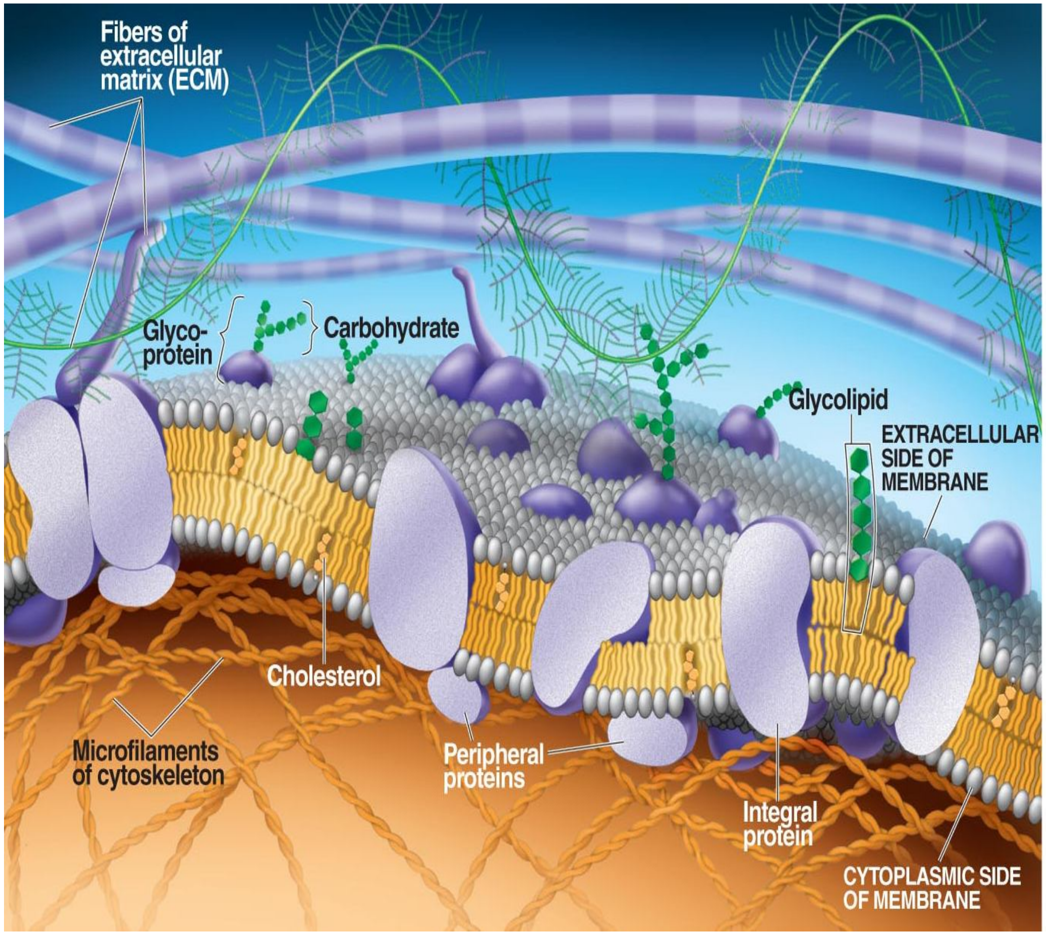
The Cell Membrane



****Note:** Cell wall structure and function is different than that of the cell membrane

The cell membrane is a dynamic and intricate structure that regulates material transported across the membrane. The membrane is selectively permeable (or semi-permeable) meaning that certain molecules can cross the membrane and others cannot.

