

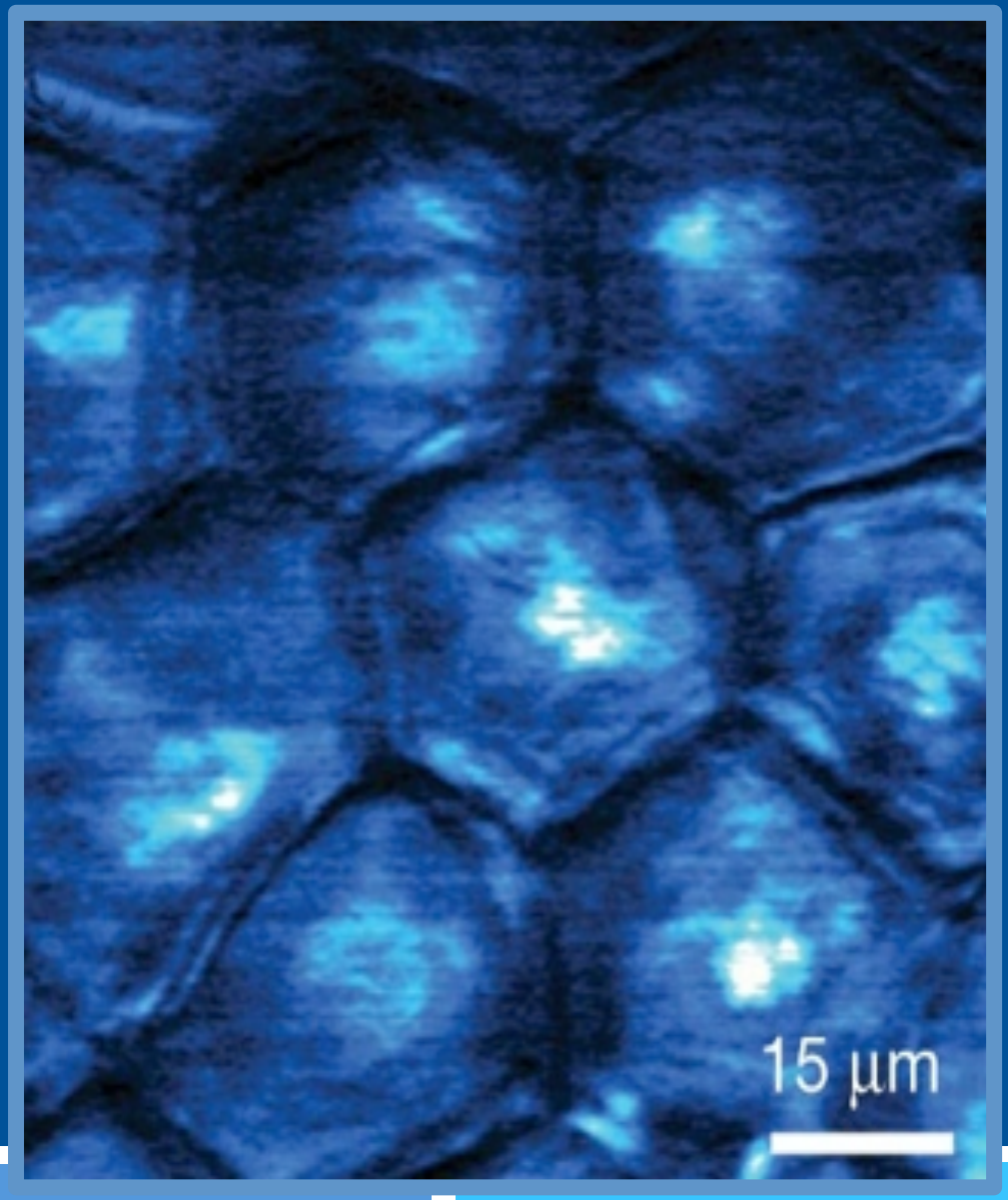

MEMBRANE STRUCTURE

Lecture 8

BIOL 266/4

2014-15

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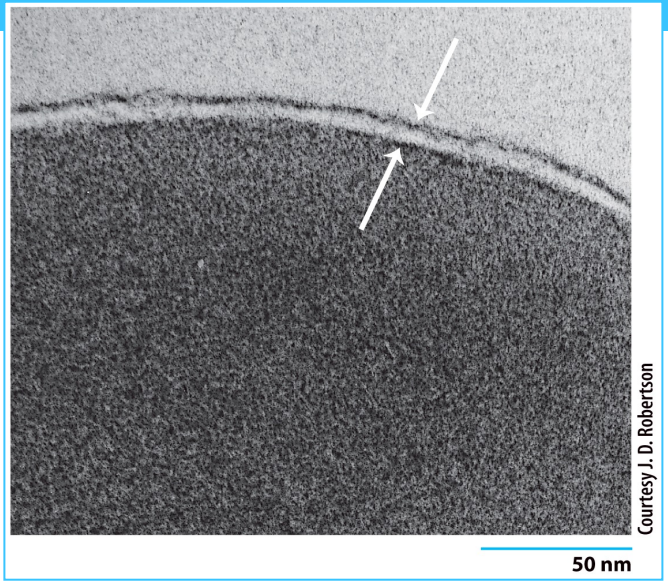
Biology Department
Concordia University

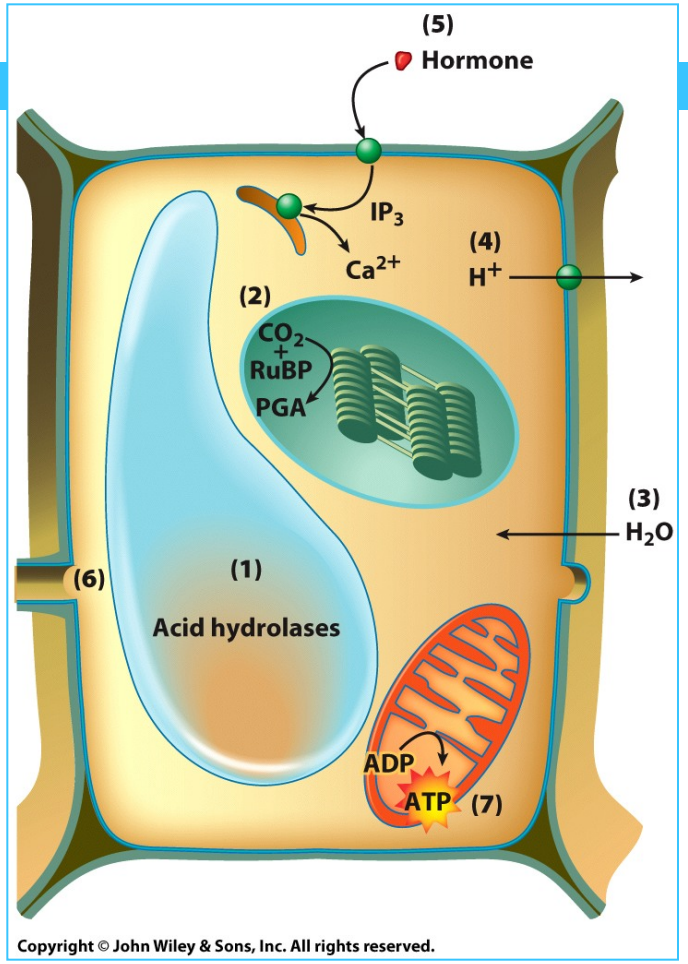
Plasma Membrane



- **Plasma membrane**: The outer boundary of the cell that separates it from the world is a thin, fragile structure about 5 – 10 nm thick.
- Not detectable with light microscope
- The 2 dark-staining layers in the electron micrographs correspond primarily to the inner & outer polar surfaces of the bilayer
- All membranes examined closely (plasma, nuclear or cytoplasmic) from plants, animals or microorganisms have the same ultrastructure

