AND HISTOLOGY
Prof. Mauro

Eukaryotic cell





Eukaryotic cell



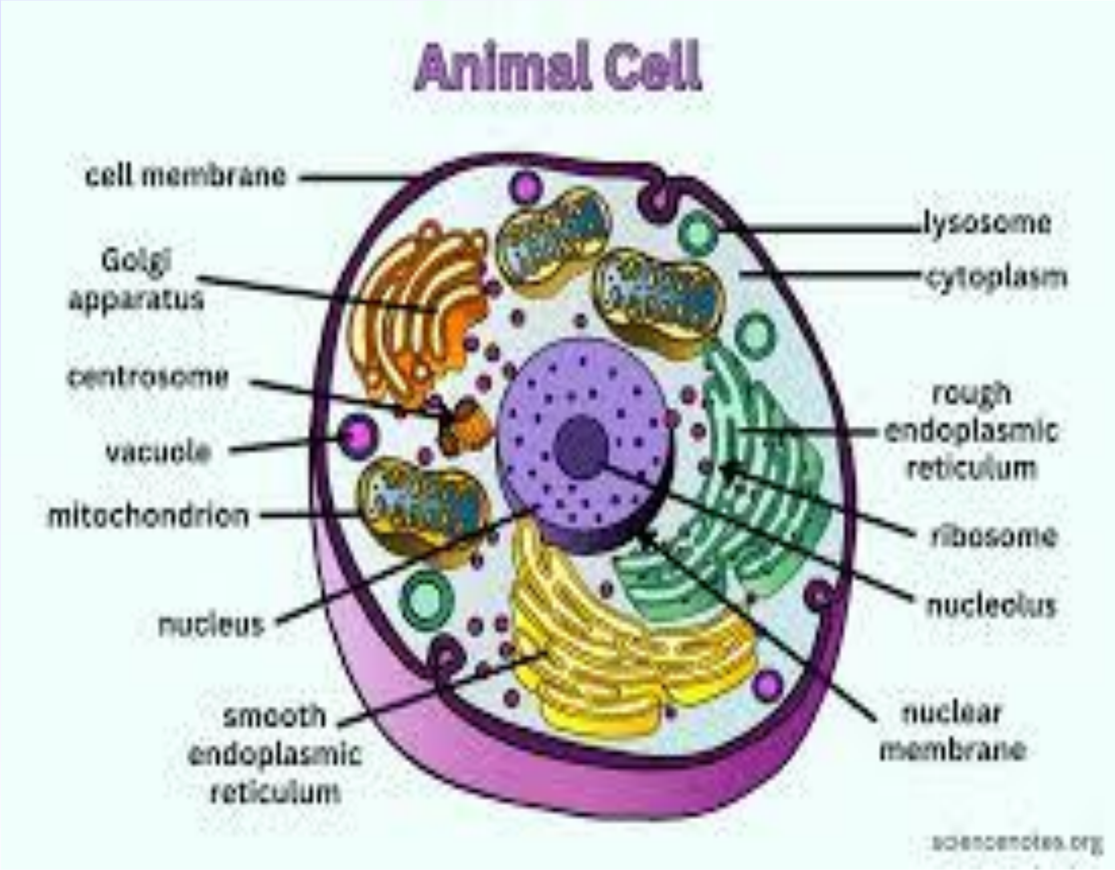
Cell Component/ Feature	Prokaryotic Cells	Eukaryotic Cells	
		Plant Cells	Animal Cells
Size	Average Diameter: 0.5-5μm	Up to 40μm diameter	
DNA	Naked DNA Circular DNA	DNA associated with histones in chromosomes	
Nucleus	Absent (DNA in cytoplasm, naked DNA)	Present (DNA within a membrane-bound nucleus)	
Organelles	Absent	Present	
Ribosomes	70S (Small)	80S (Large)	
Mitochondria	Absent	Present	
Endoplasmic Reticulum (ER)	Absent	Present	
Golgi apparatus	Absent	Present	
Lysosomes	Absent	Present	
Pili	Present	Absent	
Plasmid	Present (Sometimes)	Absent	
Flagella	Solid	Flexible/Membrane-bound	
Cell Wall	Present (Made of peptidoglycan)	Present (Made of Cellulose)	Absent
Cell Surface Membrane	Present	Present	

Advantages of compartmentalization:

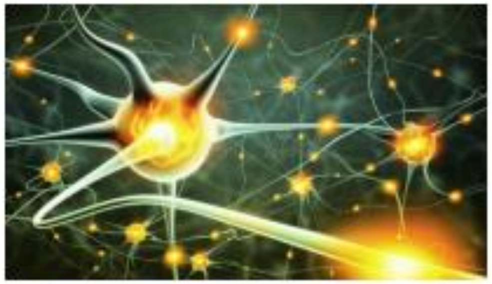
•**Microenvironment creation** → enzymes, substrates, and cofactors are concentrated → more interactions

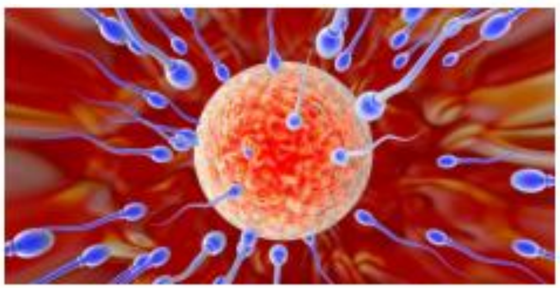
•**Control of chemical environments** → pH, ion concentration, etc.

•**Sequestration of harmful substances (e.g., drugs)** → stored in specific organelles

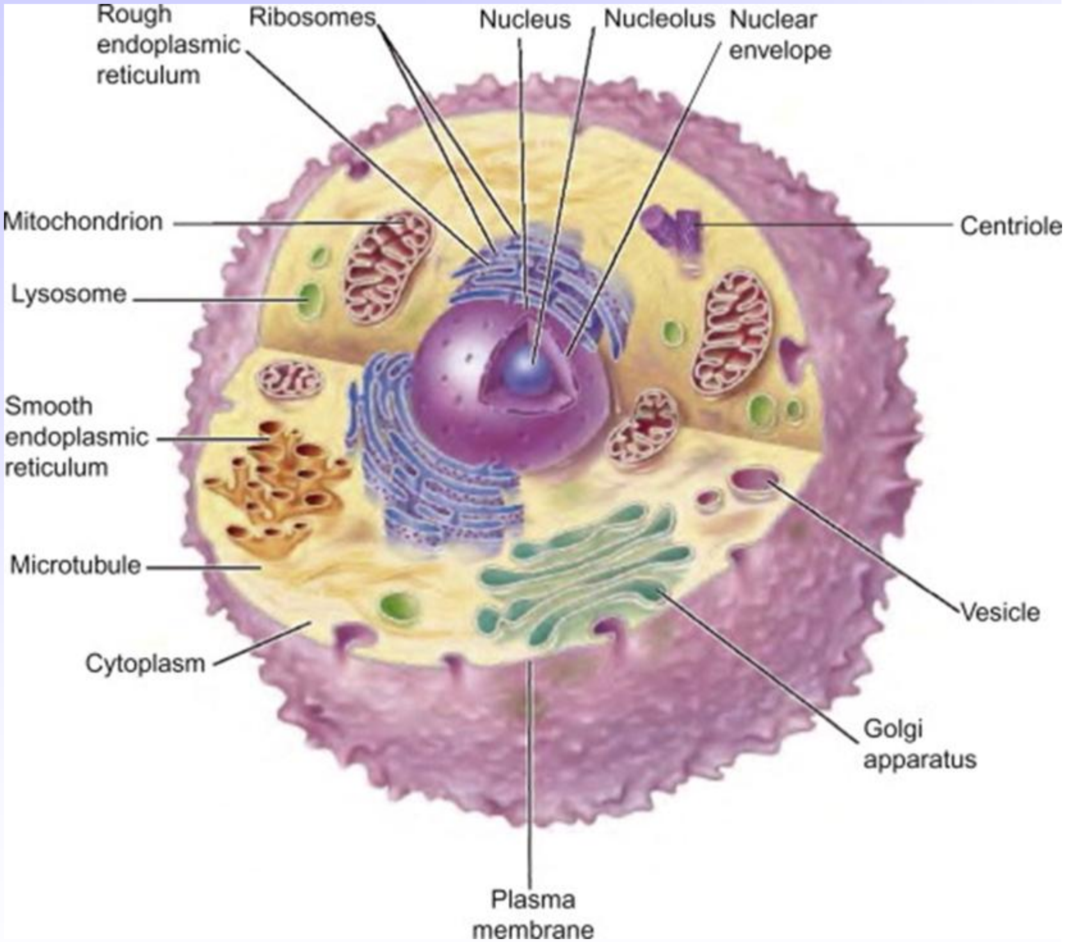


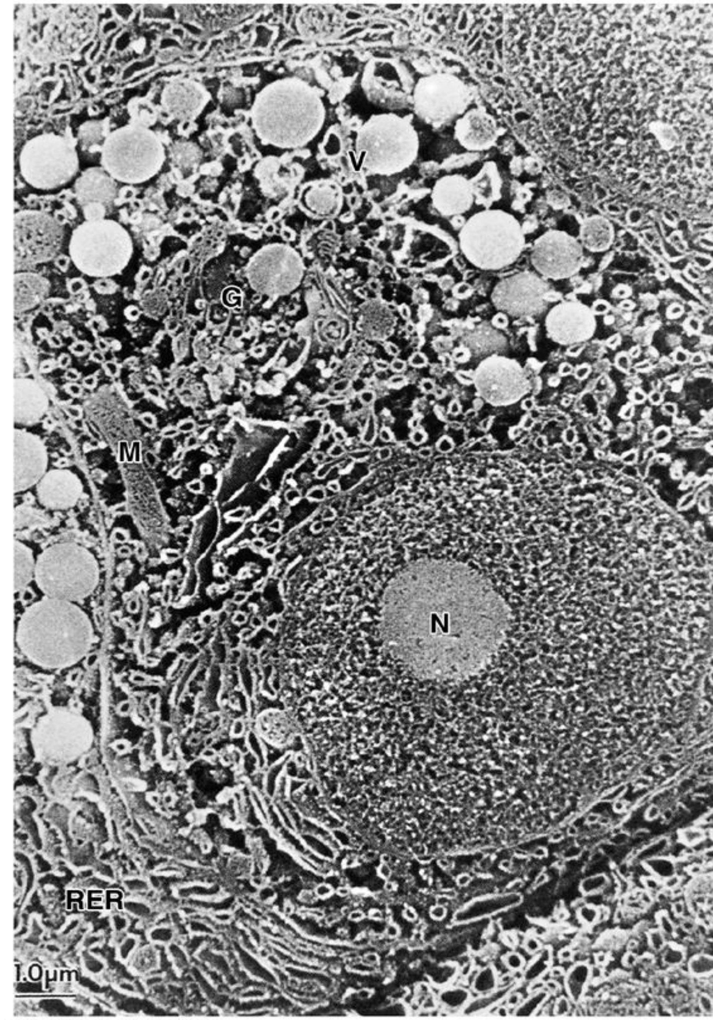
Shape of animal eukaryotic cells





Organization of the protoplasm of a eukaryotic cell



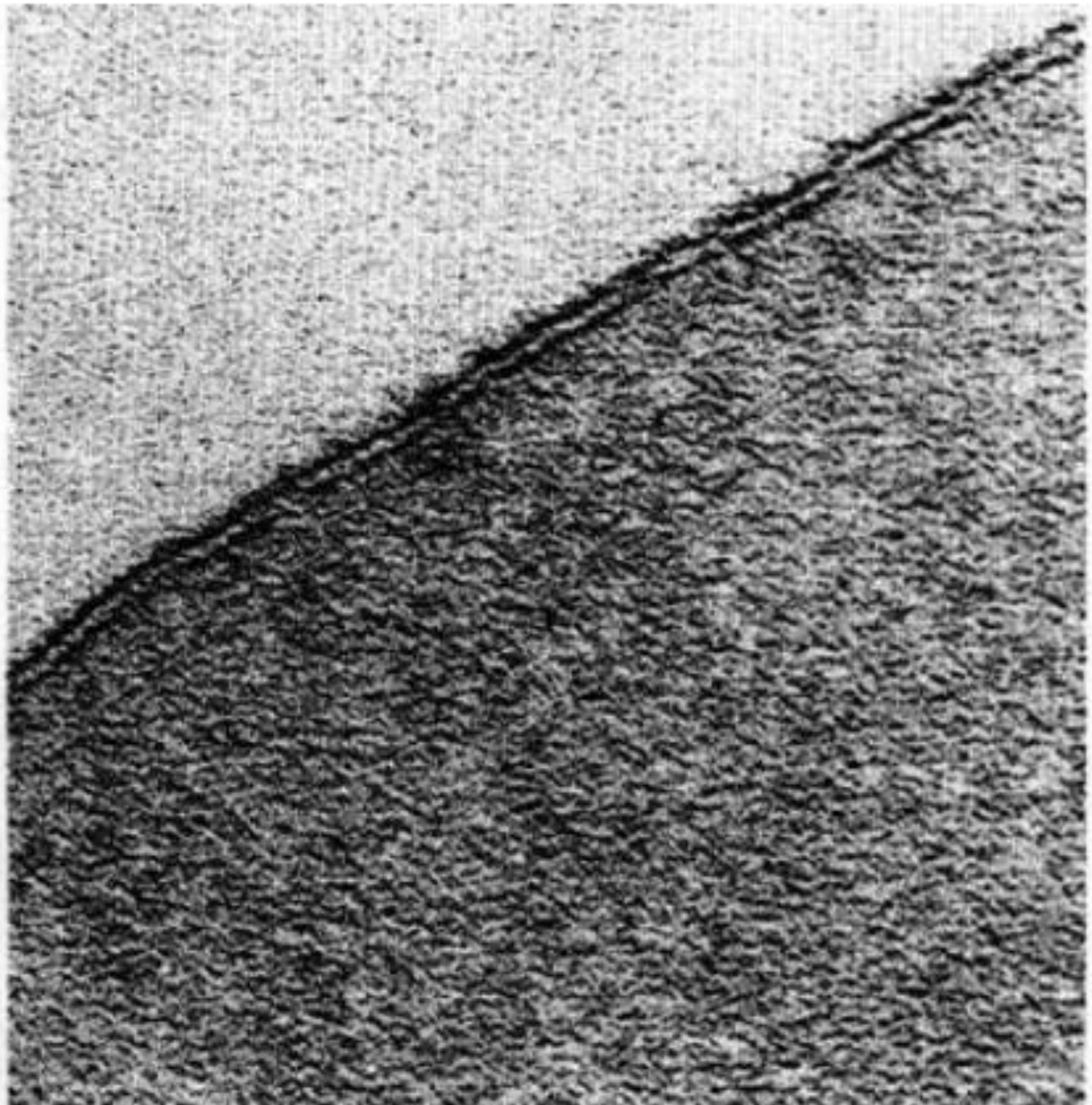


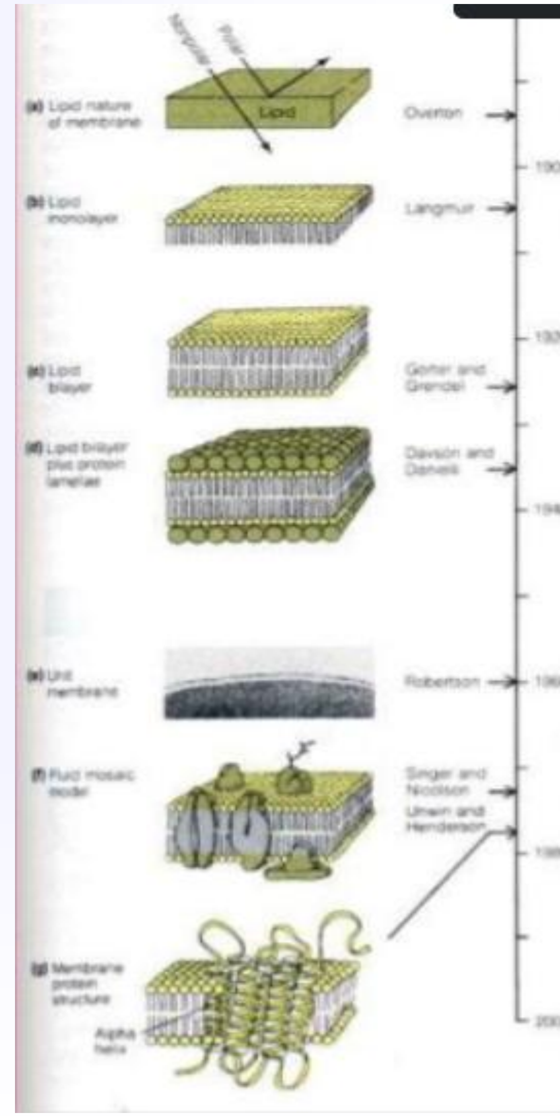
CYTOPLASM AND CELL ORGANELLES

CELL PROPERTIES

- Reproduction
- Energy
- Metabolic activities
- Growth
- Movement
- Reactivity to stimuli
- Differentiation

Plasma Membrane Structure





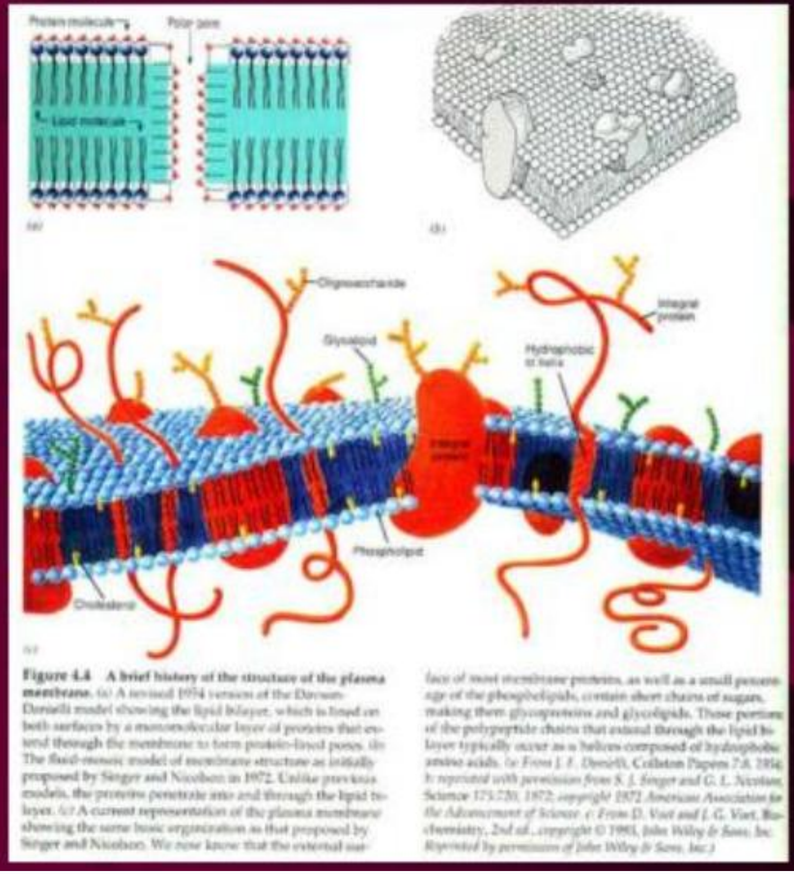
◈ **S.J.Singer and G.Nicolson(1972):**

fluid-mosaic model;

◈ K.Simons et al(1997):

lipid rafts model;

Functional rafts in Cell membranes.
Nature 387:569-572



PLASMA MEMBRANE

A thin membrane approximately 5-10 nm thick that surrounds the cell. It is not visible under a optical microscope.