Cell membranes

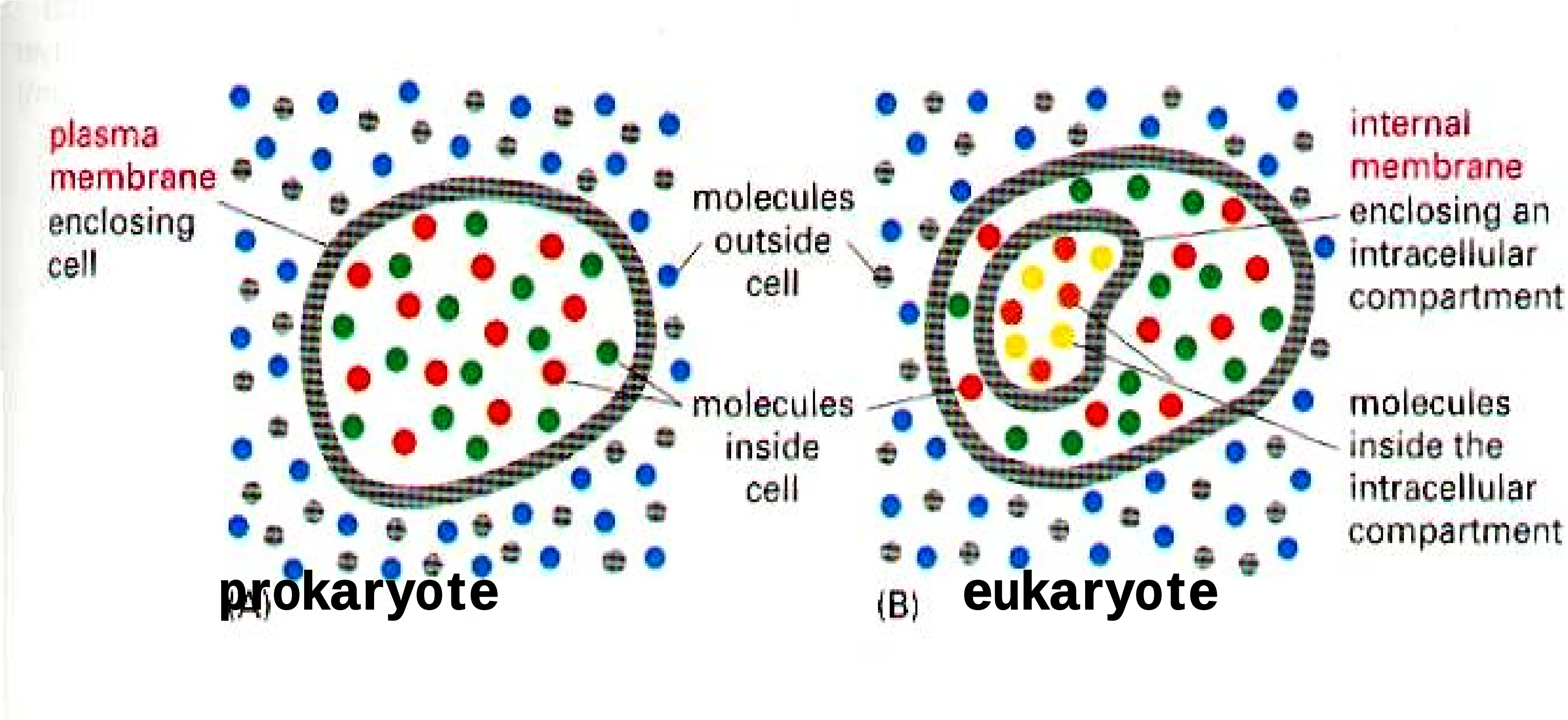
1. What are the functions of cell membranes?