An Overview of Membrane Functions

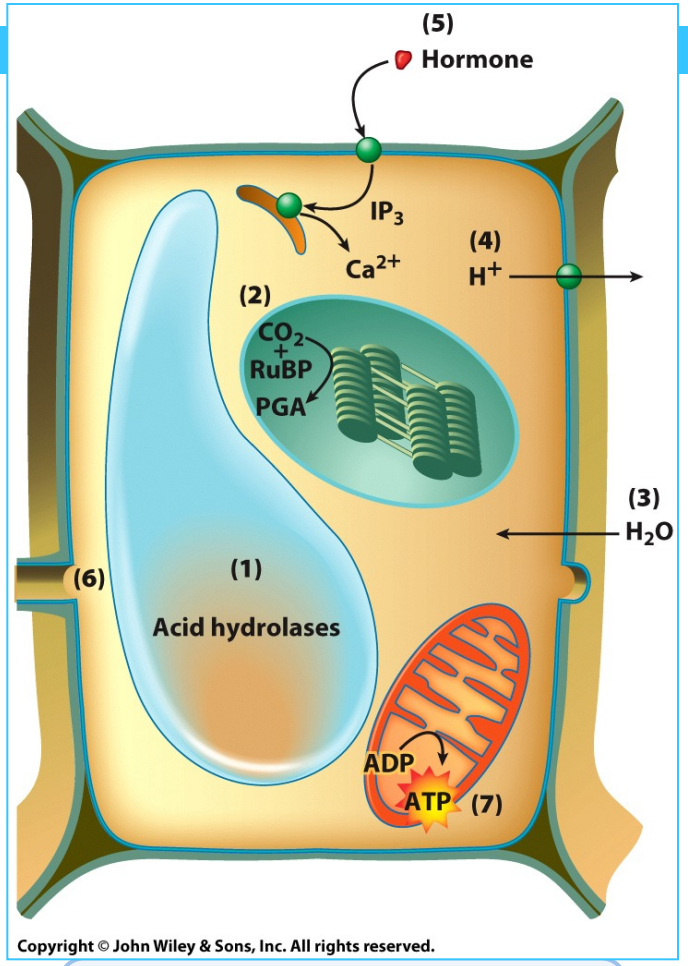
1. **Compartmentalization**
   Membranes form continuous sheets that enclose intracellular compartments.
2. **Scaffold for biochemical activities**
   Membranes provide a framework that organizes enzymes for effective interaction.
3. **Movement of solvent**
   Membranes allow movement of water between compartments.



A summary of membrane functions in a plant cell.

An Overview of Membrane Functions

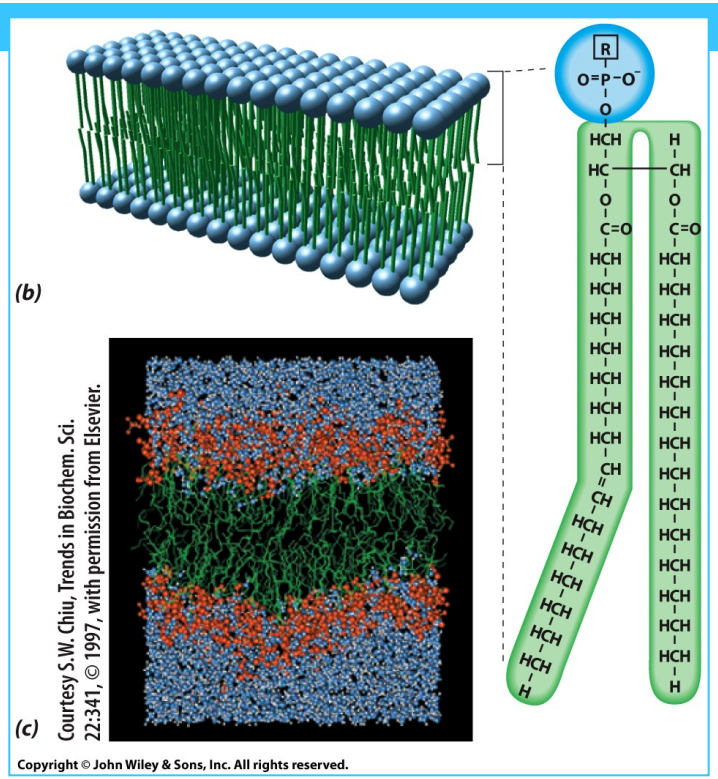
4. **Transporting solutes** Membrane proteins facilitate the movement of substances between compartments.
5. **Responding to external signals** Membrane receptors transduce signals from outside the cell in response to specific ligands.
6. **Intercellular interaction** Membranes mediate recognition and interaction between adjacent cells.
7. **Energy transduction** Membranes transduce photosynthetic energy, convert chemical energy to ATP, and store energy.



A summary of membrane functions in a plant cell.

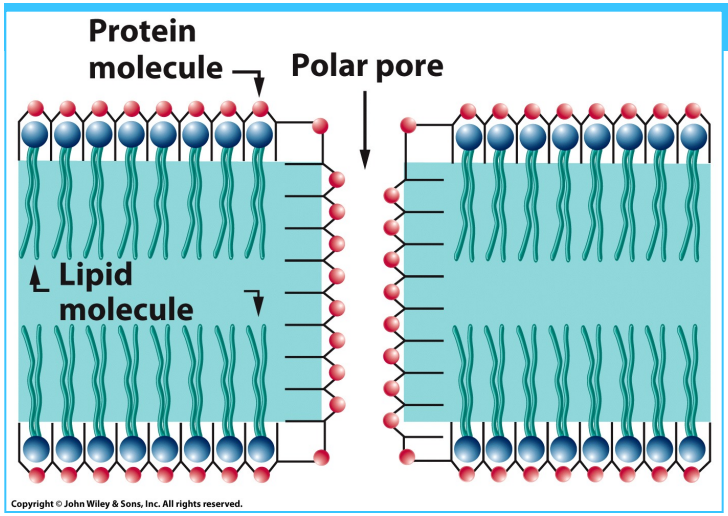
Plasma Membrane Structure

- Membranes were found to be mostly composed of lipids
- The most energetically favored orientation for polar head groups is facing the aqueous compartments outside of the bilayer

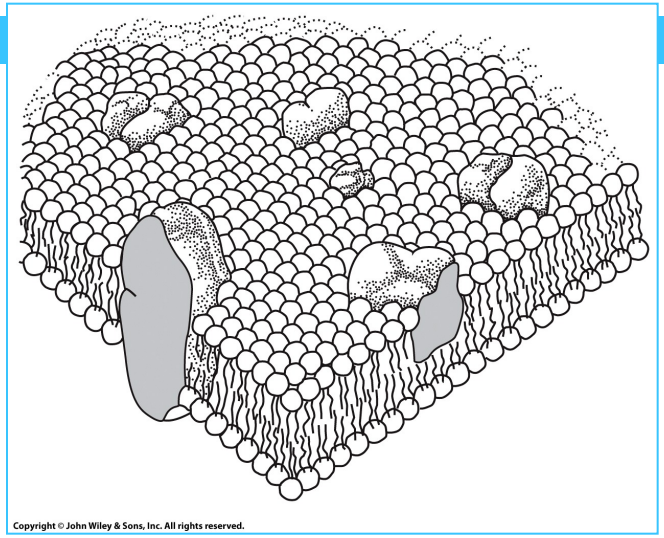


Bimolecular layer of phospholipids with water soluble head groups facing outward

Plasma Membrane Structure

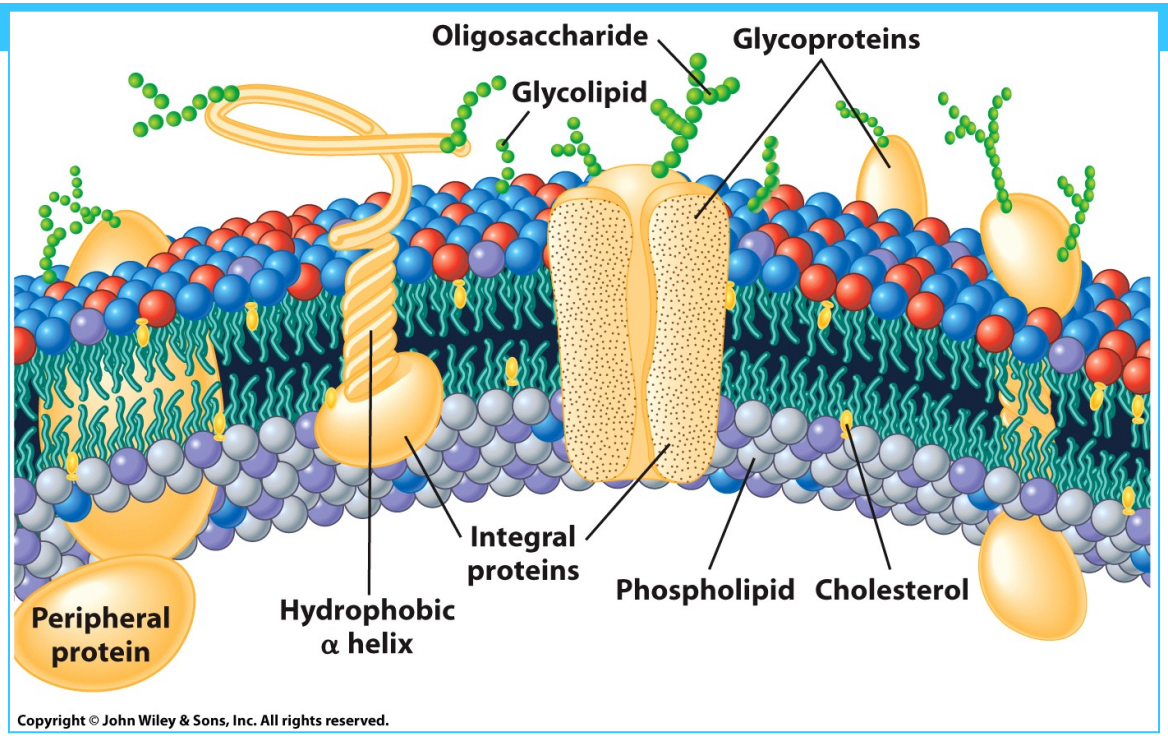


Early models representing the lipid bilayer



- The nature and importance of the lipid bilayer:
  - Lipid composition can influence the activity of membrane proteins and determine the physical state of the membrane.
  - The cohesion of bilayers to form a continuous sheet makes cells deformable and facilitates splitting and fusion of membranes.
- Protein-lined pores in the membrane account for the movement of polar solutes and ions across cell boundaries.