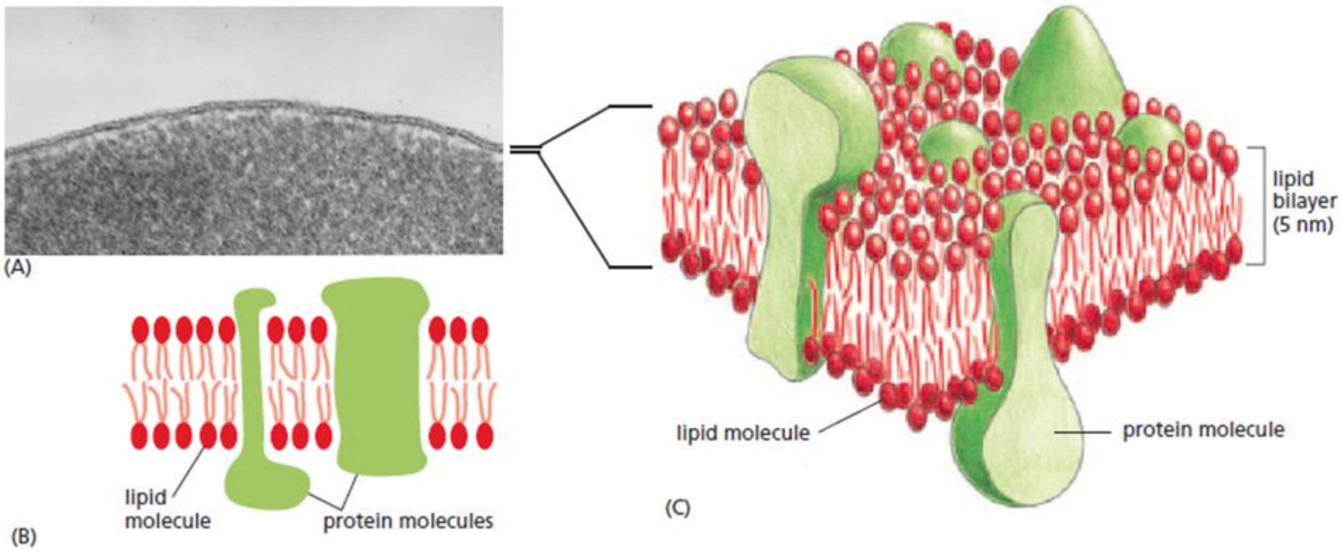
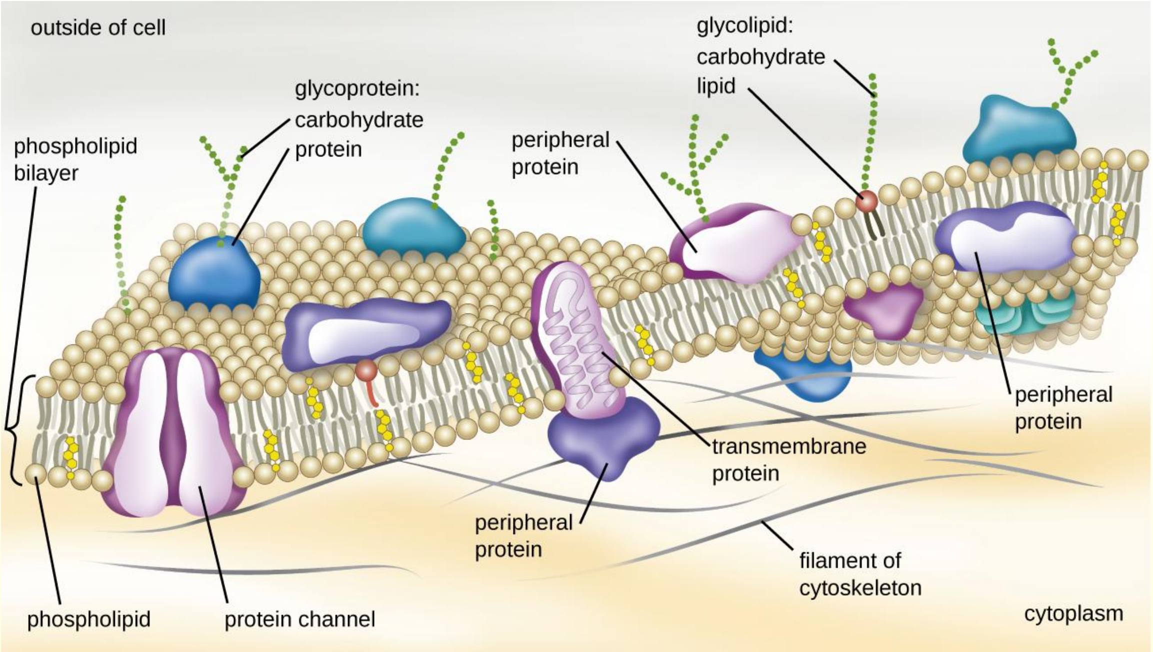


Figure 11–4 A cell membrane can be viewed in a number of ways. (A) An electron micrograph of a plasma membrane of a human red blood cell seen in cross section. (B and C) Schematic drawings showing two-dimensional and three-dimensional views of a cell membrane. (A, courtesy of Daniel S. Friend.)

The plasma membrane, cell membrane, or plasmalemma is a thin envelope that surrounds the cell, separating it from the outside environment and regulating the exchange of nutrients.

Plasma Membrane: Fluid Mosaic Model
“central dogma” of the membrane biology



- LIPIDS
- PROTEINS
- CARBOHYDARATES

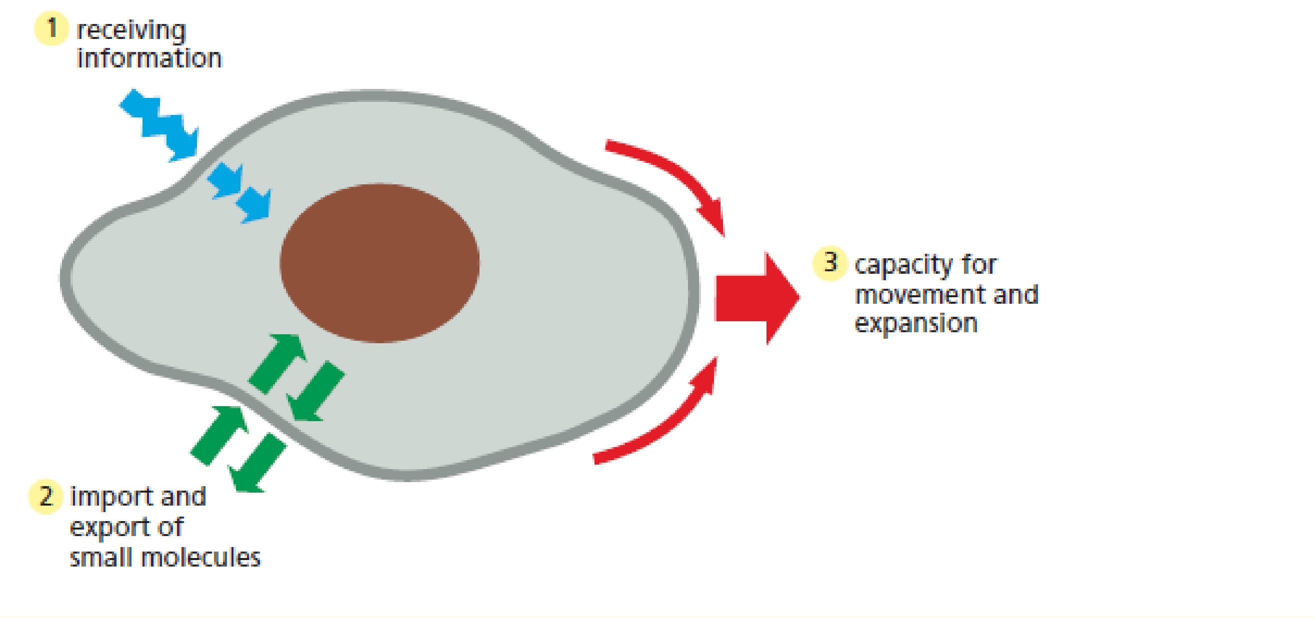
A. The core lipid bilayer exists in a fluid state, capable of dynamic movement.

B. Membrane proteins form a mosaic of particles penetrating the lipid to varying degrees.

SPECIFIC CHARACTERISTICS

-ASYMMETRICAL
-HIGHLY SELECTIVE
-FLUID
-DINAMIC

PLASMA MEMBRANE Functiom



The plasma membrane is involved in cell communication, import and export of molecules, and cell growth and motility.

(1) Receptor proteins in the plasma membrane enable the cell to receive signals from the environment;

(2) Transport proteins in the membrane enable the import and export of small molecules;

(3) the flexibility of the membrane and its capacity for expansion allow the cell to grow, change shape, and move

A. Membrane Lipids: The Fluid Part of the Model

- ❖Membrane lipids are amphipathic.
- ❖There are three major classes of lipids:

Phospholipids:

Phosphoglyceride and sphingolipids

Glycolipids

Sterols (is only found in animals)

LIPIDS

Phospholipidc Bilayer

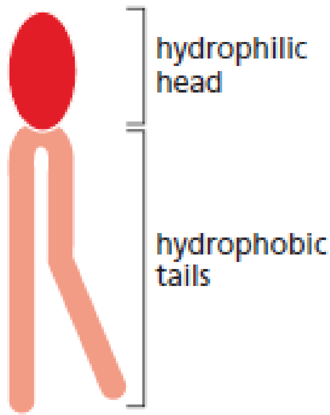
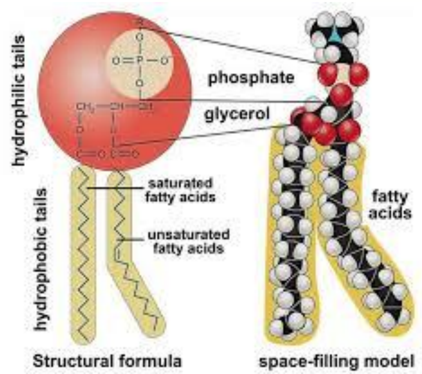
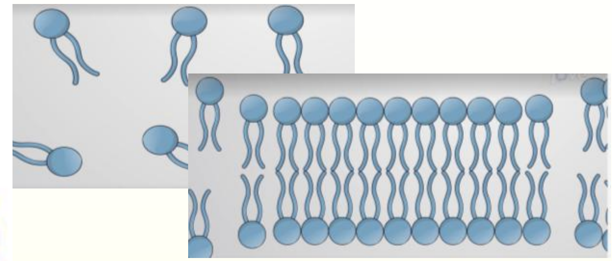
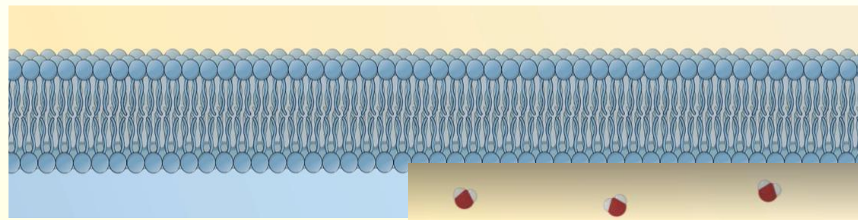


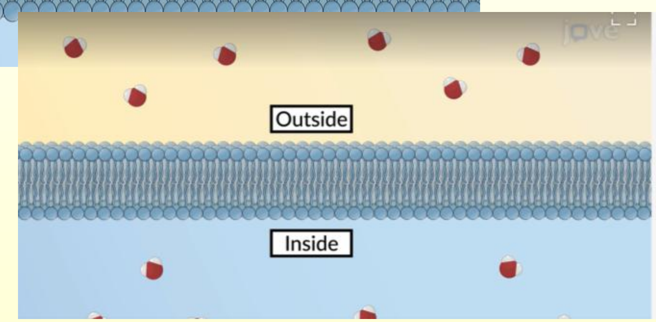
Figure 11–5 A typical membrane lipid molecule has a hydrophilic head and two hydrophobic tails.

PHOSPHOLIPIDS





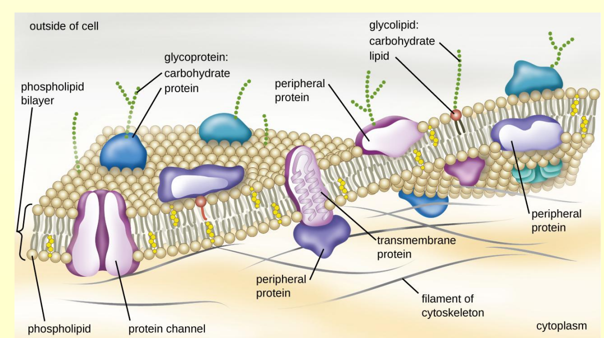




The most abundant lipids in cell membranes are the PHOSPHOLIPIDS which have a phosphate-containing, hydrophilic head linked to a pair of hydrophobic tails.

Phospholipids spontaneously arrange in water, in a continuous bilayer, with the hydrophilic polar heads face the outside and inside of the cell. The hydrophobic non-polar tails line up in the middle to avoid exposure to water.