2. What is the current model of membrane structure?

3. Evidence supporting the fluid mosaic model

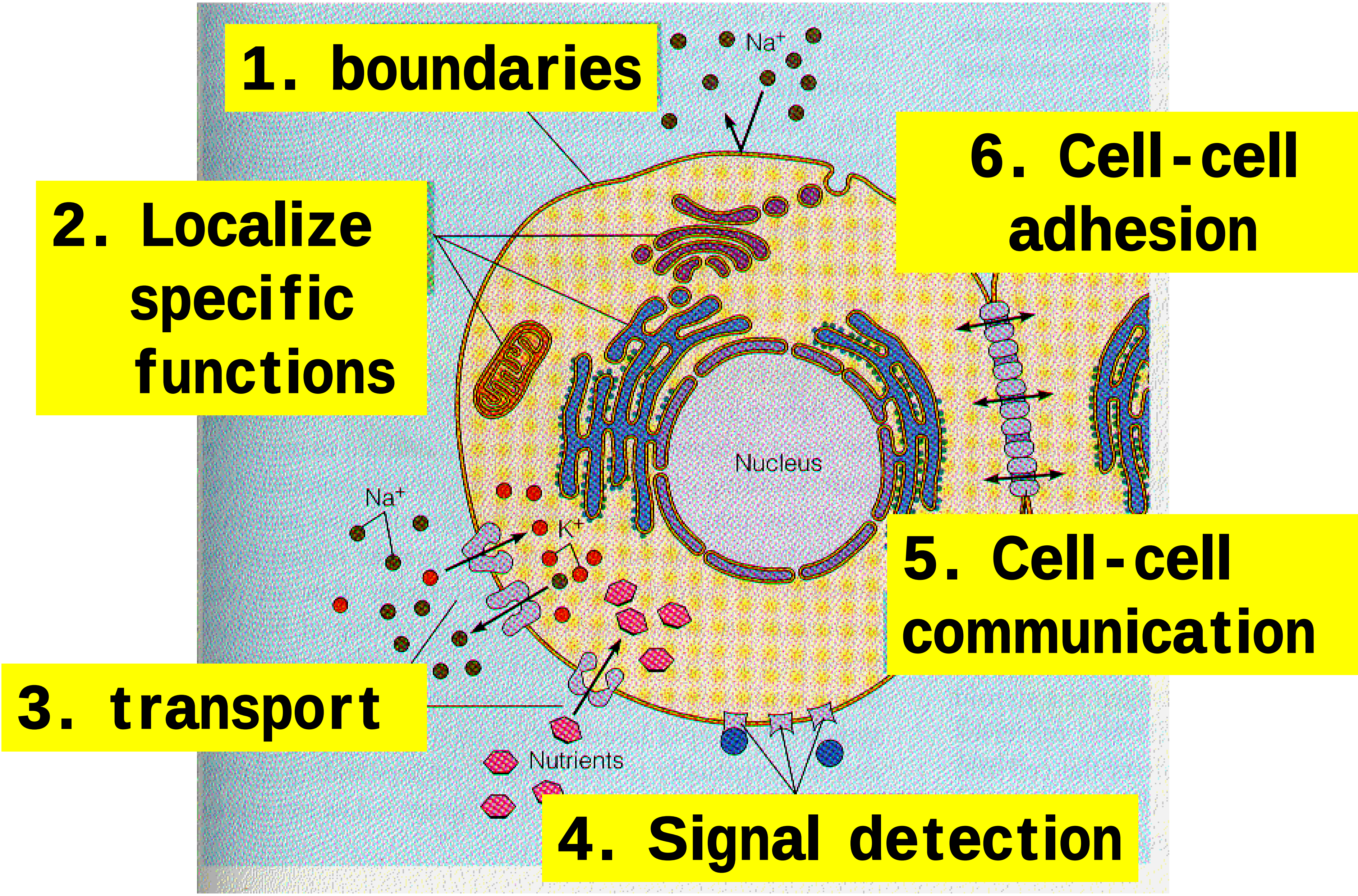
4. How appropriate fluidity is maintained

Membrane: organized arrangement of lipids and proteins that encloses and separates the cell from its surroundings



Membranes define spaces with distinctive character and function

Membrane Functions



major functions of membrane proteins

1. boundaries

2. Localize specific functions

3. transport

4. Signal detection

5. Cell-cell communication

6. Cell-cell adhesion

(a)

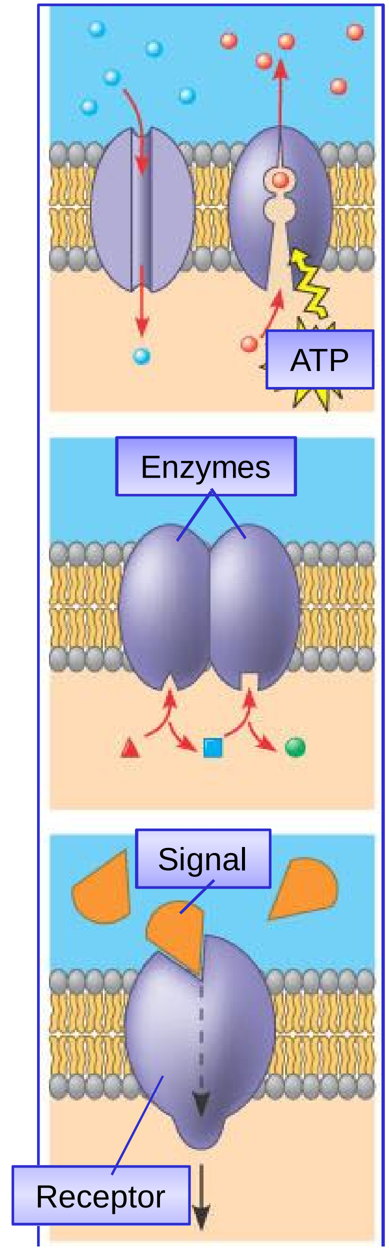
Transport. (left) A protein that spans the membrane may provide a hydrophilic channel across the membrane that is selective for a particular solute. **(right)** Other transport proteins shuttle a substance from one side to the other by changing shape. Some of these proteins hydrolyze ATP as an energy ssource to actively pump substances across the membrane.