Plasma Membrane Structure

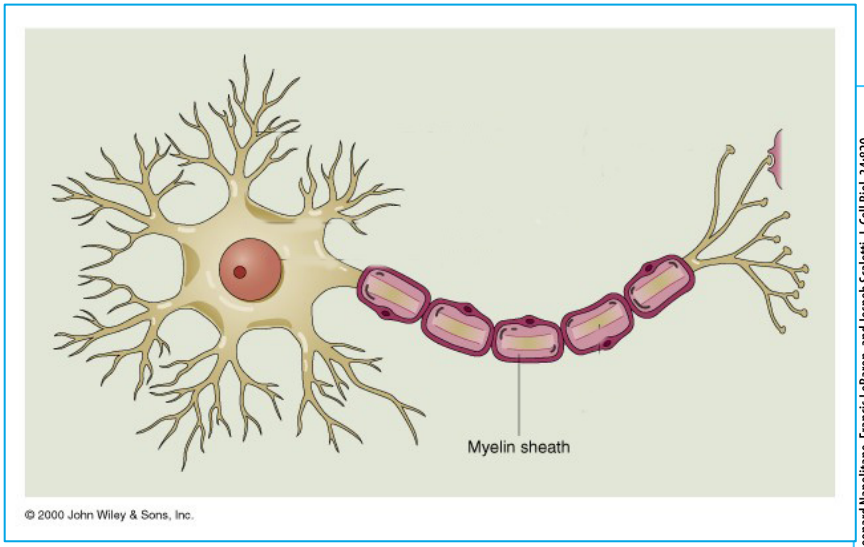


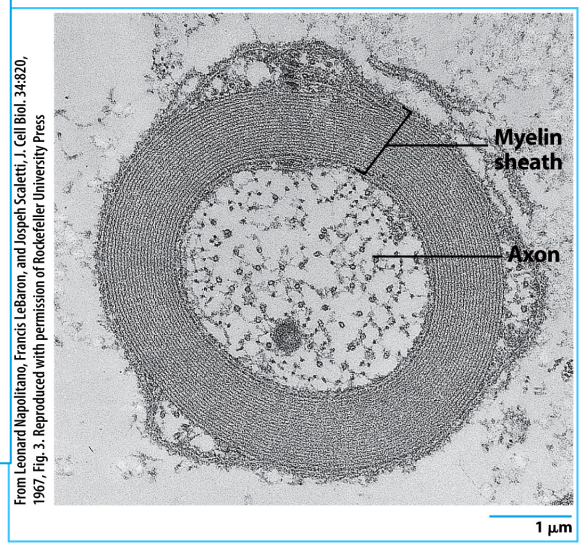
The **fluid-mosaic model**

- Core lipid bilayer exists in a fluid state, capable of movement.
- Membrane proteins form a mosaic of particles penetrating the lipids.

The Chemical Composition of Membranes

- The lipid and protein components are bound together by non-covalent bonds.
- Membranes also contain carbohydrates.
- Protein/lipid ratios vary among membrane types.

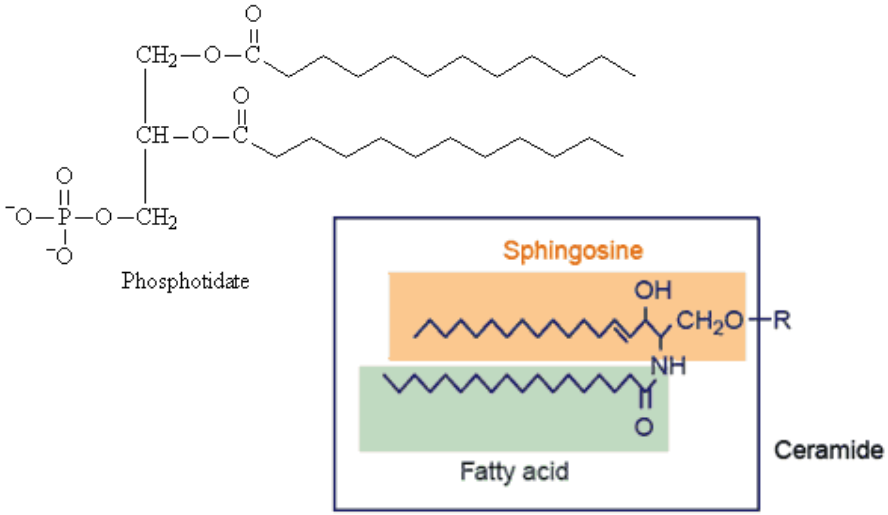




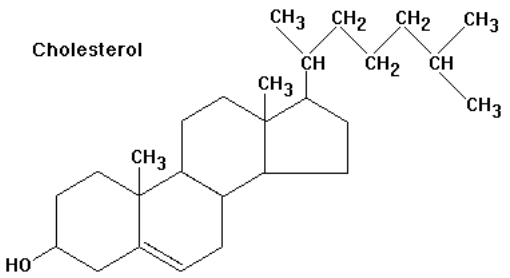
The Chemical Composition of Membranes

Membrane lipids are **amphipathic** with three main types:

1. **Phosphoglycerides** are diacylglycerides with small functional head groups linked to the glycerol backbone by phosphate ester bonds.
2. **Sphingolipids** are ceramides formed by the attachment of sphingosine to fatty acids.
3. **Cholesterol** is a smaller and less amphipathic lipid that is only found in animals.



Substituent (R)	Sphingolipid
H	Ceramide
Phosphocholine	Sphingomyelin
Sugar(s)	Glycosphingolipid

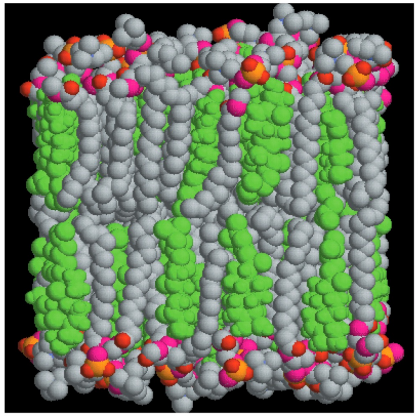


The Chemical Composition of Membranes

Chemical structure of membrane lipids

Cholesterol

- a sterol that makes up to 50% of animal membrane lipids.
- The -OH group is oriented toward membrane surface
- Carbon rings are flat and rigid; interfere with the movement of phospholipid fatty acid tails



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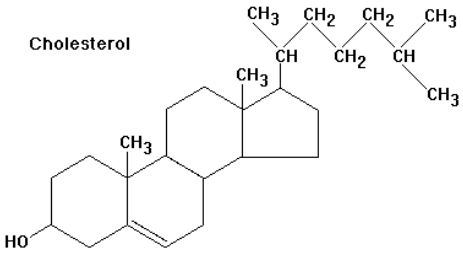
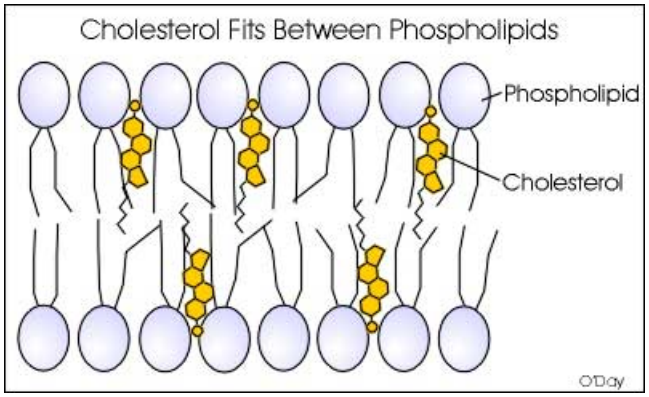
Cholesterol molecules (green)



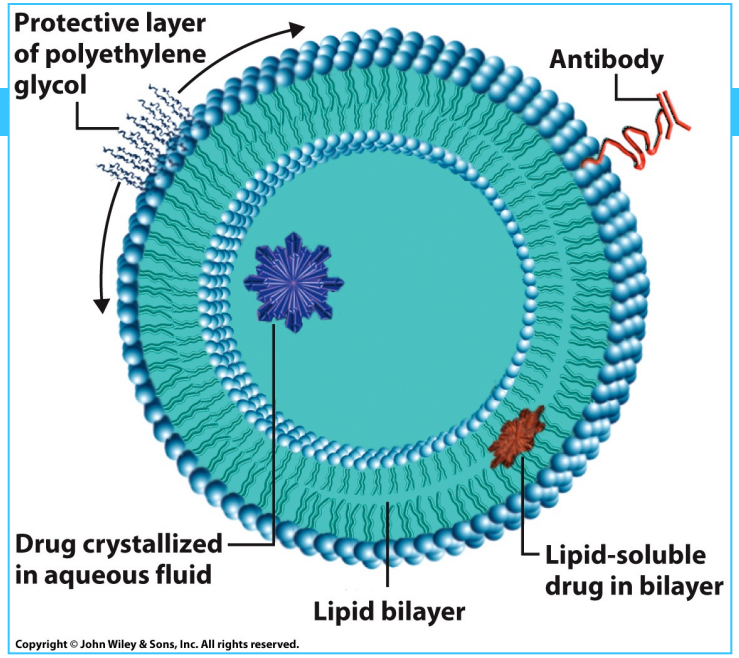


The Chemical Composition of Membranes

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.