Phospholipids provide the basic structure, the other components, the proteins and carbohydrates, associate with the phospholipids and contribute to the membrane's function



Phospholipidc Bilayer: Phosphatidylcholine

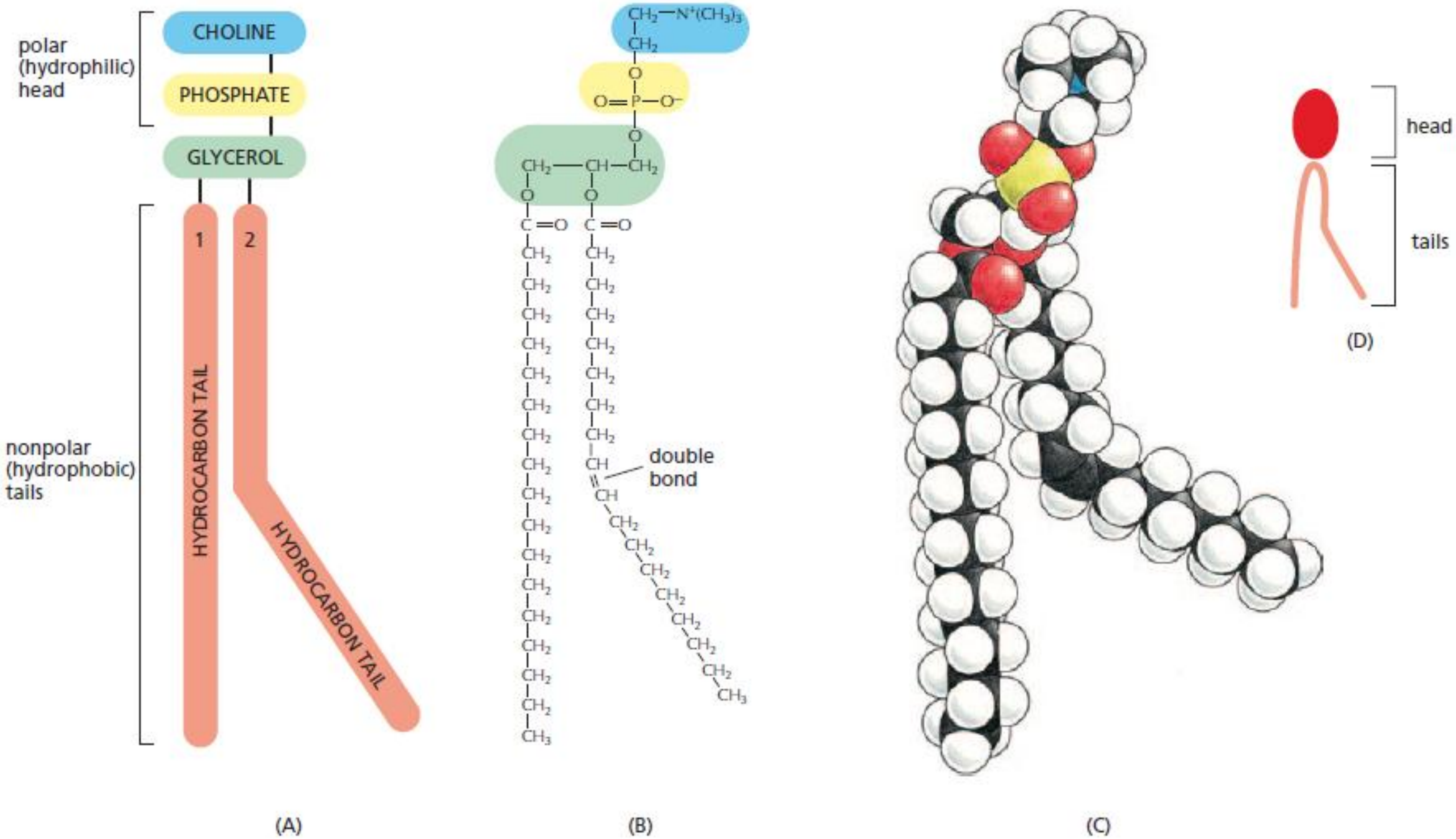


Figure 11–6 Phosphatidylcholine is the most common phospholipid in cell membranes. It is represented schematically in (A), as a chemical formula in (B), as a space-filling model in (C), and as a symbol in (D). This particular phospholipid is built from five parts: the hydrophilic head, which consists of *choline* linked to a *phosphate group*; two *hydrocarbon chains*, which form the hydrophobic tails; and a molecule of glycerol, which links the head to the tails. Each of the hydrophobic tails is a *fatty acid*—a hydrocarbon chain with a –COOH group at one end—which has been attached to glycerol via this group. A kink in one of the hydrocarbon chains occurs where there is a double bond between two carbon atoms. (The "phosphatidyl" part of the name of a phospholipid refers to the phosphate–glycerol–fatty acid portion of the molecule.)

Fatty acids in membrane lipids:

the hydrocarbon tails form a hydrophobic barrier to the diffusion of polar solutes.

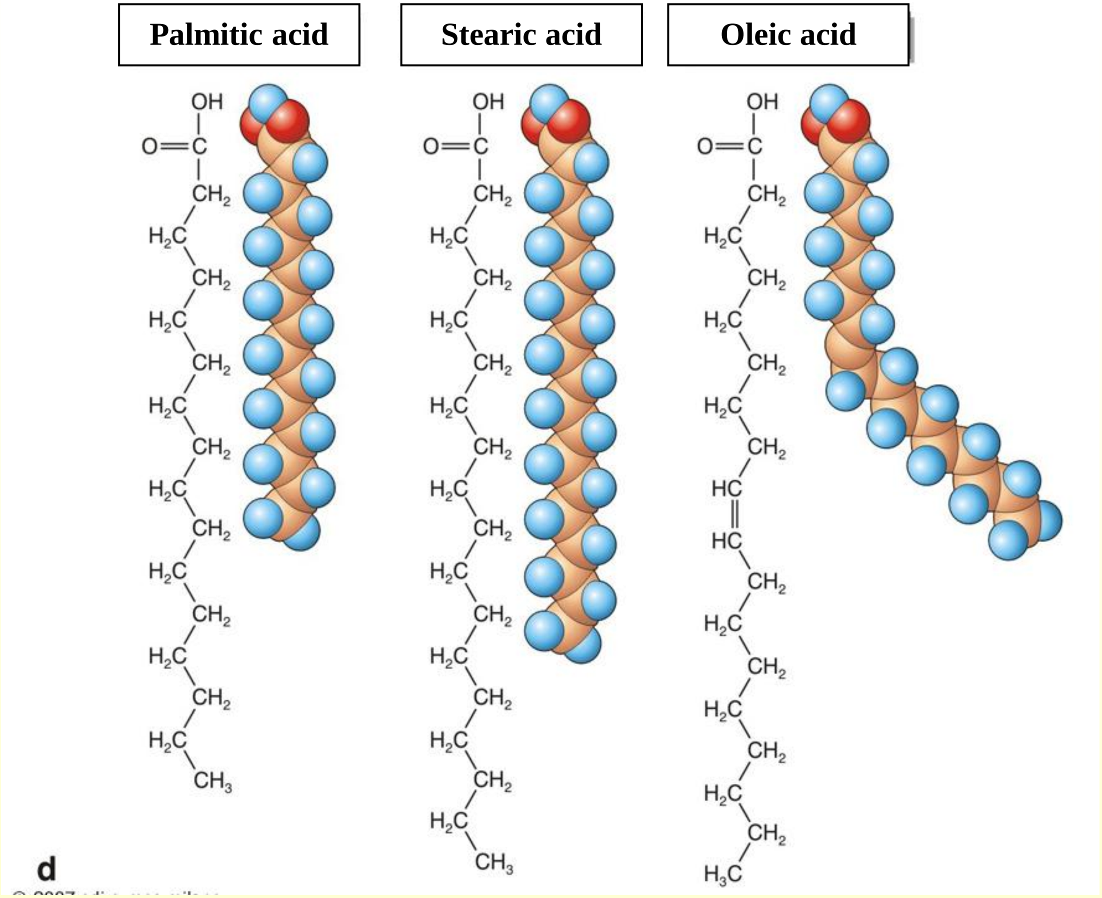
Unsaturated fats: increase membrane fluidity by hindering the packing of other molecules.

Chain length: 14-24C atoms, on average 18-20.Optimal length for the formation of a double layer 6-8 nm thick.

Single bonds

Double bonds

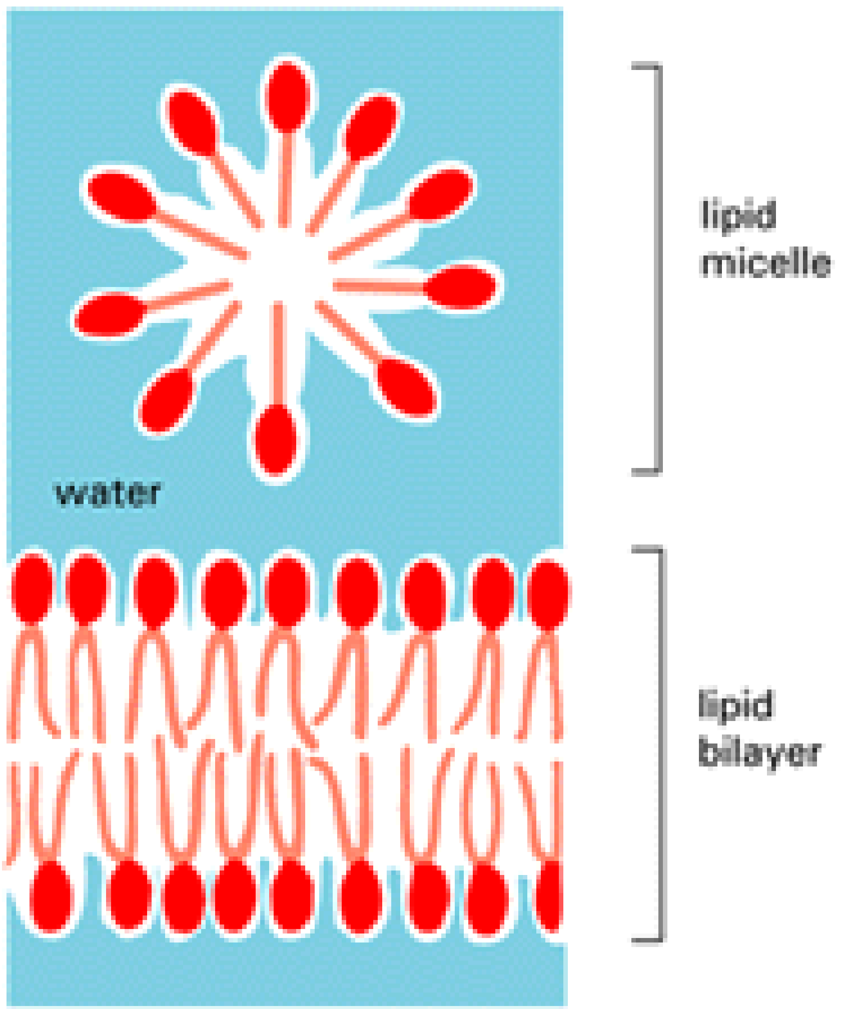
Between fatty acid chains: weak Van der Waals bonds.

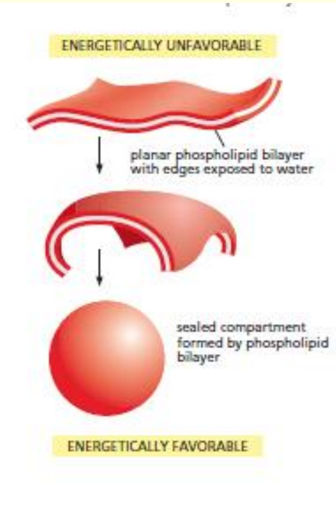


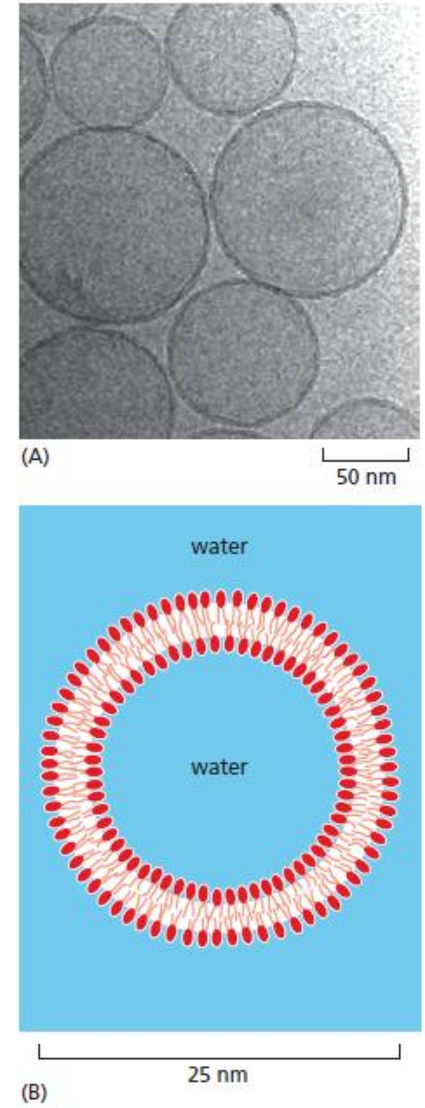
Palmitic e Stearic are saturated fatty acids. Oleic is insaturated fatty acid, with a double bond that causes the chain to bend.