(b)

Enzymatic activity. A protein built into the membrane may be an enzyme with its active site exposed to substances in the adjacent solution. In some cases, several enzymes in a membrane are organized as a team that carries out sequential steps of a metabolic pathway.

(c)

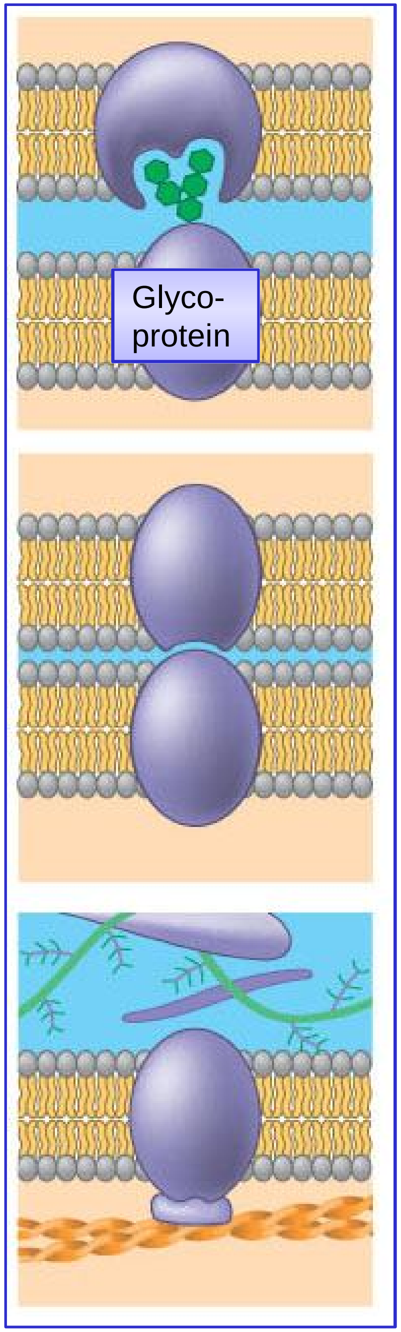
Signal transduction. A membrane protein may have a binding site with a specific shape that fits the shape of a chemical messenger, such as a hormone. The external messenger (signal) may cause a conformational change in the protein (receptor) that relays the message to the inside of the cell.



(d) **Cell-cell recognition.** Some glyco-proteins serve as identification tags that are specifically recognized by other cells.

(e) **Intercellular joining.** Membrane proteins of adjacent cells may hook together in various kinds of junctions, such as gap junctions or tight junctions (see Figure 6.31).

(f) **Attachment to the cytoskeleton and extracellular matrix (ECM).** Microfilaments or other elements of the cytoskeleton may be bonded to membrane proteins, a function that helps maintain cell shape and stabilizes the location of certain membrane proteins. Proteins that adhere to the ECM can coordinate extracellular and intracellular changes (see Figure 6.29).