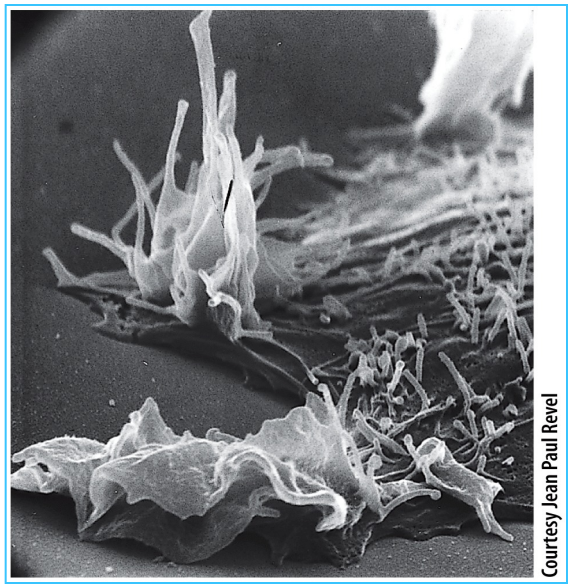
Liposomes: synthetic vesicles

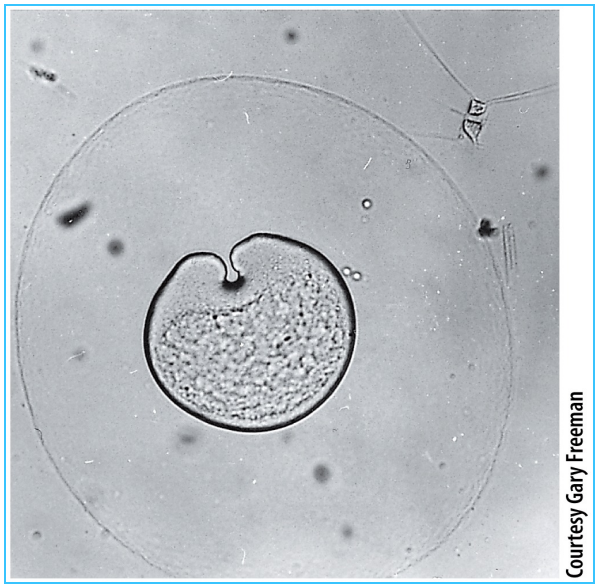
The Nature and Importance of the Lipid Bilayer

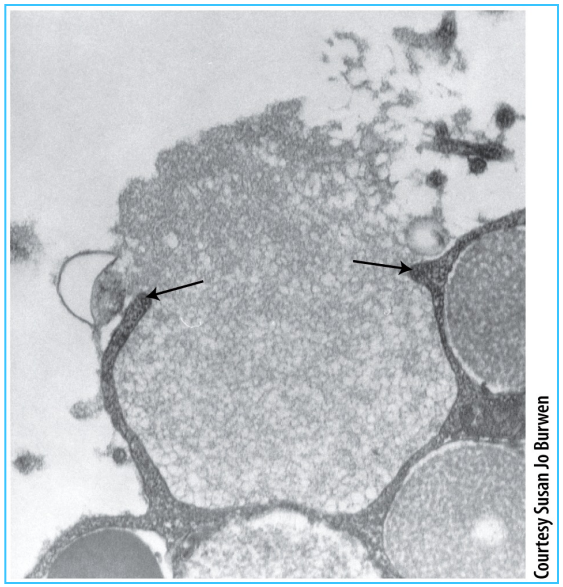
- Membrane lipid composition is characteristic of specific membranes.
- Lipid bilayers assemble spontaneously in aqueous solutions as **liposomes.**

The Chemical Composition of Membranes

The dynamic properties of plasma membranes


Courtesy Jean Paul Revel


Courtesy Gary Freeman


Courtesy Susan Jo Burwen

Movement: ruffling of the plasma membrane of a migrating cell

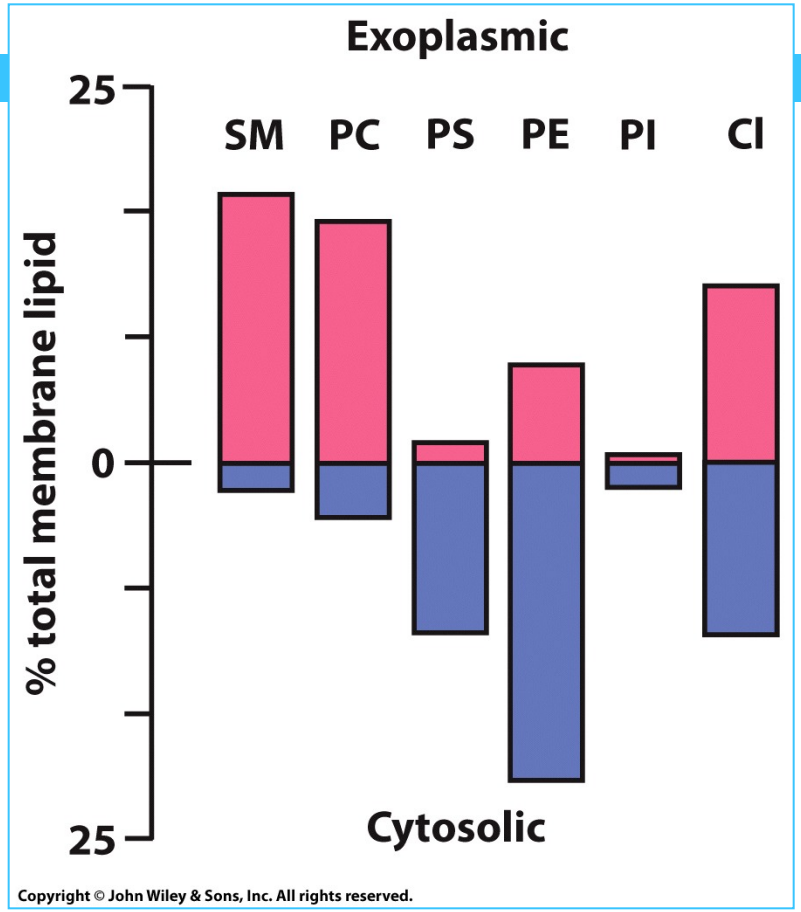
Division: invagination of the plasma membrane towards the cell center during cell division

Fusion: plasma membranes fuse

The Chemical Composition of Membranes

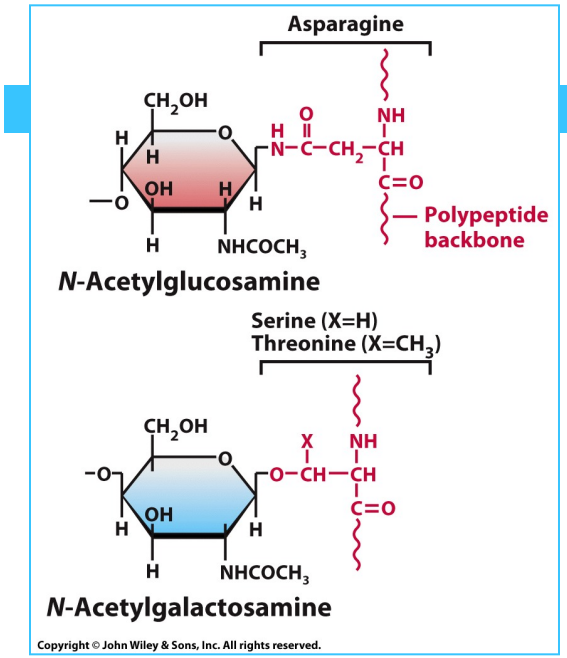
The Asymmetry of Membrane Lipids

- Inner and outer membrane leaflets have different lipid compositions.
- Provides different physico-chemical properties appropriate for different interactions