LIPIDS

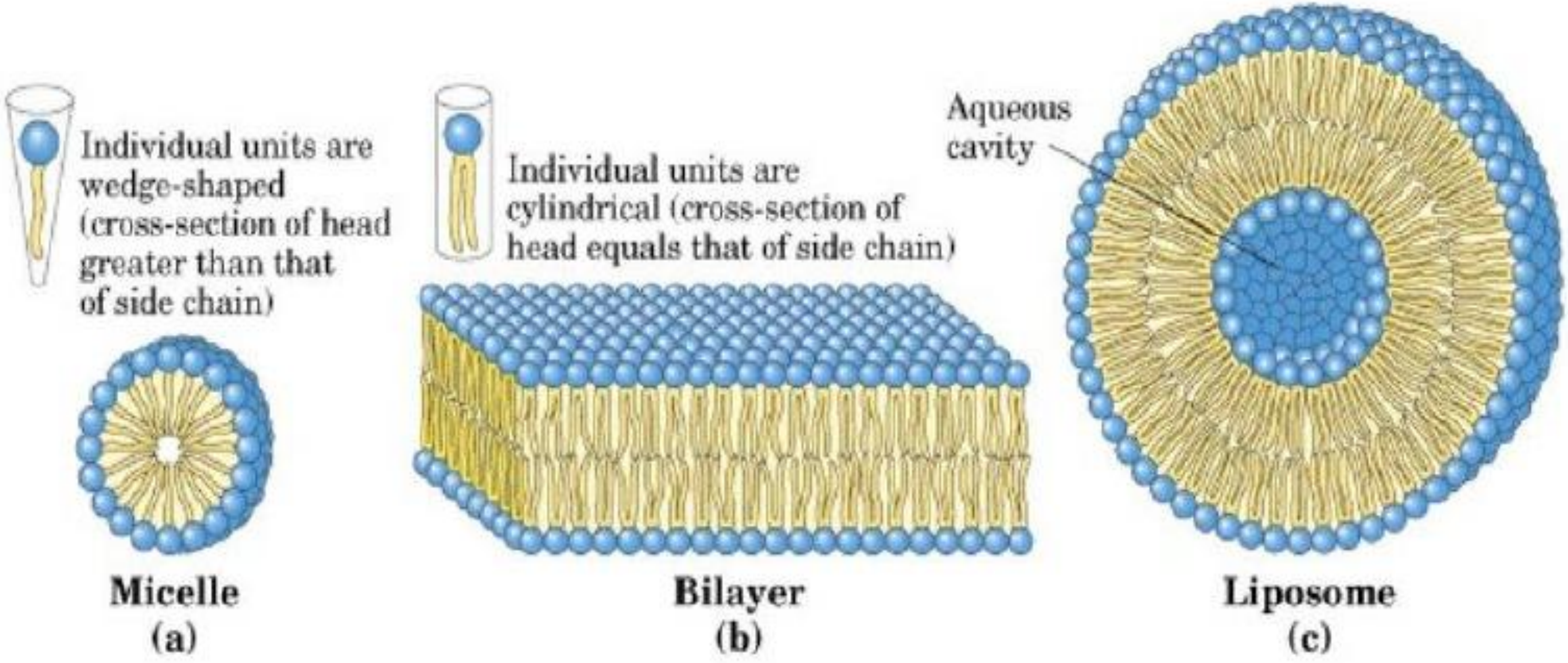
Amphipathic molecules



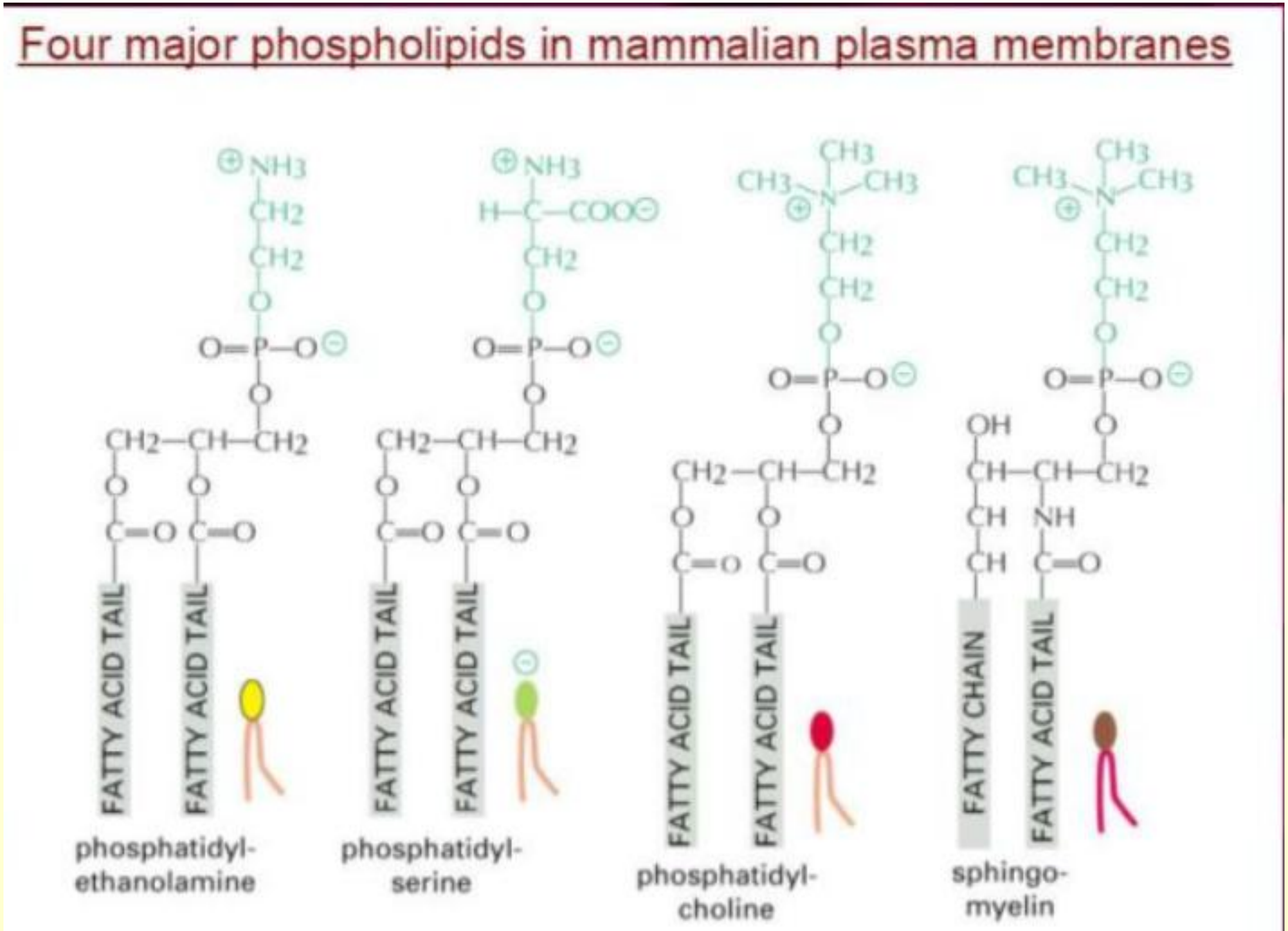




Lipid Bilayers

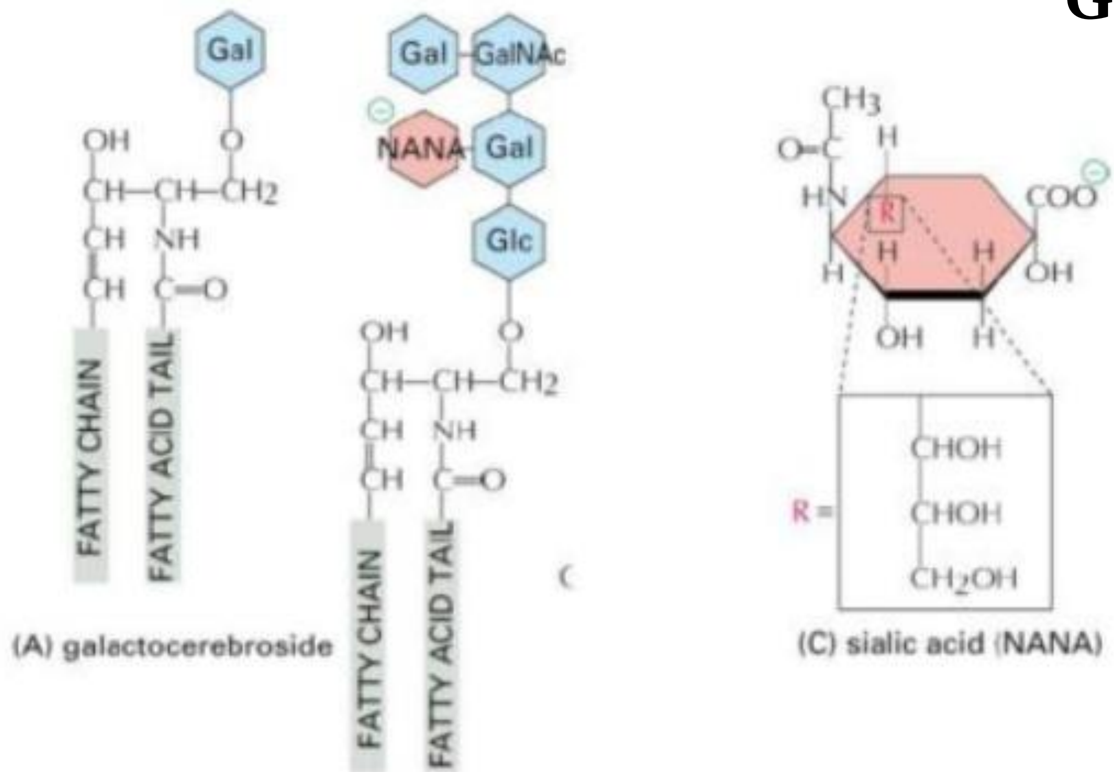


Phospholipids present in mammalian membranes



Glycolipids are found on the surface of all plasma membranes

GLYCOLIPIDS



(A) galactocerebroside

(B) GM1 ganglioside

(C) sialic acid (NANA)

Some lipids are characterized by the presence of sugar groups or carbohydrate linked to the polar head portion. These molecules are called **Glycolipids**.

Glycolipids are located mainly in the plasma membrane, and only in the noncytosolic half of the bilayer

Sterol cholesterol present in mammalian membranes

it constitutes approximately 20% of the lipids in the membrane

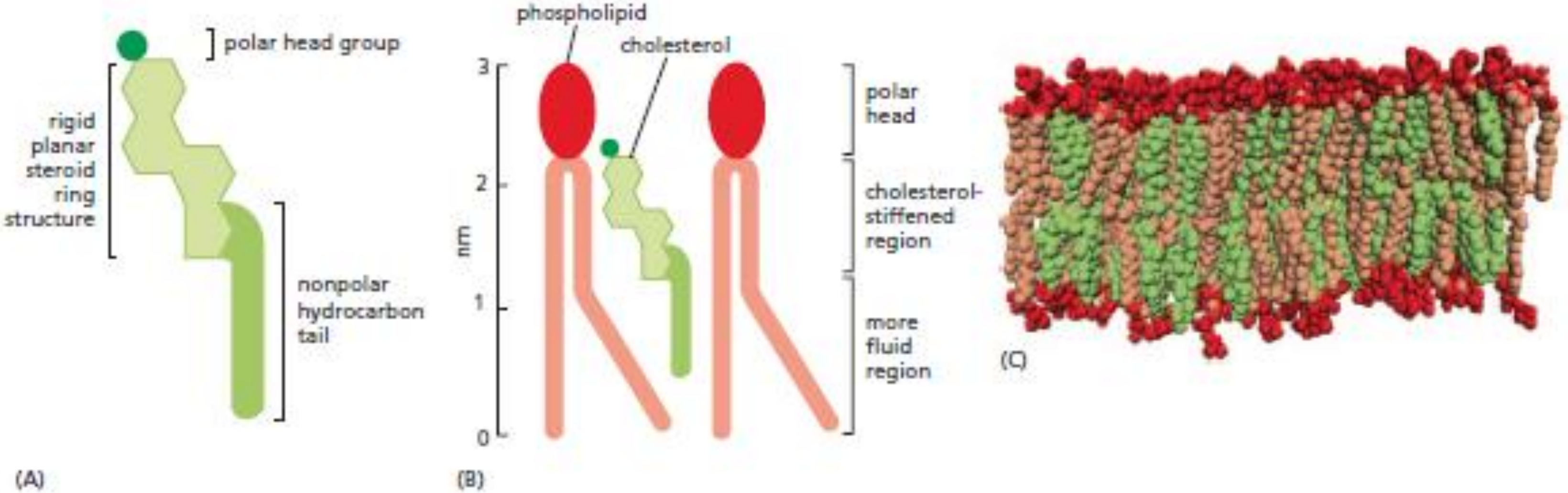


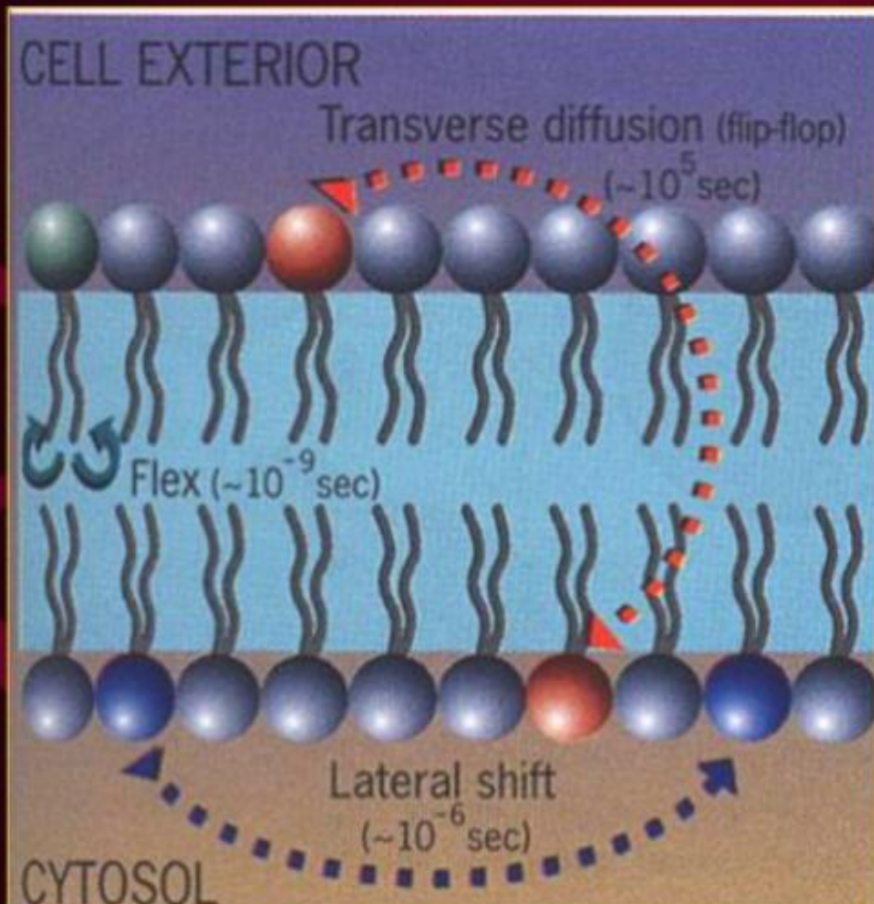
Figure 11–15 Cholesterol tends to stiffen cell membranes. (A) The shape of a cholesterol molecule. (B) How cholesterol fits into the gaps between phospholipid molecules in a lipid bilayer. (C) Space-filling model of the bilayer, with cholesterol molecules in green. The chemical formula of cholesterol is shown in Figure 11–7. (C, from H.L. Scott, *Curr. Opin. Struct. Biol.* 12: 499, 2002.)

membrane fluidity is modulated by the inclusion of the sterol cholesterol

cholesterol tends to stiffen the bilayer, making it less flexible, as well as less permeable.

membrane fluidity

❖ Three kinds of movement of Membrane lipids



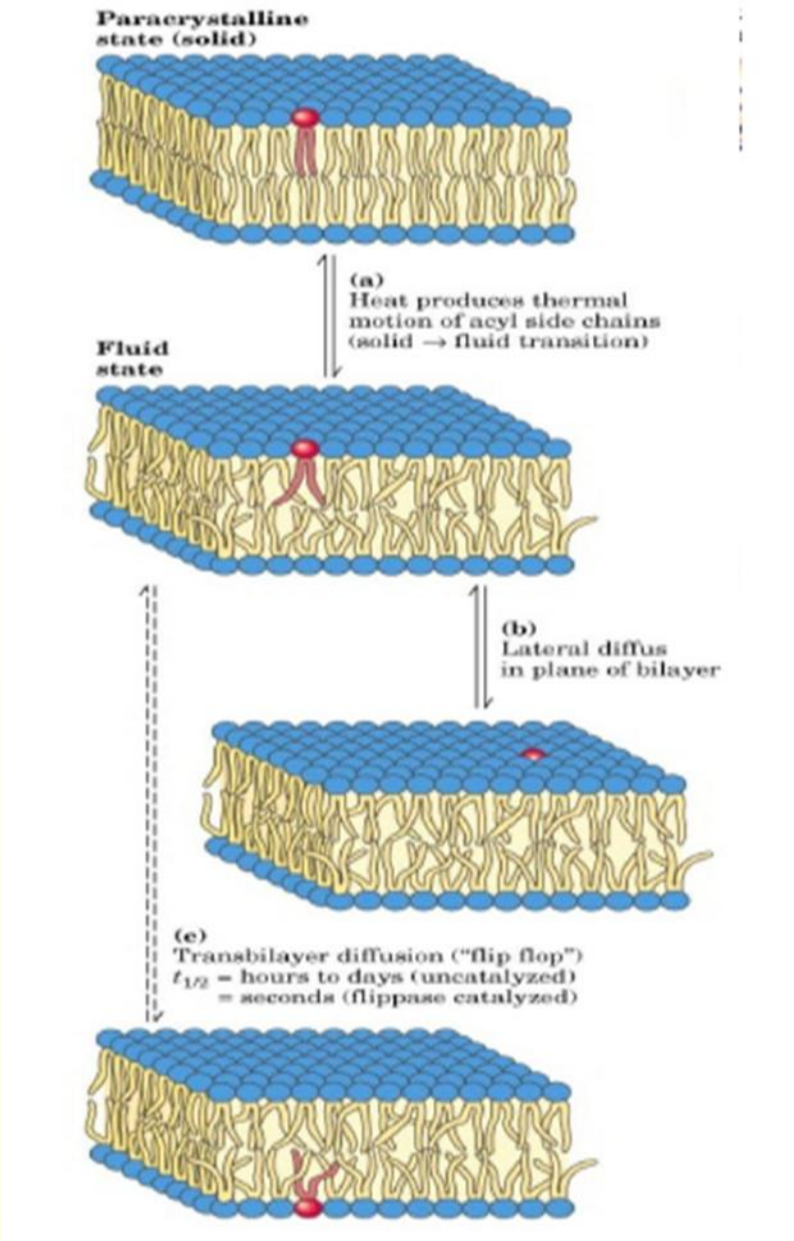
Three kinds of movement:

Rotation about its long axis;

Lateral diffusion by exchanging places;

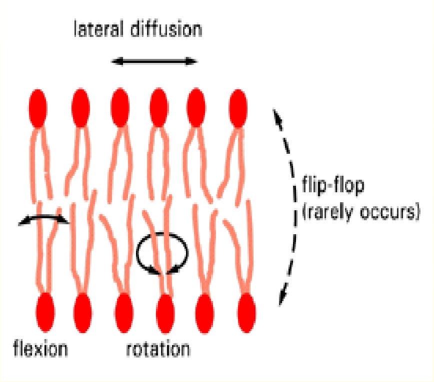
Transverse diffusion, or "flip-flop" from one monolayer to the other. Flippases catalyze the flip-flop.

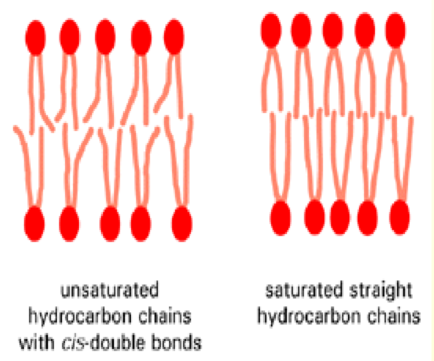
Bilayer Diffusion



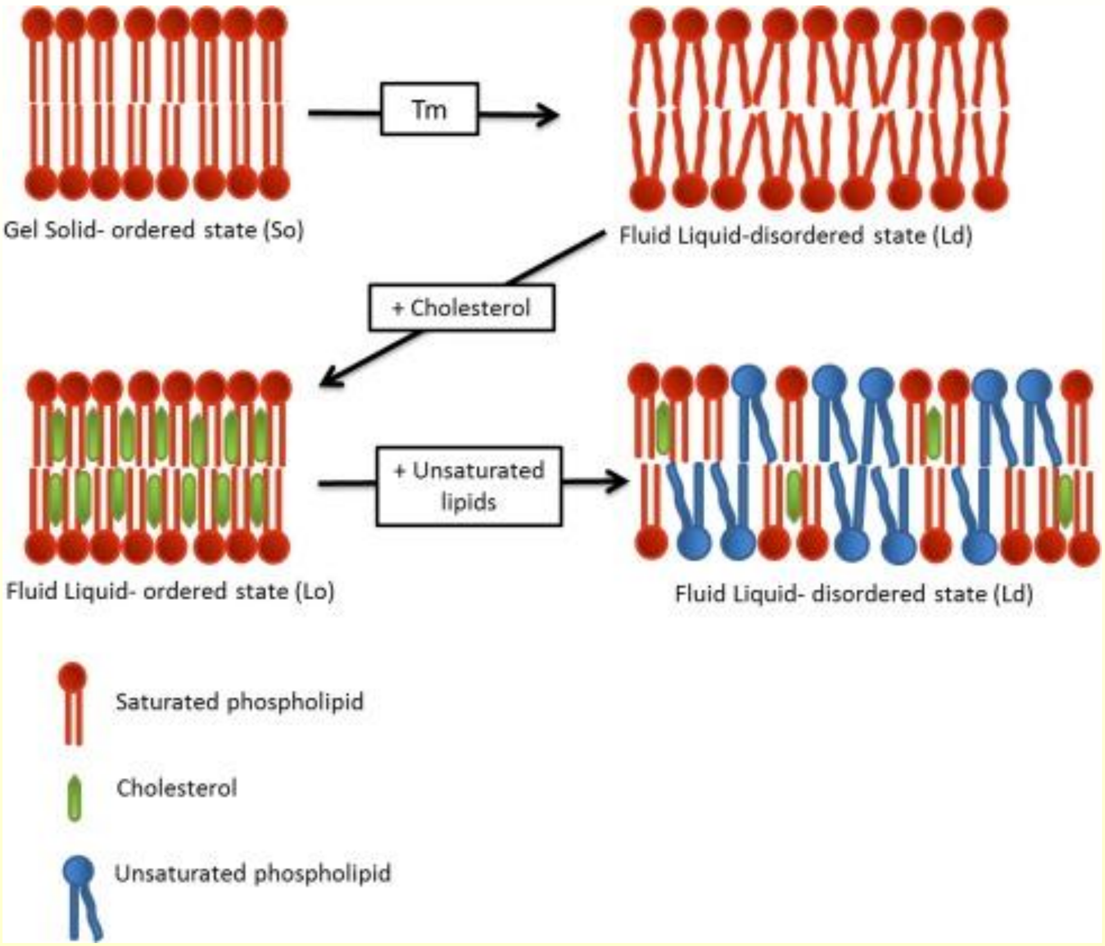
Flip-flop: a rare event

Rotation and lateral diffusion are supported, however.