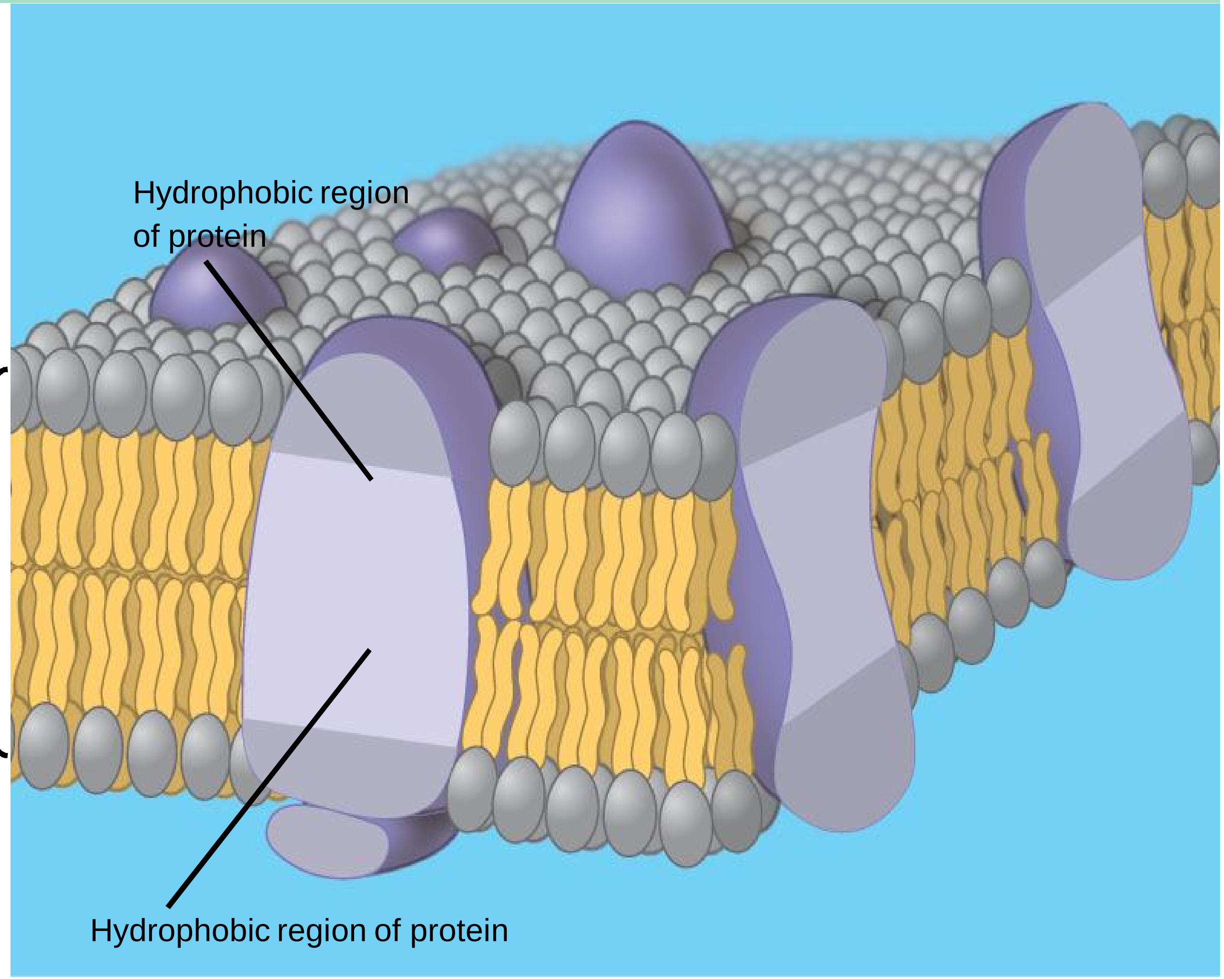


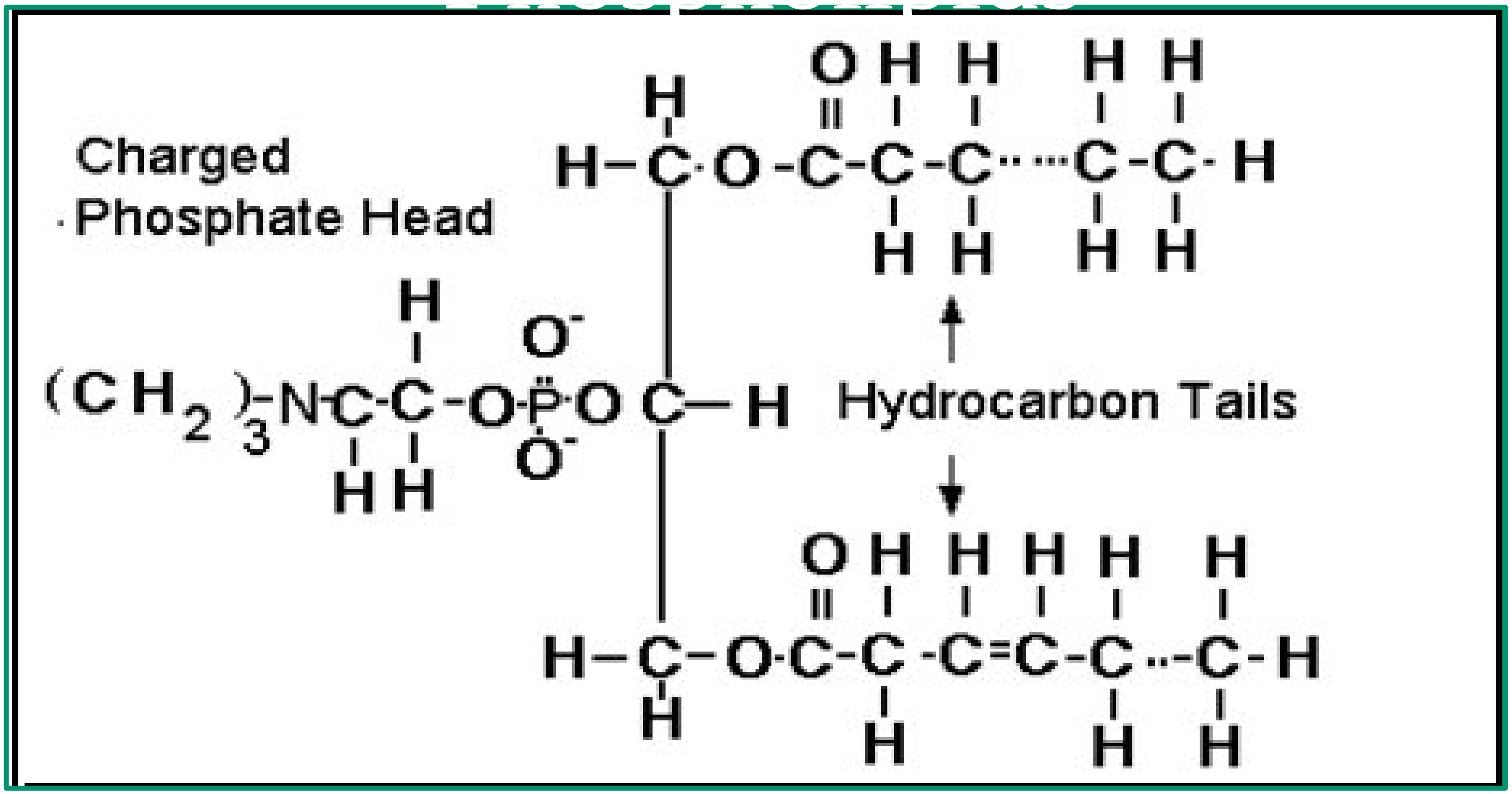
Current Understanding of Membrane Structue:
Fluid Mosaic Model