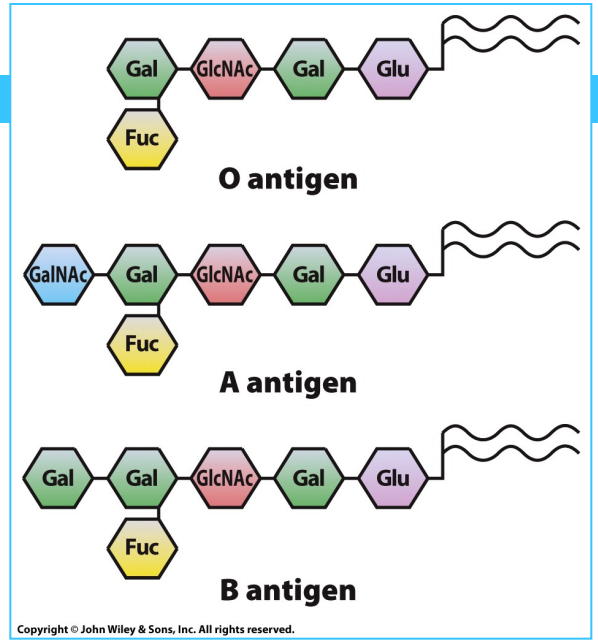
SM: sphingomyelin
PC: phosphatidylcholine
PS: phosphatidylserine
PE: phosphatidylethanolamine
PI: phosphatidylinositol
Cl: cholesterol

The Chemical Composition of Membranes



Two types of linkages that join sugars to a polypeptide chain

Blood-group antigens

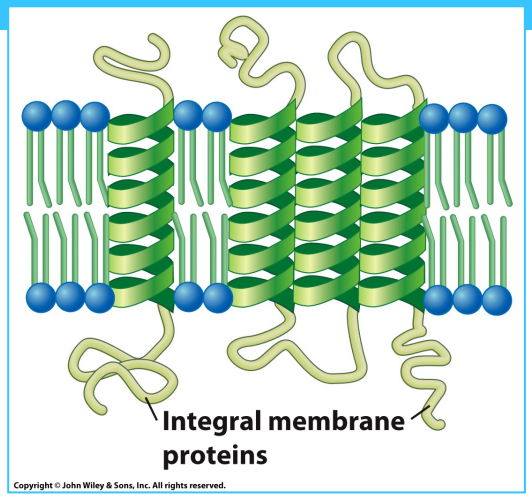


Membranes contain carbohydrates covalently linked to lipids and proteins on the **extracellular surface** of the bilayer.

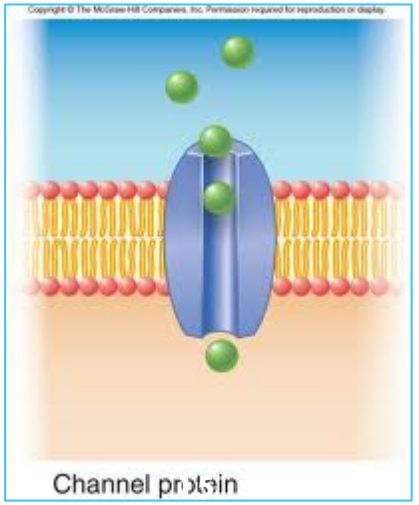
- Glycoproteins have short, branched carbohydrates for interactions with other cells and structures outside the cell.
- Glycolipids have larger carbohydrate chains that may be cell-to-cell recognition sites.

The Structure and Functions of Membrane Proteins

- Membrane proteins attach to the bilayer asymmetrically, giving the membrane a distinct "sidedness"
- Membrane proteins can be grouped into three distinct classes:
  1. **Integral proteins**
     - Penetrate and pass through lipid bilayer
     - Make up 20 -30% of all encoded proteins
     - Are amphipathic, with hydrophobic domains anchoring them in the bilayer and hydrophilic regions forming functional domains outside of the bilayer.
     - Channel proteins have hydrophilic cores that form aqueous channels in the membrane-spanning region.



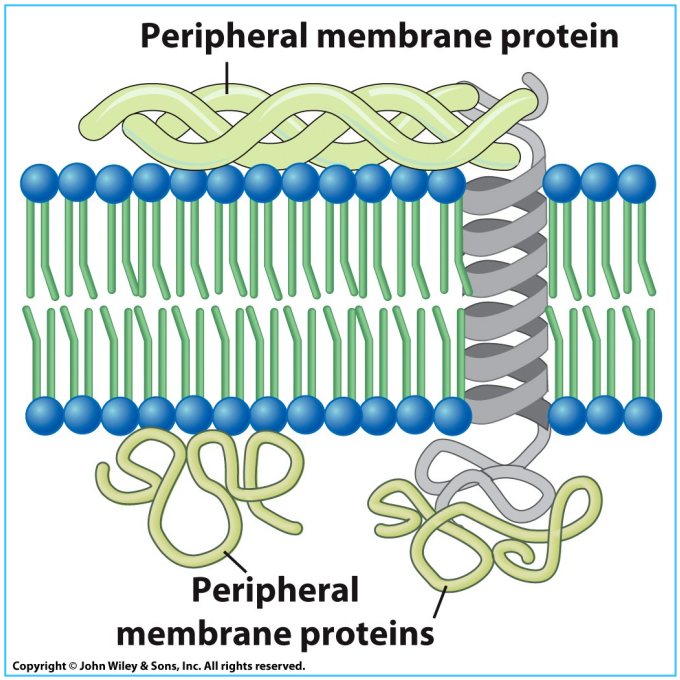
Integral proteins



The Structure and Functions of Membrane Proteins

2. Peripheral proteins

- Attached to the polar head groups of the lipid bilayer and/or to an integral membrane protein by weak bonds
- Easily solubilized.
- Located entirely outside of bilayer on either the extracellular or cytoplasmic side

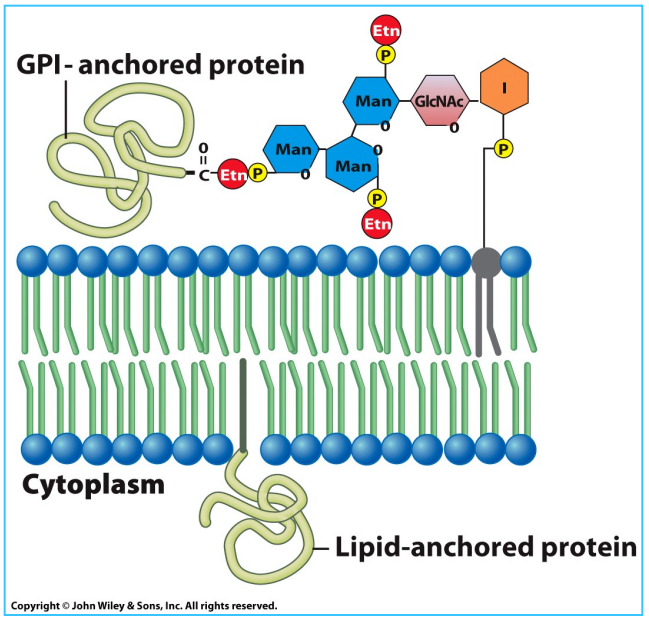


Peripheral proteins

The Structure and Functions of Membrane Proteins

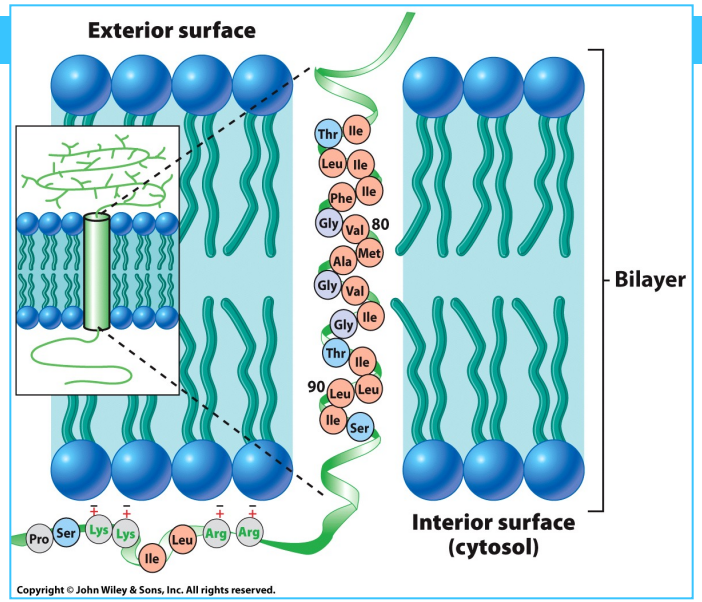
3. Lipid-anchored membrane proteins

- Covalently bonded to a lipid group that resides within the membrane
- Glycophosphatidylinositol **(GPI)-linked proteins** found on the outer leaflet can be released by inositol-specific phospholipases.
- Some inner-leaflet proteins are anchored to membrane lipids by long hydrocarbon chains.