Factors that influence membrane fluidity



- <u>Temperature</u>:
  - Increases fluidity: Higher temperatures give phospholipids more kinetic energy, causing them to move more freely.
  - Decreases fluidity: Lower temperatures reduce kinetic energy, causing the phospholipids to pack more tightly.
- <u>Fatty acid saturation</u>:
  - Increases fluidity: Unsaturated fatty acids have "kinks" in their tails due to double bonds, which prevent close packing and increase fluidity.
  - Decreases fluidity: Saturated fatty acids have straight tails that can pack together tightly, decreasing fluidity.
- <u>Fatty acid tail length</u>:
  - Increases fluidity: Shorter fatty acid tails have less surface area for interactions, leading to less entanglement and greater fluidity.
  - Decreases fluidity: Longer fatty acid tails have more surface area for intermolecular interactions, leading to more entanglement and less fluidity.
- <u>Cholesterol</u>:
  - At high temperatures: Cholesterol limits the movement of phospholipids, decreasing fluidity and stabilizing the membrane.
  - At low temperatures: Cholesterol disrupts tight packing, preventing the membrane from solidifying and increasing fluidity

Lipid composition of different cell membranes, expressed as the **percentage of total lipid by weight**

TABLE 10–1 Approximate Lipid Compositions of Different Cell Membranes

	PERCENTAGE OF TOTAL LIPID BY WEIGHT					
LIPID	LIVER CELL PLASMA MEMBRANE	RED BLOOD CELL PLASMA MEMBRANE	MYELIN	MITOCHONDRION (INNER AND OUTER MEMBRANES)	ENDOPLASMIC RETICULUM	*E. COLI* BACTERIUM
Cholesterol	17	23	22	3	6	0
Phosphatidylethanolamine	7	18	15	25	17	70
Phosphatidylserine	4	7	9	2	5	trace
Phosphatidylcholine	24	17	10	39	40	0
Sphingomyelin	19	18	8	0	5	0
Glycolipids	7	3	28	trace	trace	0
Others	22	13	8	21	27	30

B. Membrane Proteins: The "Mosaic" Part of the Model

❖Membranes contain integral, peripheral, and lipid-anchored proteins:

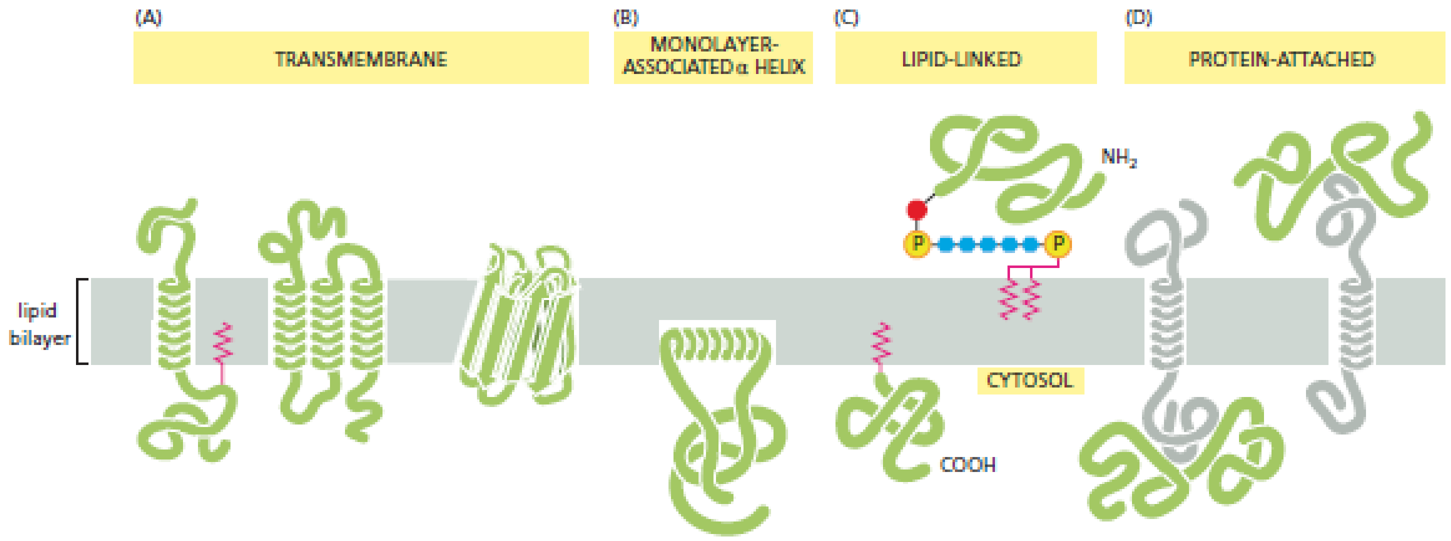
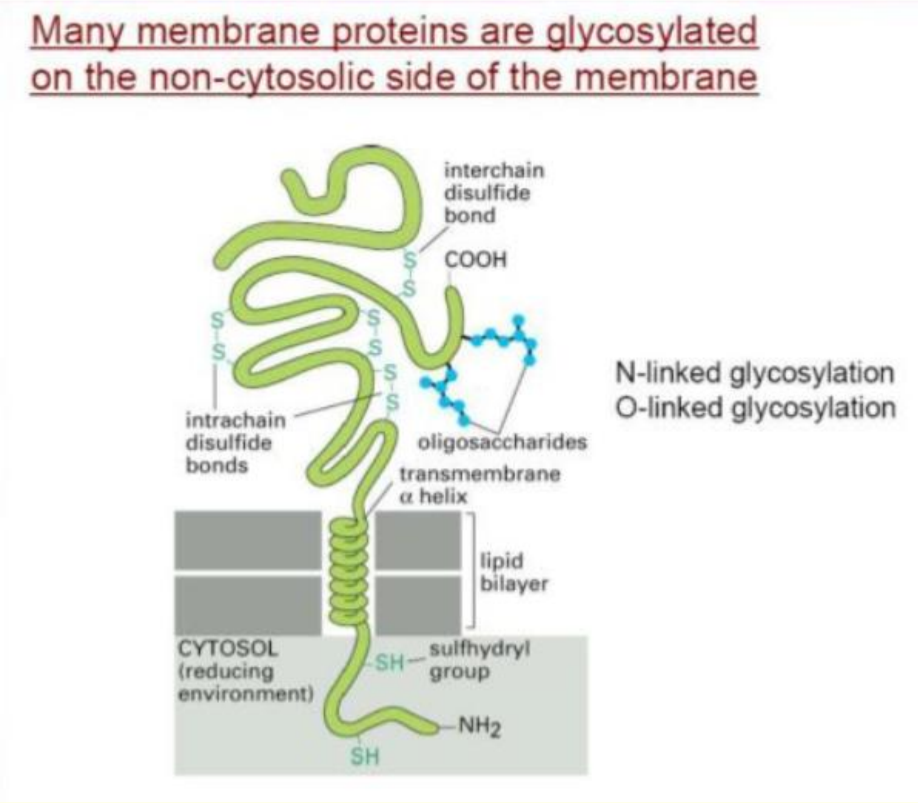
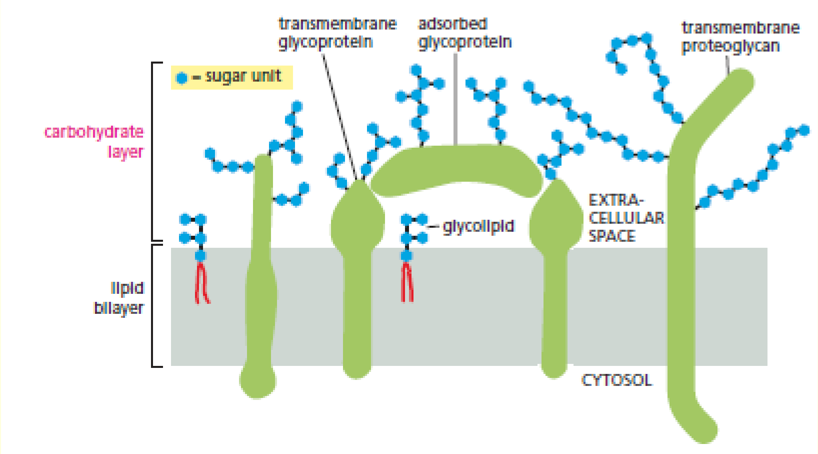


Figure 11–20 Membrane proteins can associate with the lipid bilayer in different ways. (A) Transmembrane proteins extend across the bilayer as a single α helix, as multiple α helices, or as a rolled-up β sheet (called a β barrel). (B) Some membrane proteins are anchored to the cytosolic half of the lipid bilayer by an amphipathic α helix. (C) Others are linked to either side of the bilayer solely by a covalently attached lipid molecule (red zigzag lines). (D) Many proteins are attached to the membrane only by relatively weak, noncovalent interactions with other membrane proteins. All except (D) are *integral membrane proteins*.

PLASMA MEMBRANE PROTEINS

GLYCOPROTEINS

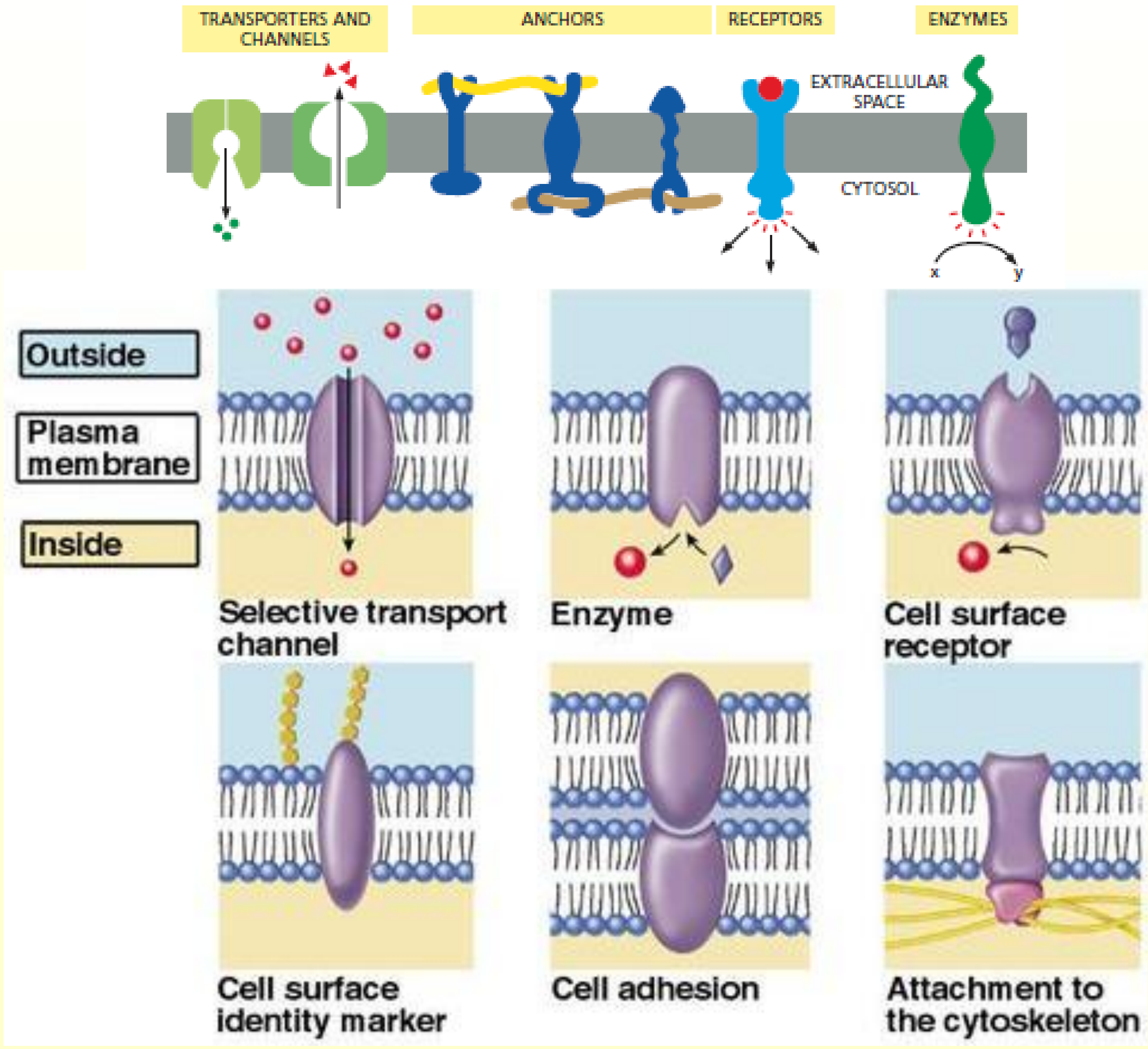




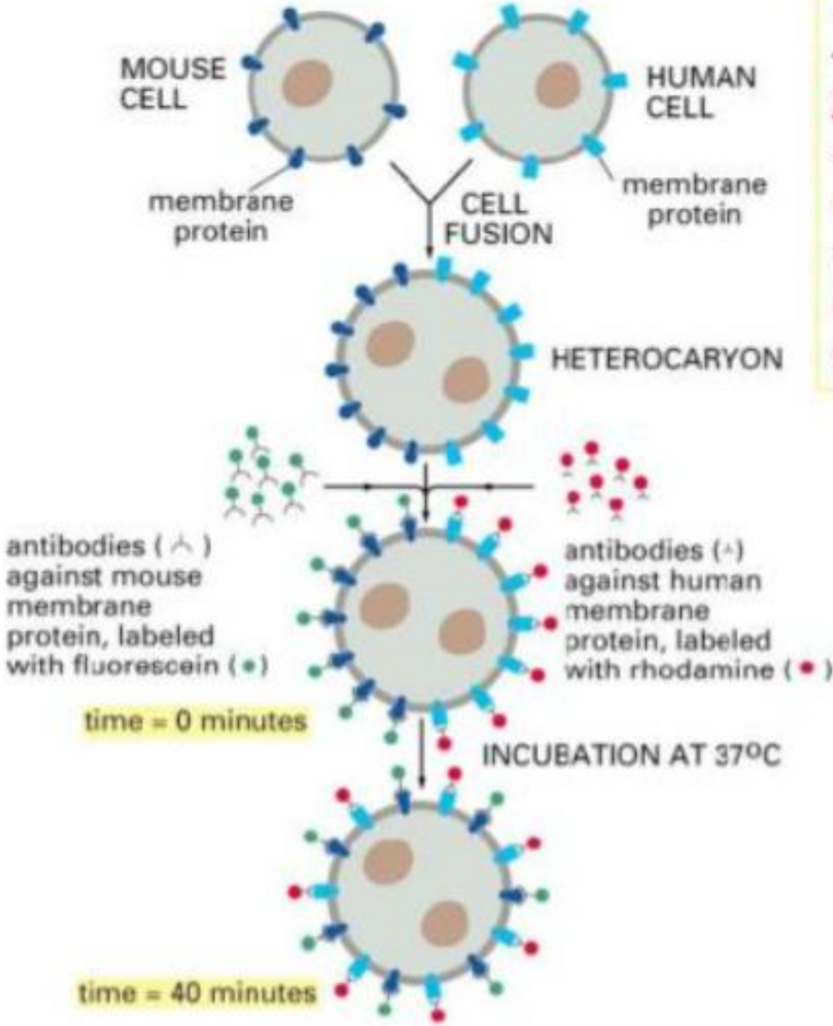
All of the carbohydrate on the glycoproteins is located on the outside of the plasma membrane,

where it forms a sugar coating called the *carbohydrate layer* or **glycocalyx**

FUNCTIONS OF PLASMA MEMBRANE PROTEINS



Plasma membrane proteins can move laterally in the lipid bilayer

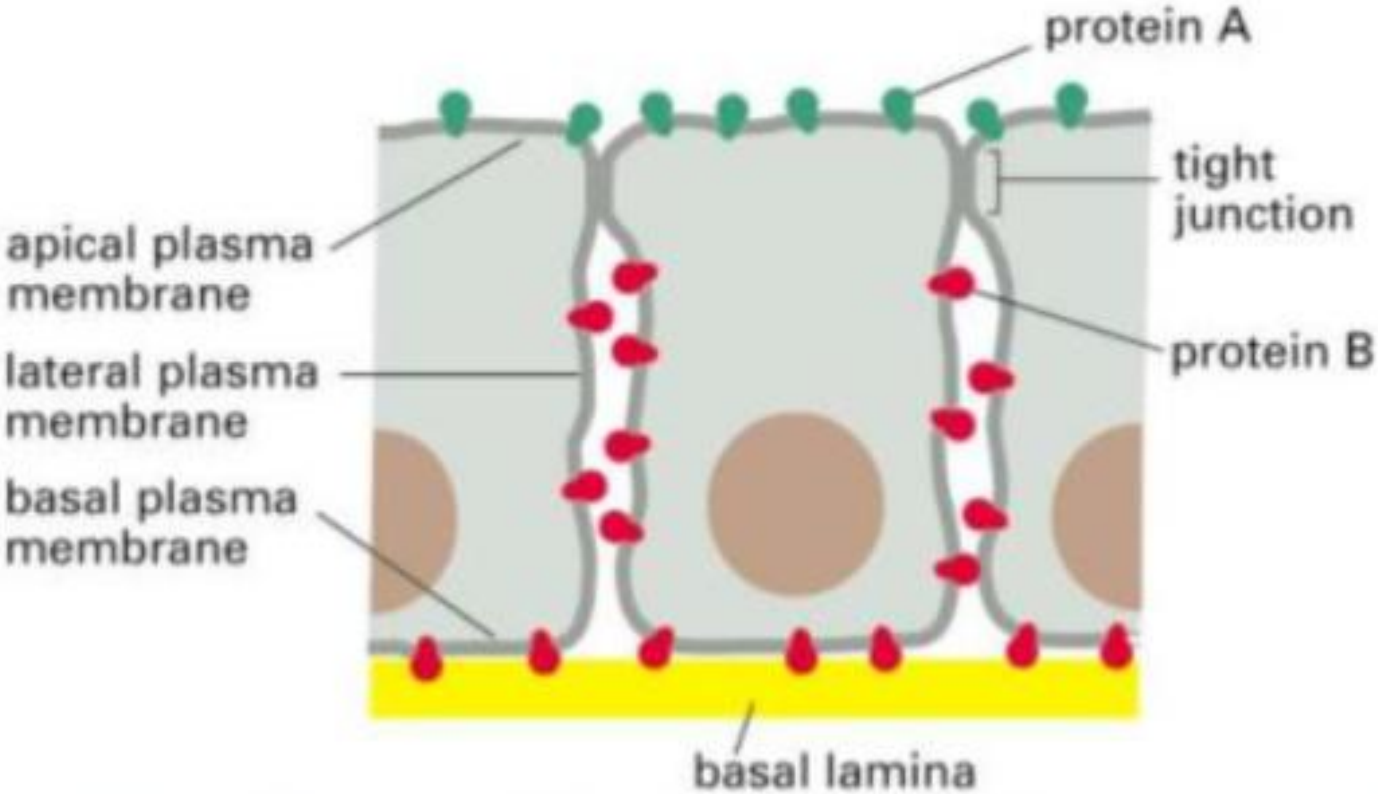


The mobility of membrane proteins can be shown experimentally by the mixing of membrane proteins that occurs when two cells are tagged with different fluorescent labels and then induced to fuse

Many membrane proteins vary in their mobility.