1972 Singer & Nicholson

Proteins embedded and floating in a sea of phospholipids

Familiar features?

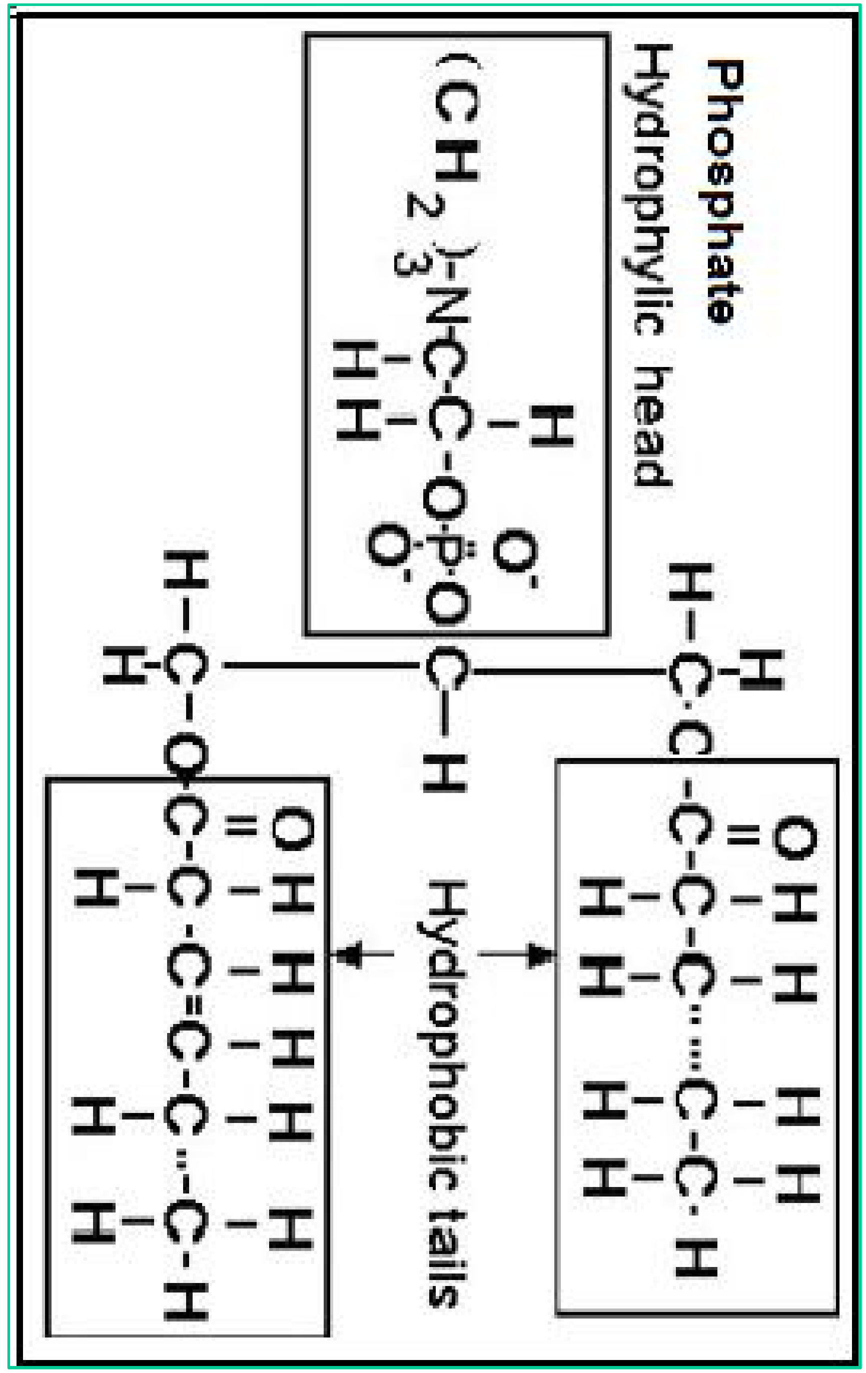
Problems ?