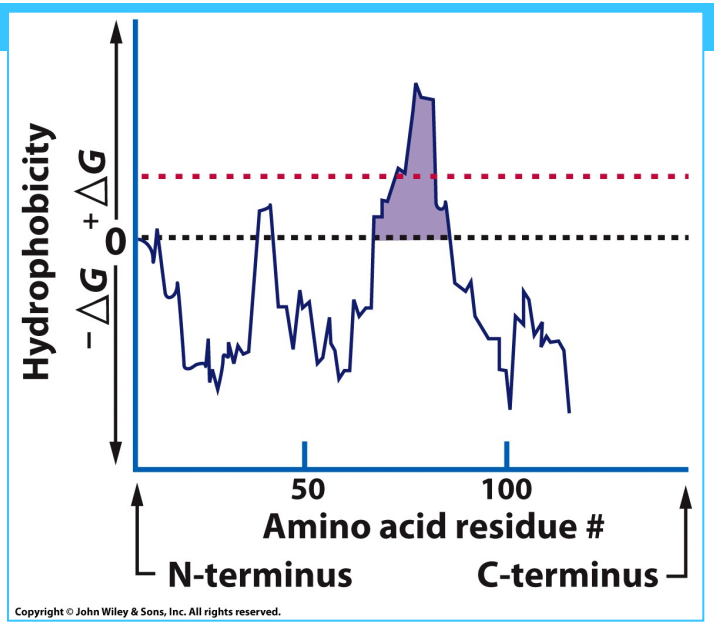


Lipid-anchored proteins

The Structure and Functions of Membrane Proteins



Glycophorin A, an integral protein with a single transmembrane domain with a Gly-X-X-X-Gly sequence



Hydropathy plot for glycophorin A demonstrates a single pass domain

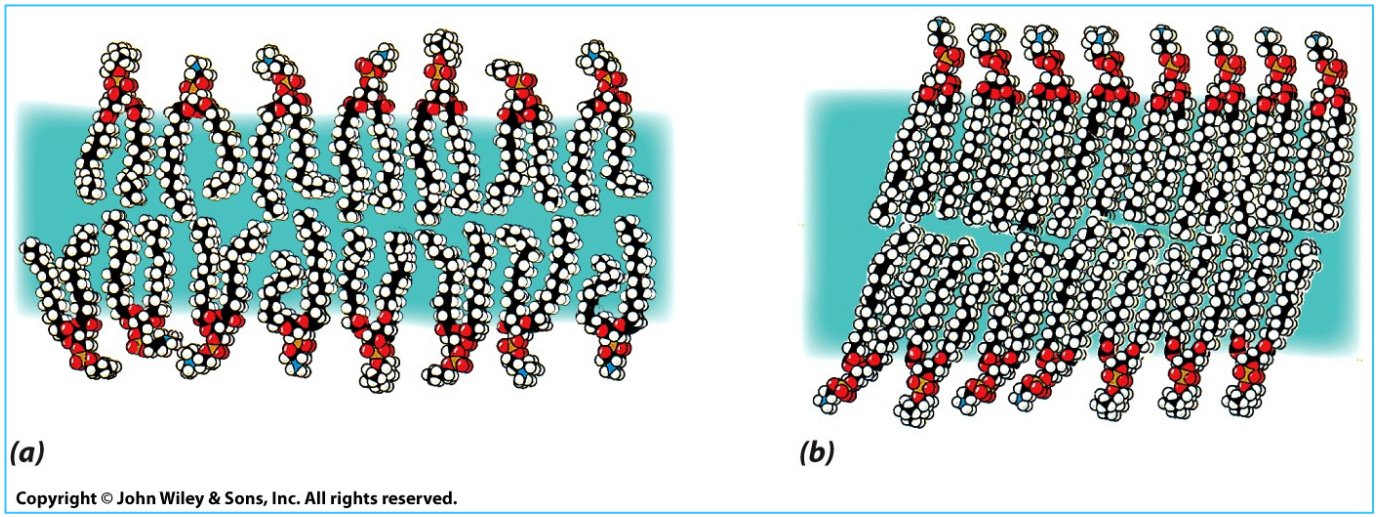
Studying the Structure and Properties of Integral Membrane Proteins

- Identifying transmembrane domains: A string of 20-30 hydrophobic amino acids from hydropathy plots identifies a membrane-spanning domain.

Membrane Lipids and Membrane Fluidity

- Membrane lipids exist in gel or liquid-crystal phases depending on temperature, lipid composition, saturation and presence of cholesterol.
- Liquid-crystal membranes predominate
- When lowering the temperature, a point is reached where liquid-crystal phase → gel phase occurs which is known as the ***transition temperature***
- The greater the degree of unsaturation of fatty acids of the bilayer is, the lower the transition temperature is for the membrane.

Membrane Lipids and Membrane Fluidity



Liquid-Crystal phase **Gel phase**

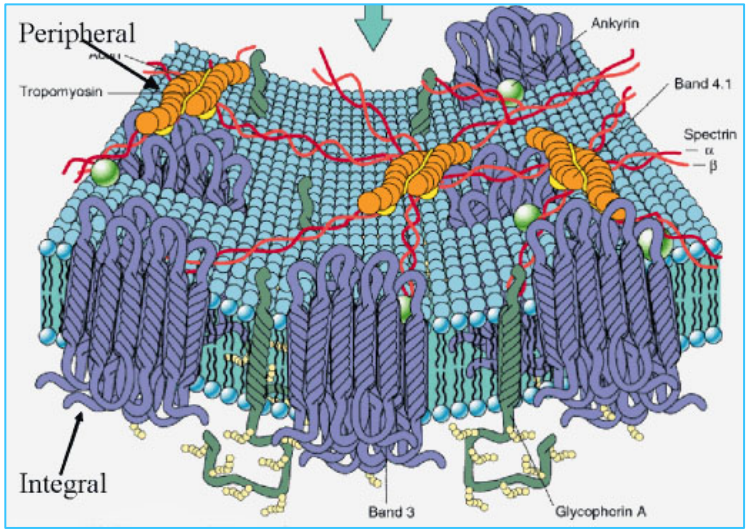
Structure of the lipid bilayer depends on the temperature: above and below the transition temperature.

Membrane Lipids and Membrane Fluidity

Structure depends on the temperature

Membrane Fluidity

- The fluidity of membranes is a compromise between structural rigidity and complete fluidity.
- Membrane fluidity makes it possible for proteins to move in the membrane and for membranes to assemble and grow.



Membrane Lipids and Membrane Fluidity

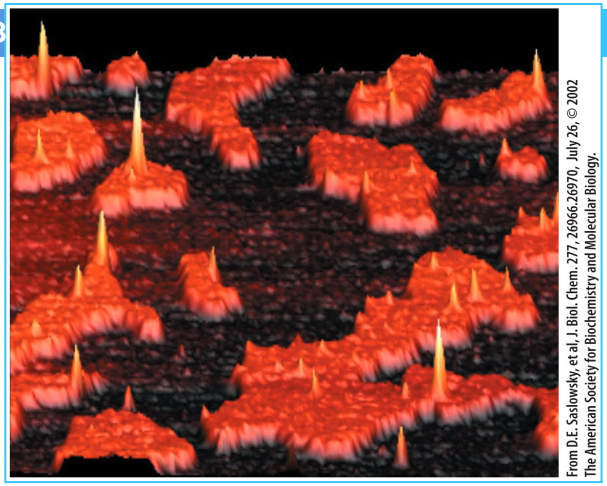
Structure depends on the temperature

Maintaining Membrane Fluidity

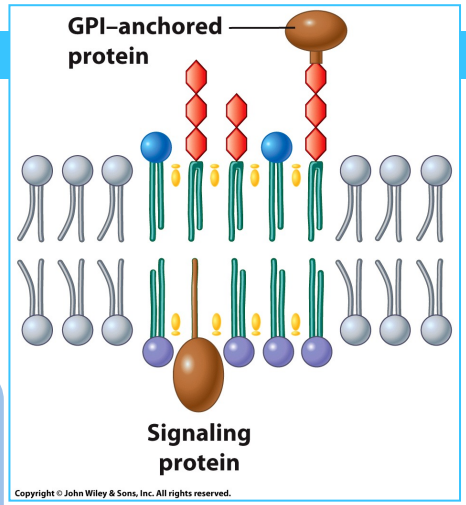
- The internal temperature of most organisms (other than birds and mammals) fluctuate with temperature.
- Membrane fluidity is maintained as temperature changes by altering the composition of membrane lipids.
- ***Remodeling*** lipid bilayers involves saturation or desaturation of acyl chains and replacement of acyl chains by the action of *phospholipases* or *acyltransferases*.
- The importance of these mechanisms has been verified using mutants unable to carry out certain desaturation reactions in response to cold.