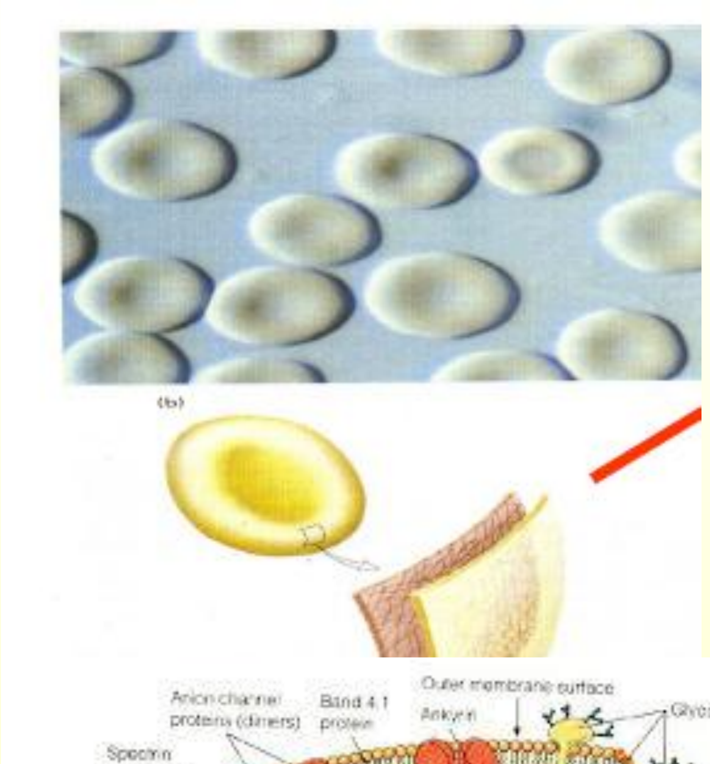
Protein movements are limited by interactions with the cytoskeleton, other proteins and ECM.

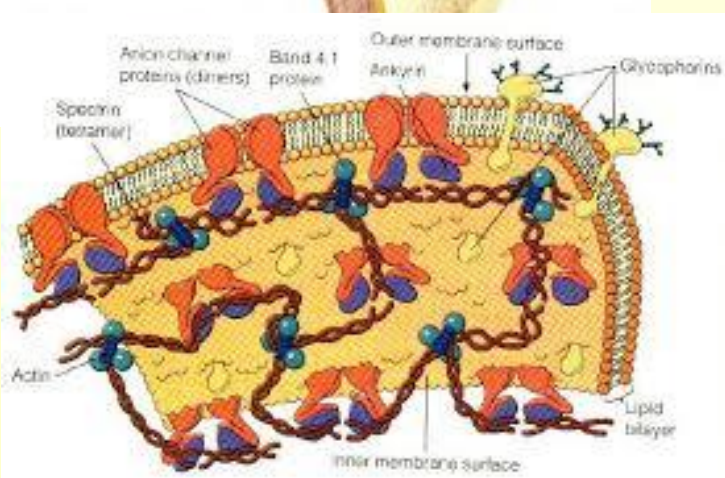
Membrane proteins and lipids can be confined to s specific domain

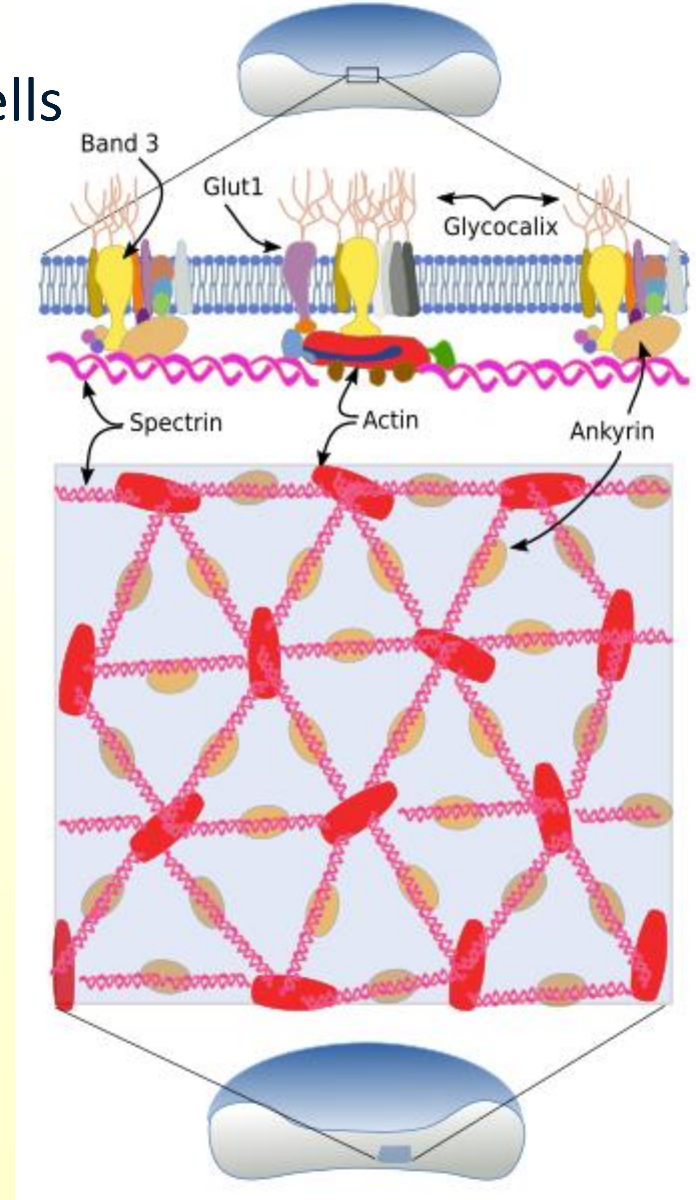


Membrane proteins are restricted to particular domains of the plasma membrane of epithelial cells in the gut membrane proteins in the cytosolic inner face establish bonds with the cytoskeletal proteins

Red blood cells





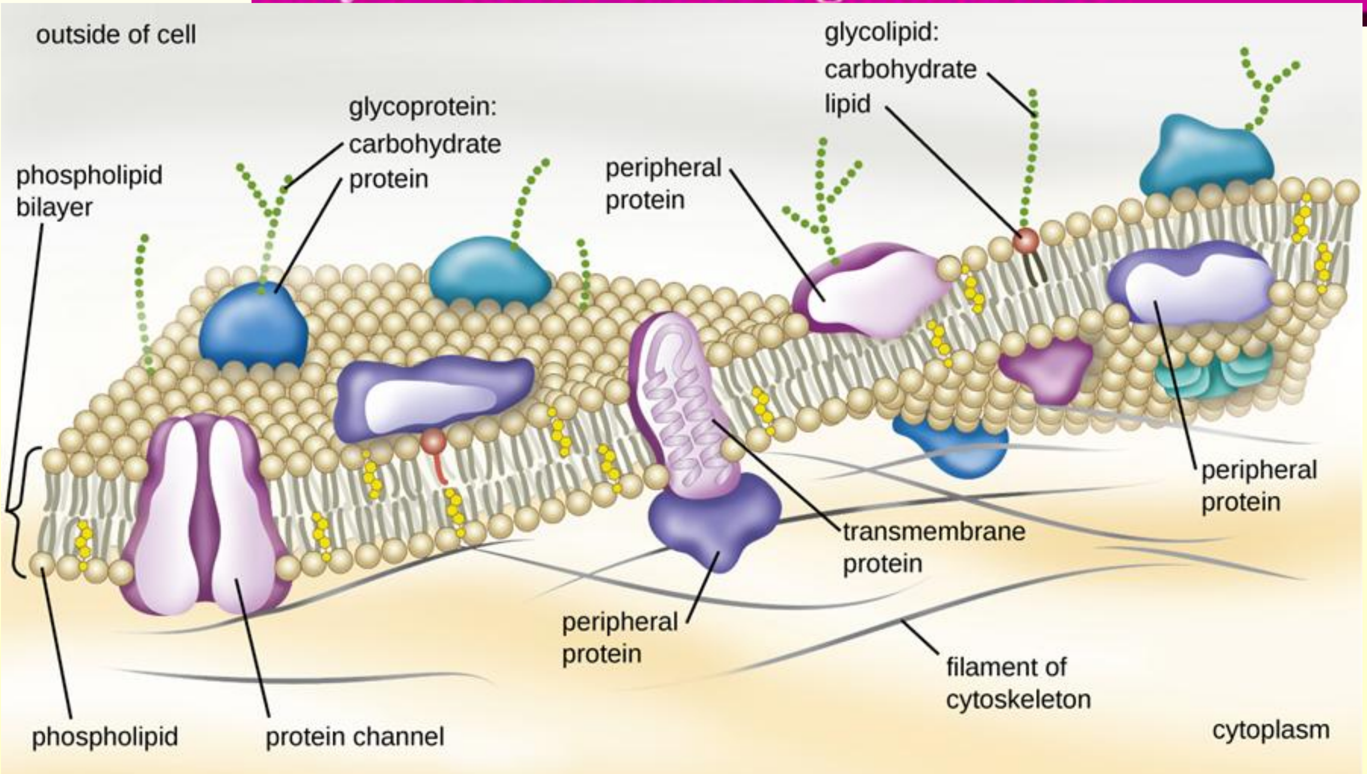


C. Membrane Carbohydrates

❖ Membrane contain carbohydrates convalently linked to lipids and proteins on the extracellular surface of the bilayer.

❖ Glycoproteins have short , branched carbohydrates for interactions with other cells and structures outside the cell.

❖ Glycolipids have larger carbohydrate chains that may be cell-to-cell recognition sites.



GLYCOCALYX

The Glycocalyx:

- Is the "sugar coat" located on the outer surface of the outer leaflet of the Cell membrane.
- Is responsible for the "fuzziness" seen on Electron Microscope.
- Composition: Consists of polar oligosaccharide side chains covalently linked to proteins and some lipids of the plasma membrane.
- Functions:

  (a) The glycocalyx aids in **attachment of some cells** to extracellular matrix components.

  (b) It **binds** antigens and enzymes to the cell surface.

  (c) It facilitates **cell-cell recognition and interaction.**

  (d) It **protects** cells from injury by preventing contact with inappropriate substances.

  (e) It assists T cells and antigen-presenting cells in **aligning with each** other.

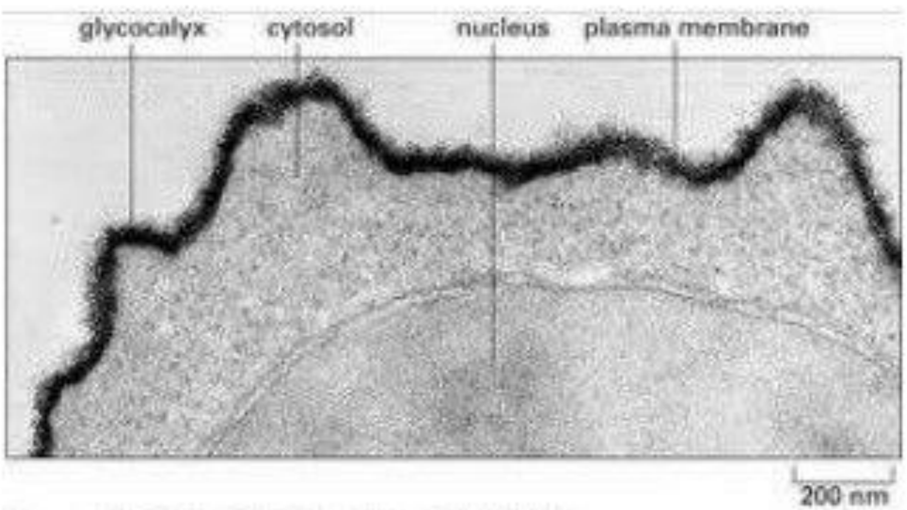
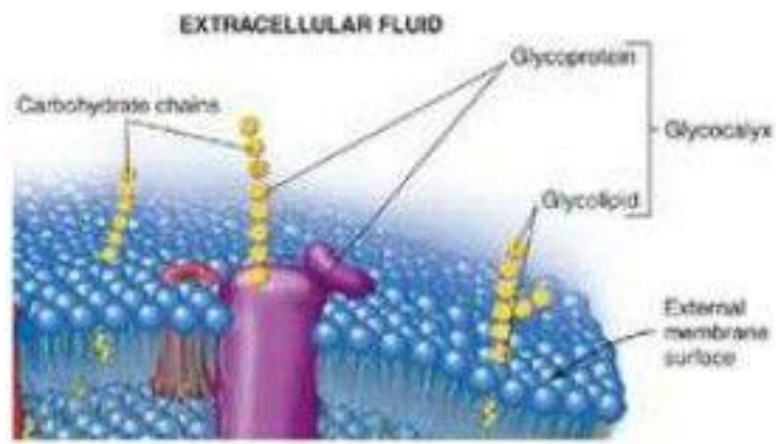
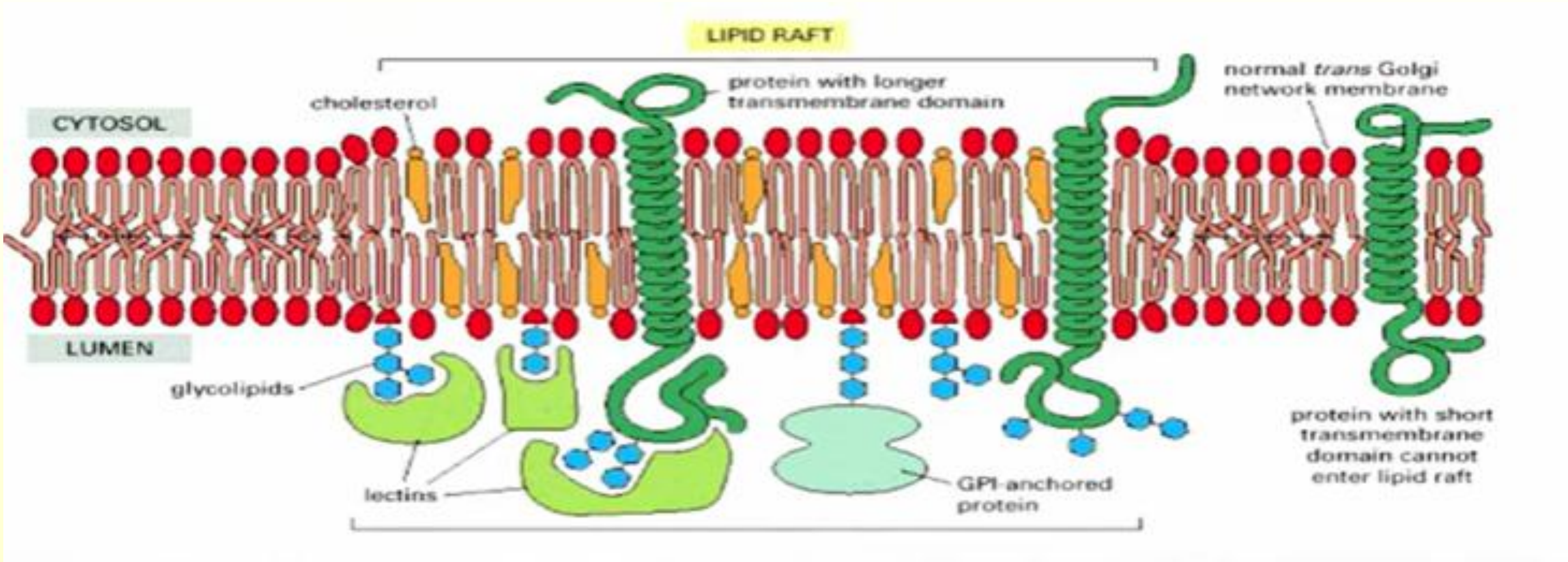


Figure 10-44. Molecular Biology of the Cell, 4th Edition.