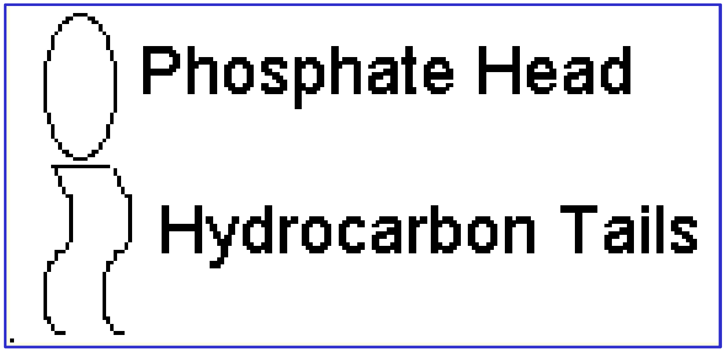




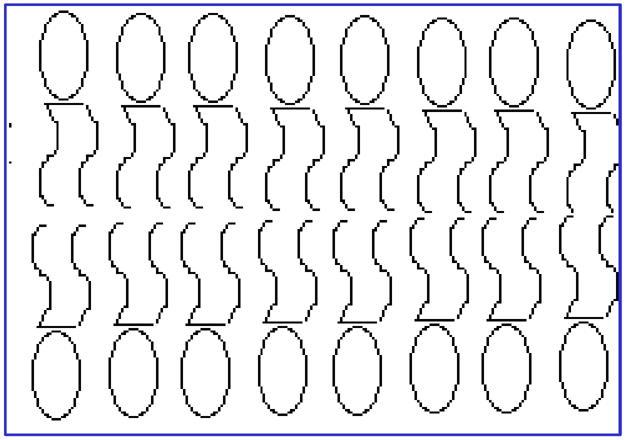
All cells have plasma membranes and many of their organelles also have membranes. All membranes are made from a bilayer of phospholipids.