Membrane Lipids and Membrane Fluidity

Lipid Rafts



Sphingomyelin organizing into orange-colored rafts



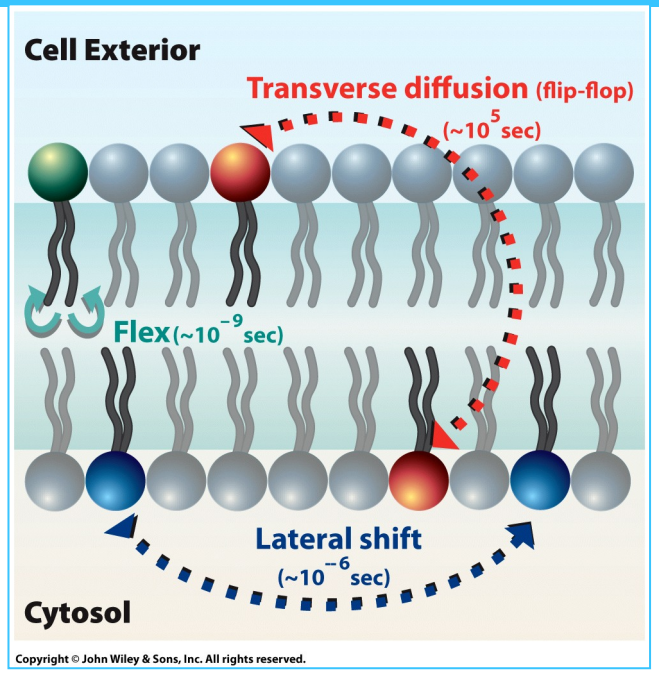
Schematic model of a lipid raft

Lipid Rafts

- **Cholesterol** and **Sphingolipids** tend to pack together to form highly ordered micro-domains forming **lipids rafts** that float within the more fluid and disordered environment.
- Provide a favorable environment for cell-surface receptors and GPI-anchored proteins.

The Dynamic Nature of the Plasma Membrane

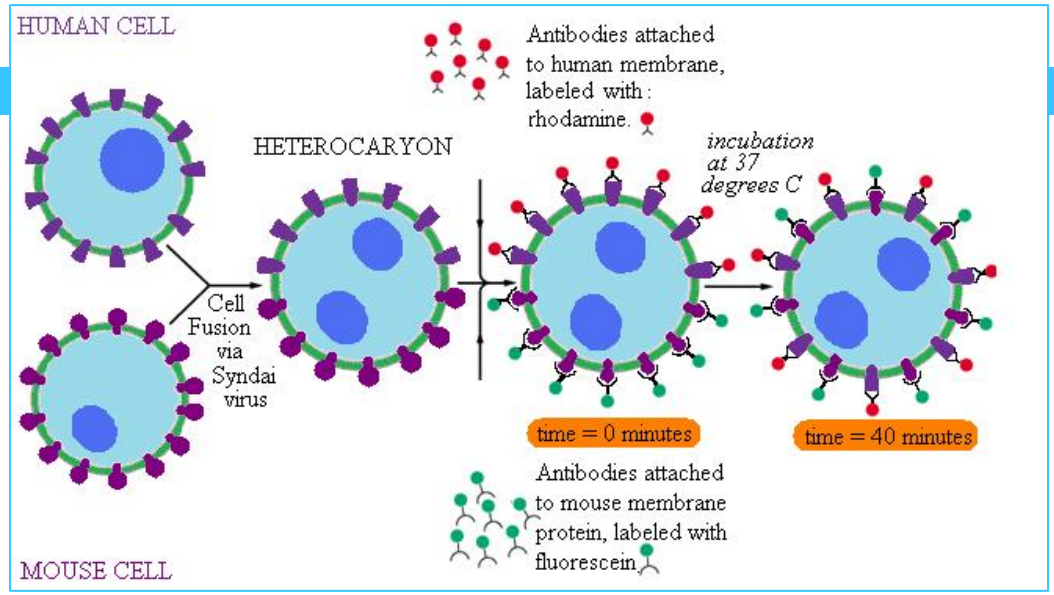
- Lipid bilayer can exist in a relatively fluid state.
- A phospholipid can move laterally within the same leaflet with considerable ease (Lateral shift)
- In contrast, it takes a phospholipid molecule a matter of hours to days to move across to the other leaflet (flip-flop).
- Hydrophilic head group of the lipid must pass through the internal hydrophobic sheet of the membrane for a flip flop movement, which is thermodynamically unfavorable.
- The physical state of the lipid is an important determinant of the mobility of integral proteins.

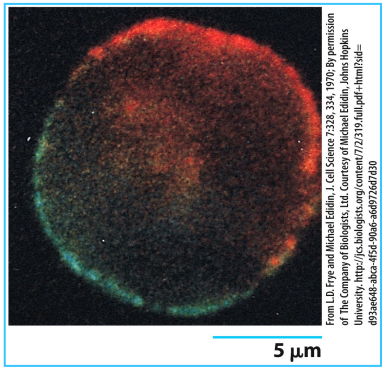


The possible movements of phospholipids in a membrane

The Dynamic Nature of the Plasma Membrane

Cell fusion to reveal mobility of membrane proteins: fusion of human and mouse cells



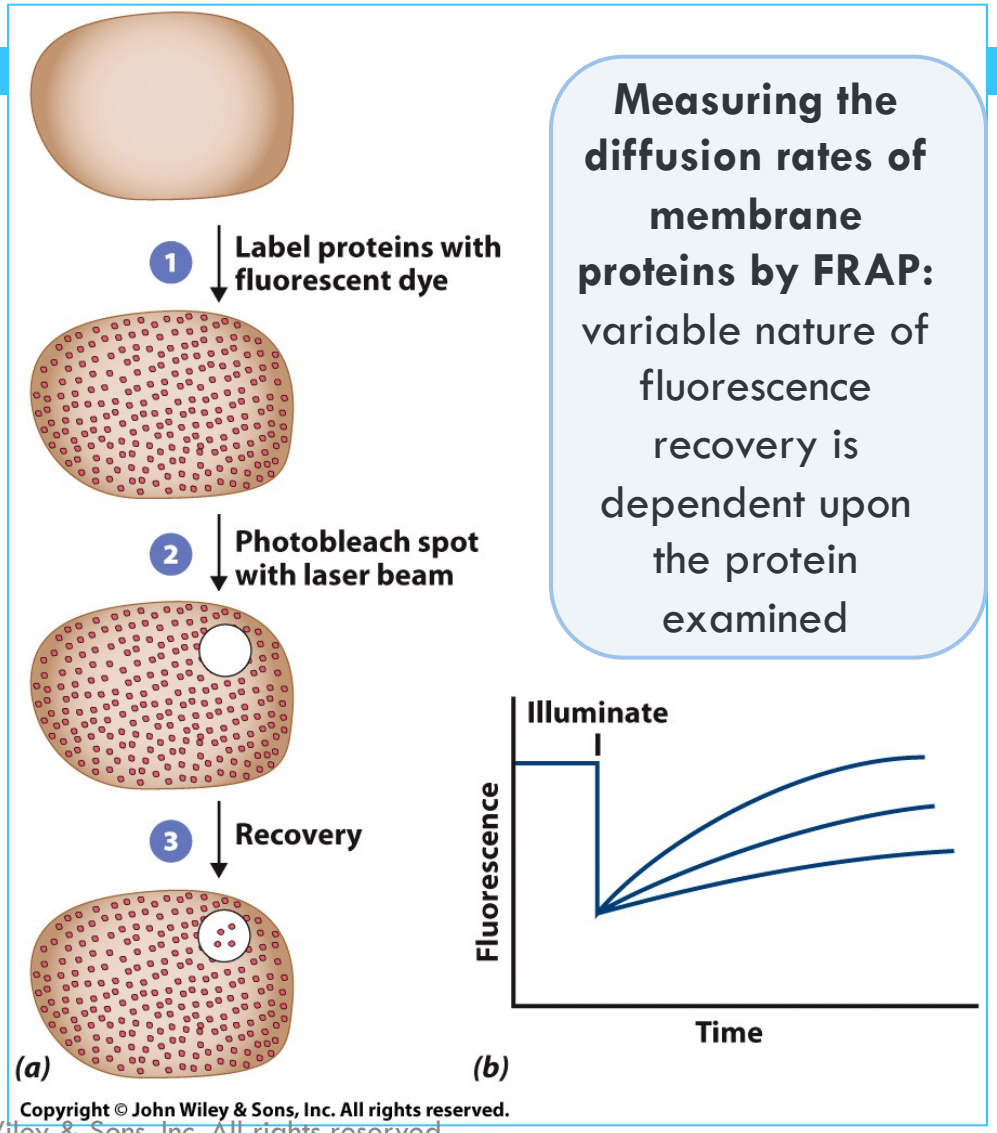


Diffusion of Membrane Proteins after Cell Fusion

- **Cell fusion** is a technique whereby two different types of cells, or cells from two different species, can be fused to produce one cell with a common cytoplasm and a single, continuous plasma membrane.
- **Cell fusion** be induced by certain viruses, or with polyethylene glycol.
- Labeled proteins have shown that membrane proteins can move between fused cell.