❖ Lipid composition can influence the activity of membrane proteins and determine the physical state of the membrane.

❖Biomembrane have agglomeration



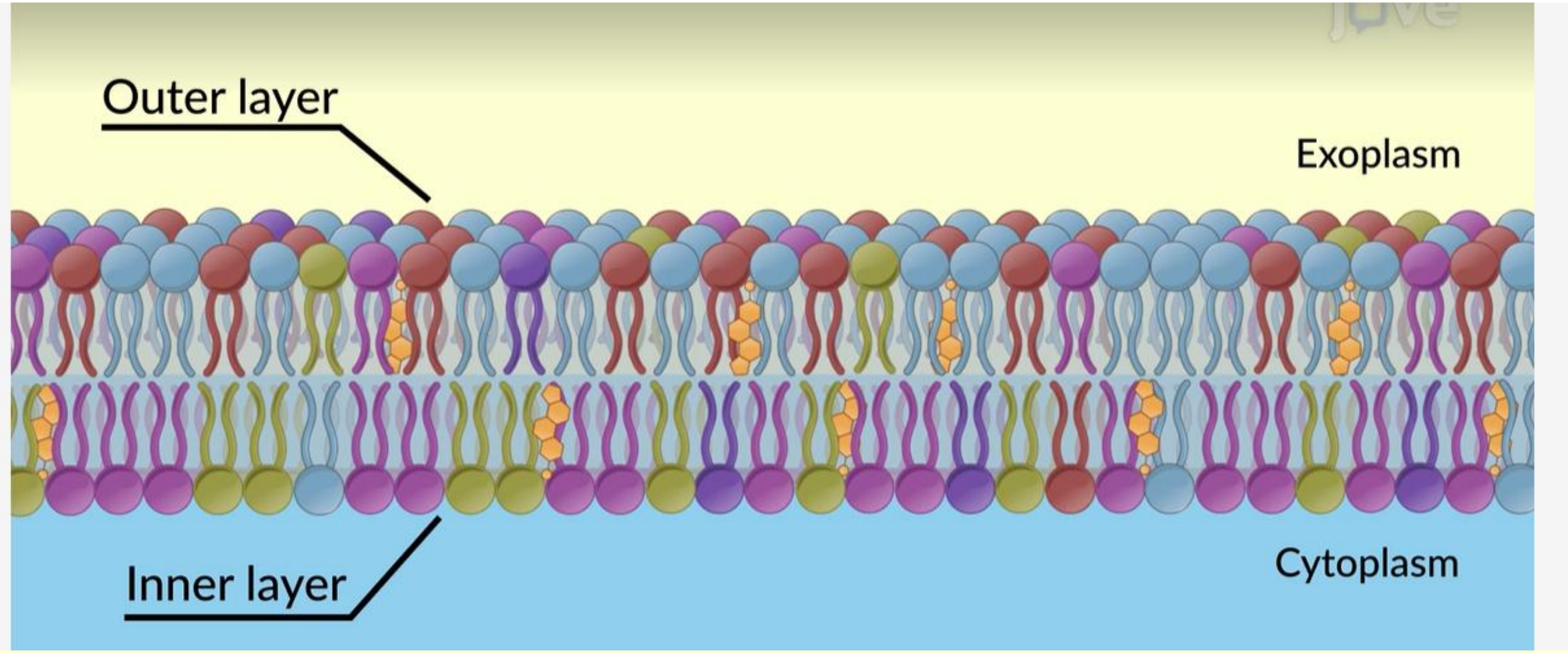
Lipid rafts are dynamic microdomains in the plasma membrane that are enriched in cholesterol and sphingolipids, creating ordered platforms that organize proteins and regulate cellular functions like signaling, membrane trafficking, and cholesterol homeostasis

CELL MEMBRANES HAVE DIFFERENT COMPOSITIONS
DEPENDING ON THE **CELL TYPE** AND **ORGANELLE**.

Chemical composition of some membranes (by percentage)

Membrane	Proteins	Lipids	Carbohydrates
Myelin	18%	79%	3%
Red blood cell (Erythrocyte)	49%	43%	8%
Liver cell (Hepatocyte)	46%	52%	4%
Inner mitochondrial membrane	76%	24%	0%

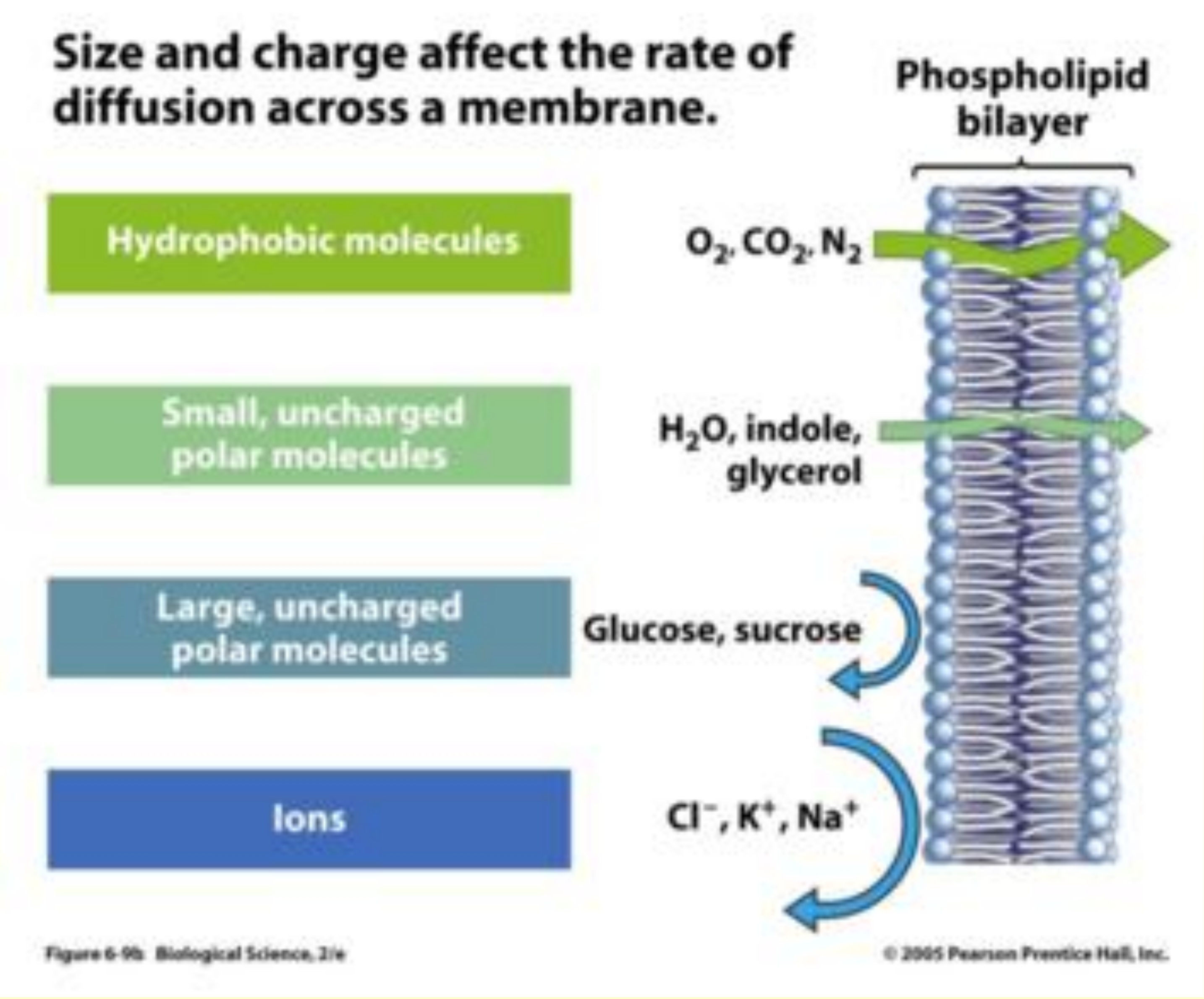
Membrane ASYMMETRY



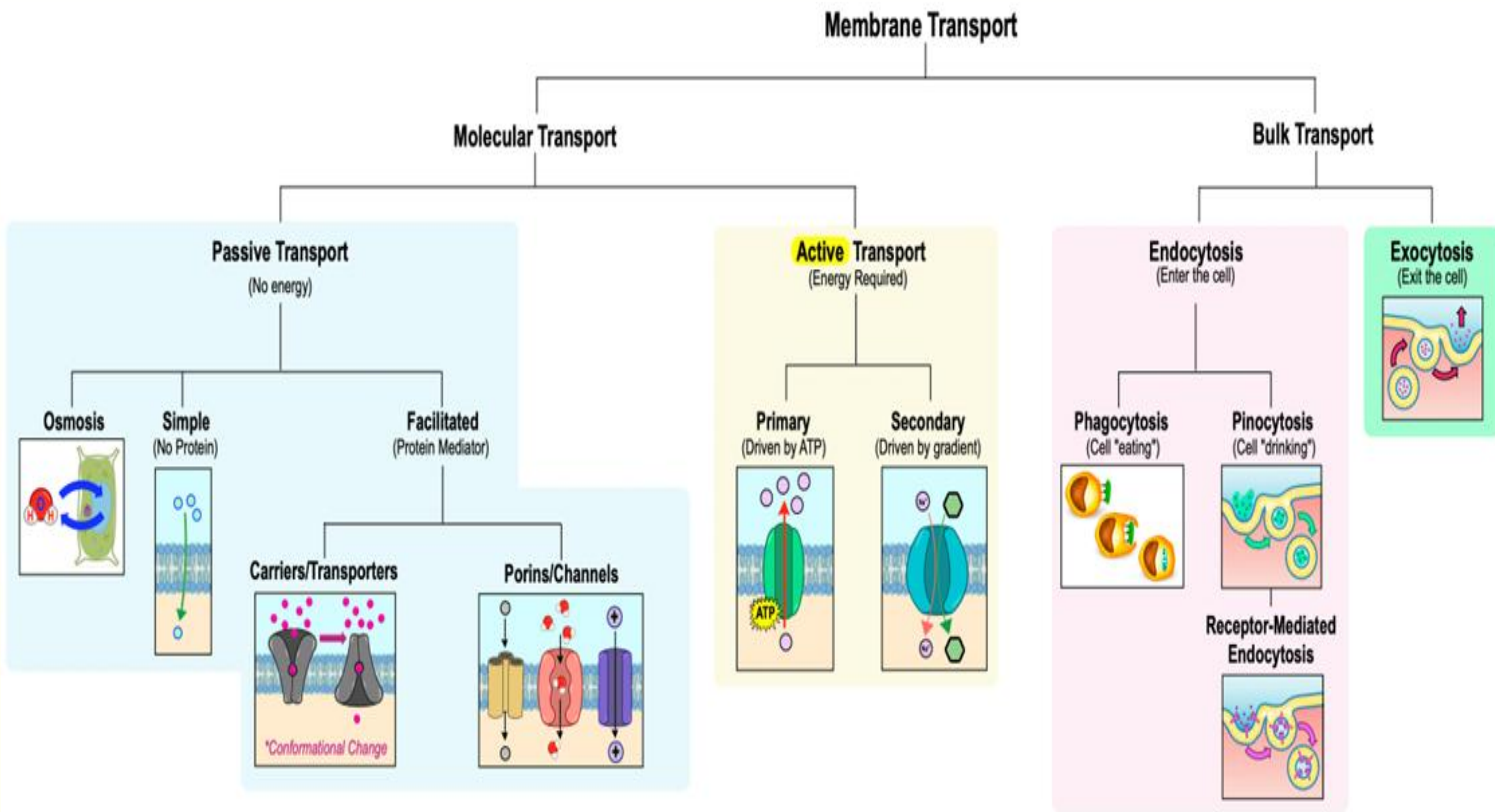
- The inner and outer layers of the plasma membrane have different lipid compositions
- Due to the membrane asymmetry, the inside and outside membrane faces can each function distinctly.

https://app.jove.com/embed/player?id=11659&access=543926bbac&t=1&s=1&fpv=1

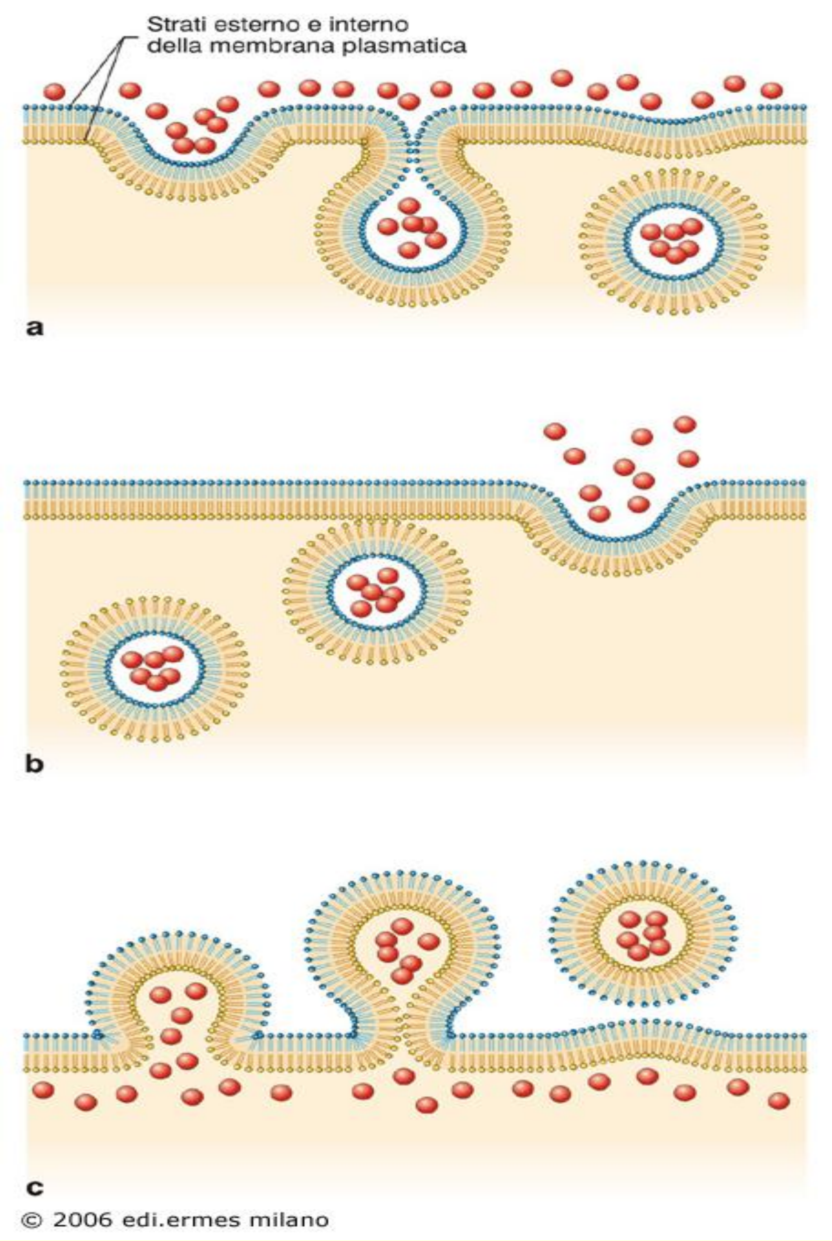
Membrane SEMIPERMEABLE.



CATEGORIES OF TRANSPORT BASED ON ENERGY REQUIREMENTS



Bulk transport

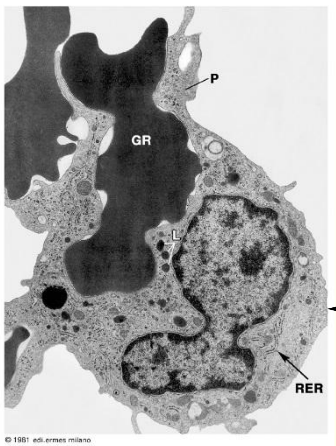


ENDOCYTOSIS

EXOCYTOSIS

MEMBRANE BUDDING

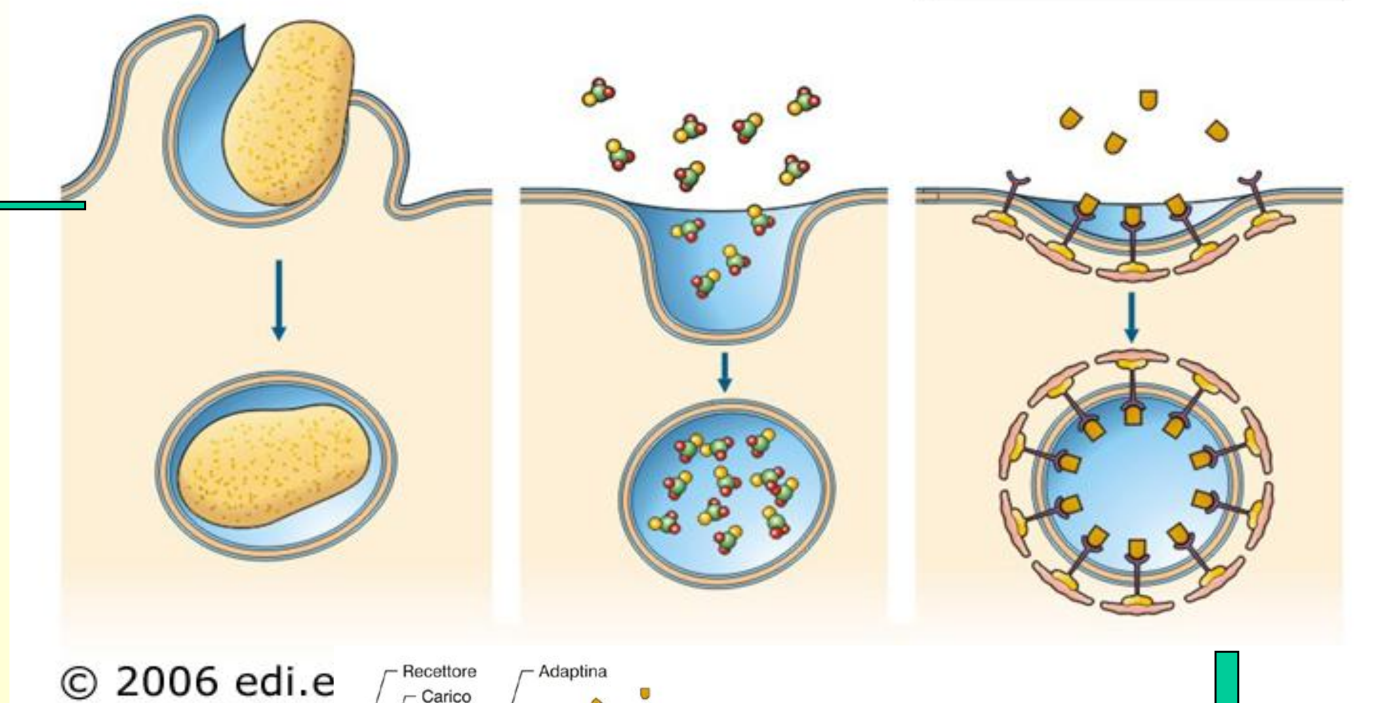
ENDOCYTOSIS

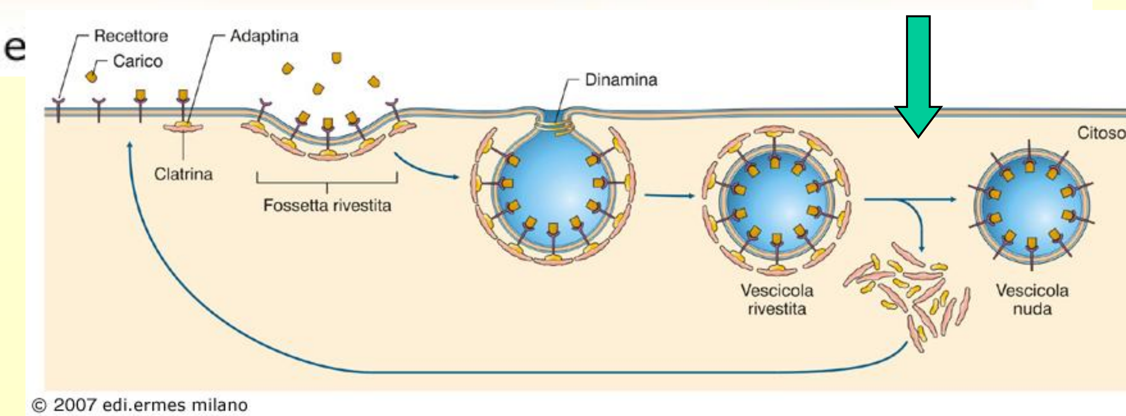


Phagocytosis

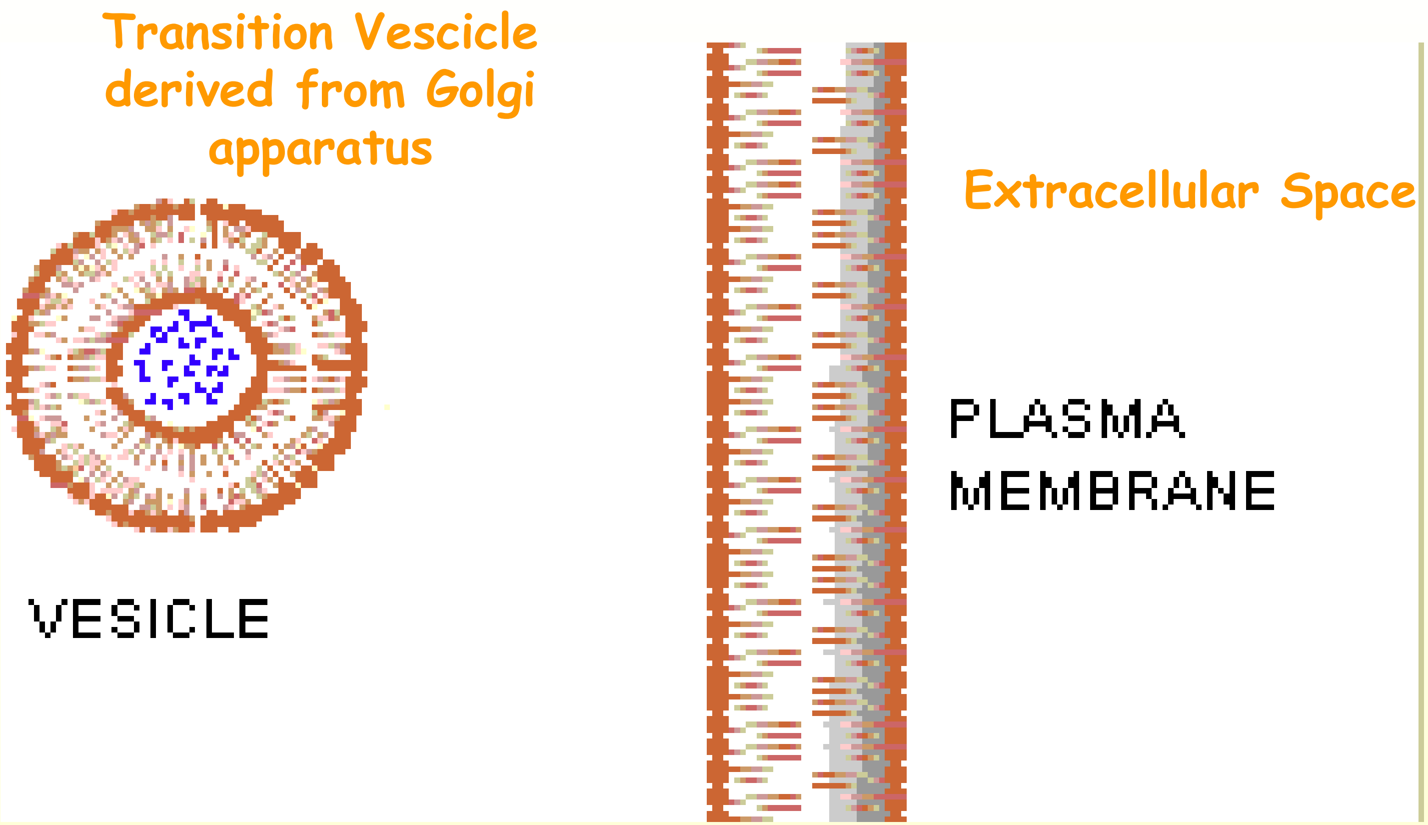
Pinocytosis

Receptor-mediated endocytosis



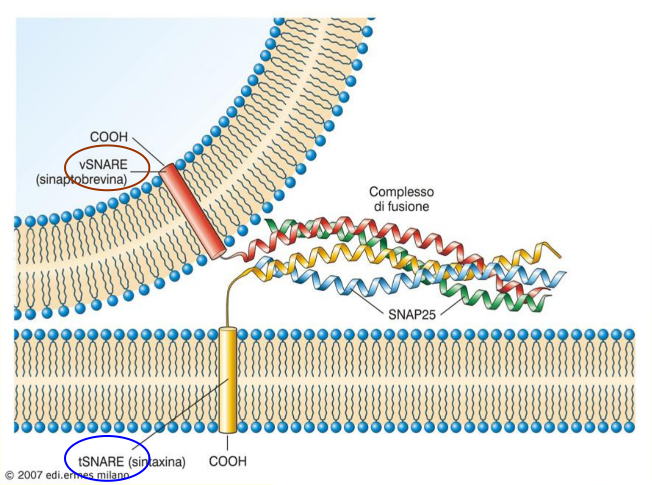


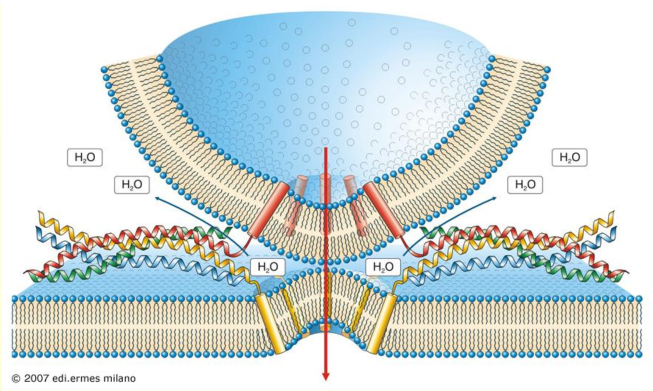
EXOCYTOSIS

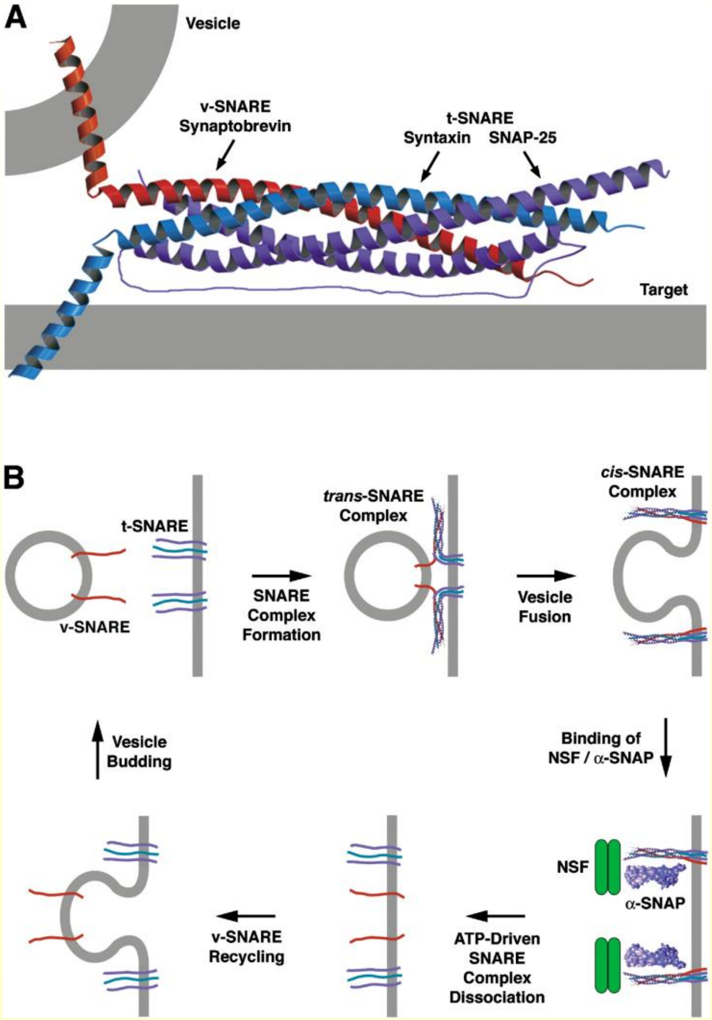


The proteins produced in the RER bud off as transition vesicles, are transported to the Golgi apparatus, and detach as condensation vesicles; then, as secretory vesicles, they migrate to the apical cytoplasm where the membranes fuse, coating the contents on the outside.

Fusion of transition vesicles

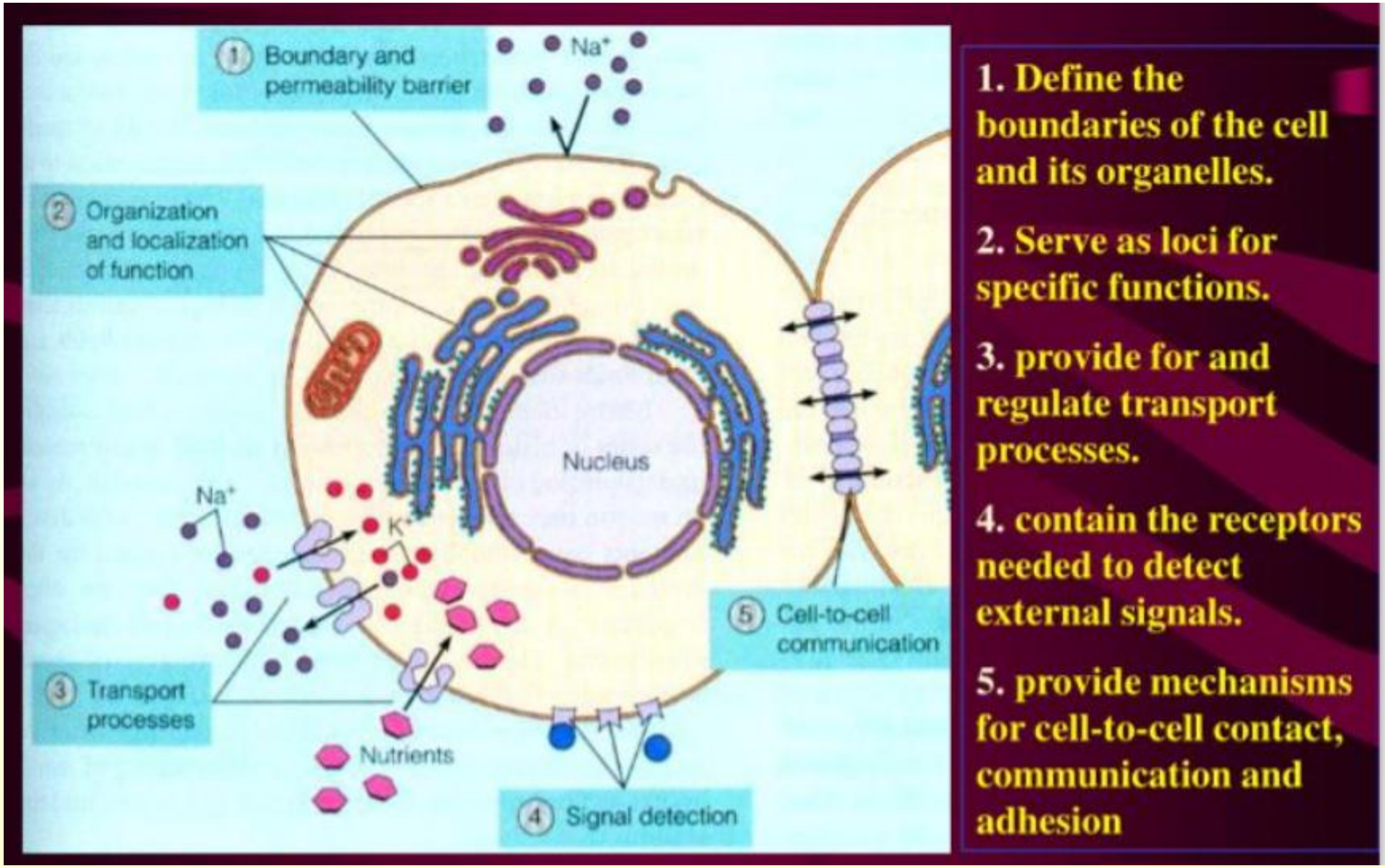






The fusion of vesicles is regulated by the presence of specific proteins called **SNARE**.

Overview of delle membrane functions



Specialized Membranes Functions

nuclear membrane, mitochondrial, Golgi and RER, vesicles, lysosomes, etc …

Essential Concepts

• Cell membranes enable cells to create barriers that confine particular molecules to specific compartments. They consist of a continuous double layer—a bilayer—of lipid molecules in which proteins are embedded.
• The lipid bilayer provides the basic structure and barrier function of all cell membranes.
• Membrane lipid molecules are amphipathic, having both hydrophobic and hydrophilic regions. This property promotes their spontaneous assembly into bilayers when placed in water, forming closed compartments that reseal if torn.
• There are three major classes of membrane lipid molecules: phospholipids, sterols, and glycolipids.
• The lipid bilayer is fluid, and individual lipid molecules are able to diffuse within their own monolayer; they do not, however, spontaneously flip from one monolayer to the other.
The two lipid monolayers of a cell membrane have different lipid compositions, reflecting the different functions of the two faces of the membrane.
• Cells that live at different temperatures maintain their membrane fluidity by modifying the lipid composition of their membranes.
• Membrane proteins are responsible for most of the functions of cell membranes, including the transport of small, water-soluble molecules across the lipid bilayer.
• Transmembrane proteins extend across the lipid bilayer, usually as one or more α helices but sometimes as a β sheet rolled into the form of a barrel.
• Other membrane proteins do not extend across the lipid bilayer but are attached to one or the other side of the membrane, either by noncovalent association with other membrane proteins, by covalent attachment of lipids, or by association of an exposed amphipathic α helix with a single lipid monolayer.
• Most cell membranes are supported by an attached framework of proteins. An especially important example is the meshwork of fibrous proteins that forms the cell cortex underneath the plasma membrane.
• Although many membrane proteins can diffuse rapidly in the plane of the membrane, cells have ways of confining proteins to specific membrane domains. They can also immobilize particular membrane proteins by attaching them to intracellular or extracellular macromolecules.
• Many of the proteins and some of the lipids exposed on the surface of cells have attached sugar chains, which form a carbohydrate layer that helps protect and lubricate the cell surface, while also being involved in specific cell–cell recognition