The Dynamic Nature of the Plasma Membrane

- Restrictions on Protein and Lipid Mobility
  - Proteins can be labeled and tracked by **fluorescence recovery after photobleaching (FRAP)** and **single particle tracking (SPT).**
  - Proteins can be immobile, mobile in a directed manner, or exhibit random movement.

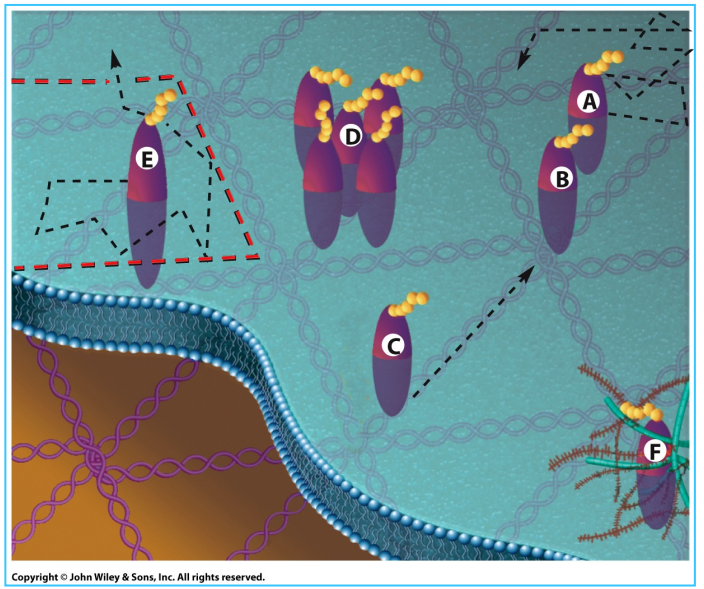


Measuring the diffusion rates of membrane proteins by FRAP: variable nature of fluorescence recovery is dependent upon the protein examined

The Dynamic Nature of the Plasma Membrane

Control of Membrane Protein Mobility

- Protein movements are slower than predicted by protein size and membrane viscosity.
- Protein movements are limited by interactions with the cytoskeleton, other proteins, and extracellular materials.
- Techniques that can drag tagged proteins within the membrane, indicate that some proteins have barriers to lateral diffusion.
- Genetically modified proteins missing either intracellular or extracellular domains are less restricted.

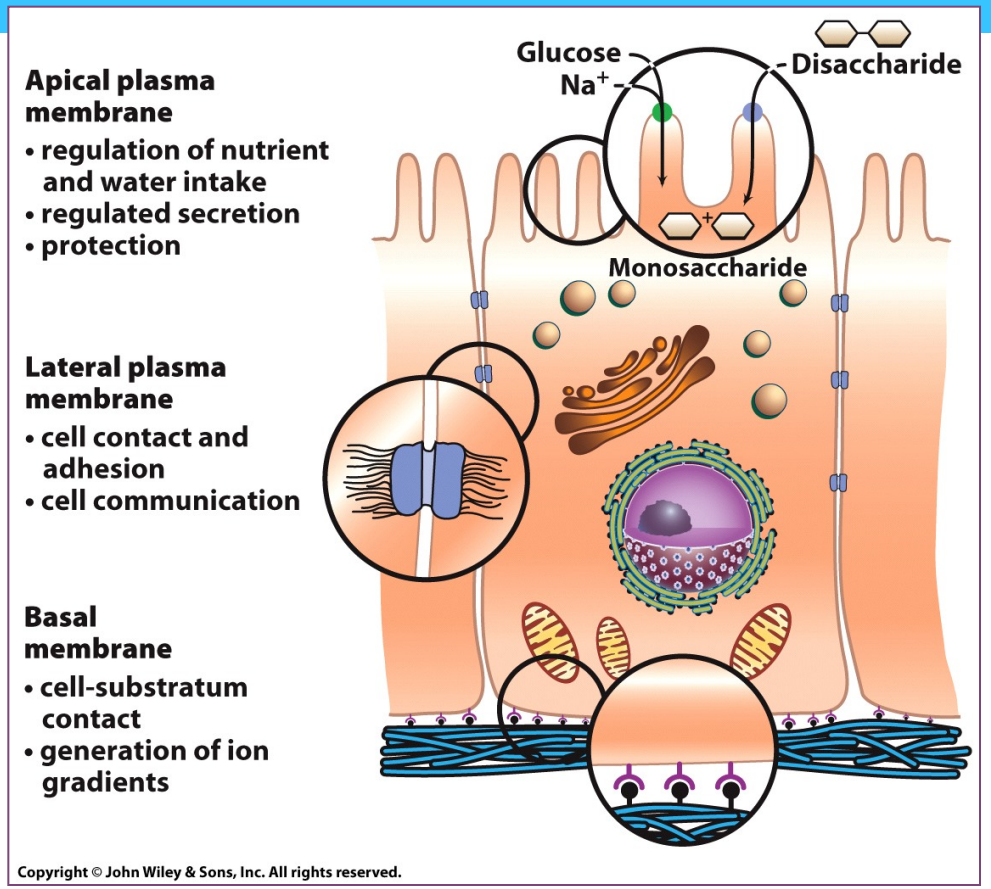


Patterns of movement of integral membrane proteins

The Dynamic Nature of the Plasma Membrane

Differences in protein distribution in the plasma membrane are evident in cells of organized tissues.

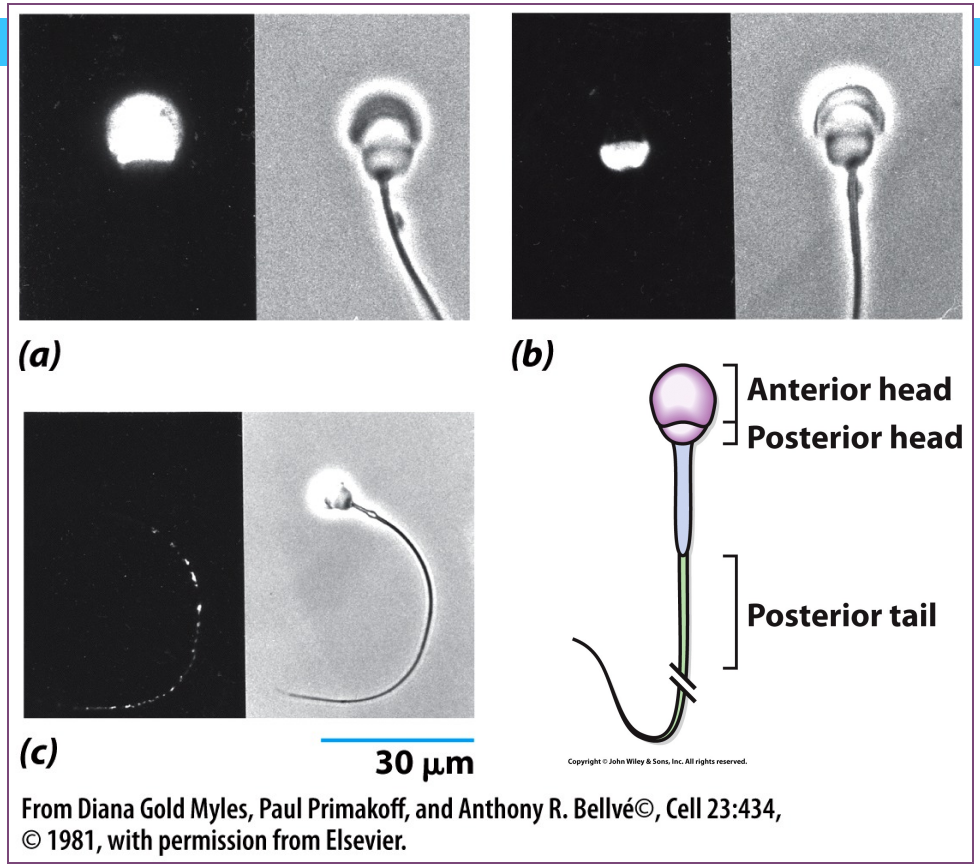
1. In the epithelia, the proteins of the apical membrane are distinct from those of the lateral and basal membranes



Differentiated functions of the plasma membrane of an epithelial cell.

The Dynamic Nature of the Plasma Membrane

2. Highly differentiated sperm has a head, midpiece and tail that is covered by a continuous membrane.
   - Can distinguish these regions with antibody staining.



From Diana Gold Myles, Paul Primakoff, and Anthony R. Bellvé©, Cell 23:434, © 1981, with permission from Elsevier.

Differentiation of the mammalian sperm plasma membrane as revealed by fluorescent antibodies.

Some interesting links

https://www.youtube.com/watch?v=moPJkCbKjBs
https://www.youtube.com/watch?v=Pfu1DE9PK2w

Put your thinking cap on….

1. How are liposomes formed?
2. Design an experiment to demonstrate that embrane proteins can diffuse after cell fusion.