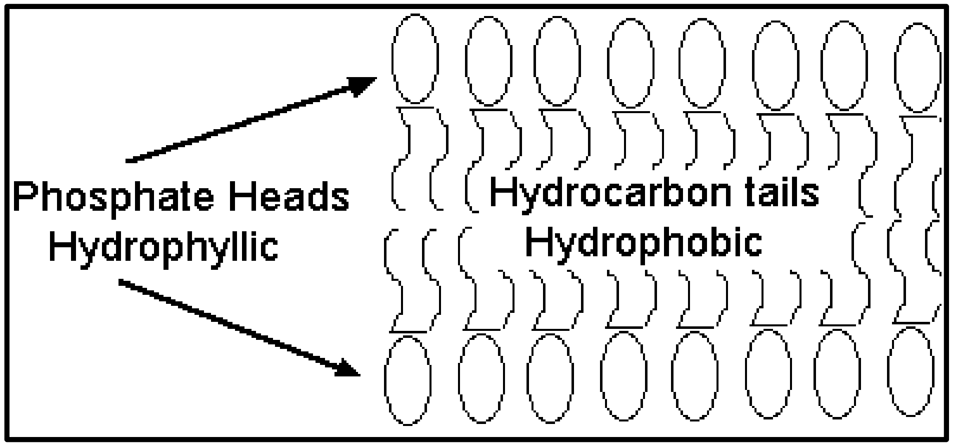
Phospholipids have hydrophilic heads and hydrophobic tails.

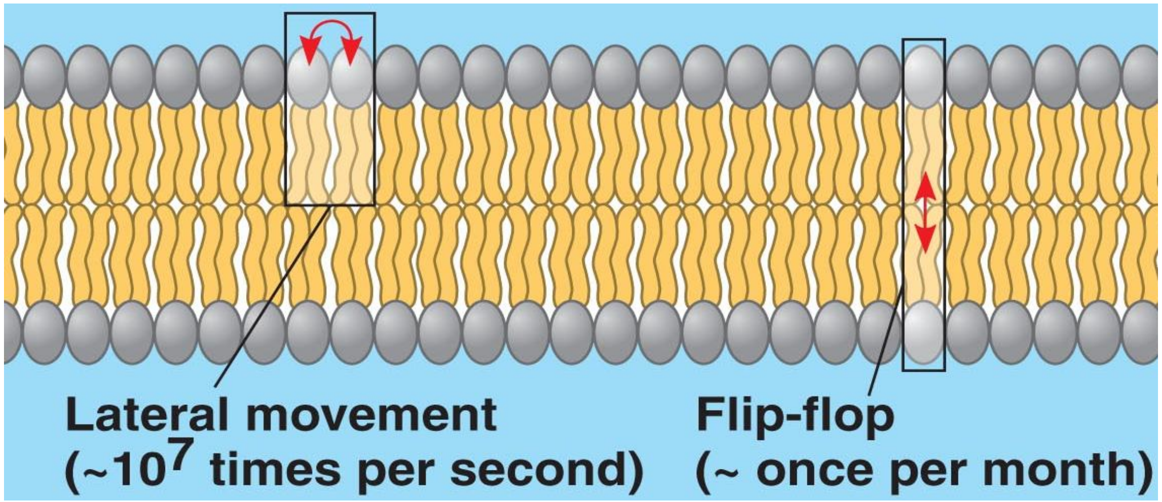




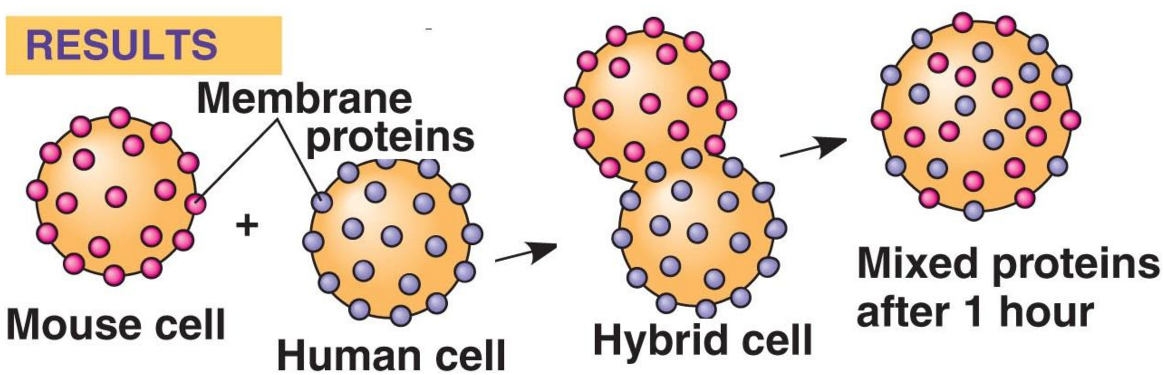
The cell membrane has two layers of phospholipids as shown below. The hydrophilic heads are facing an aqueous environment and the hydrophobic tails are facing one another.

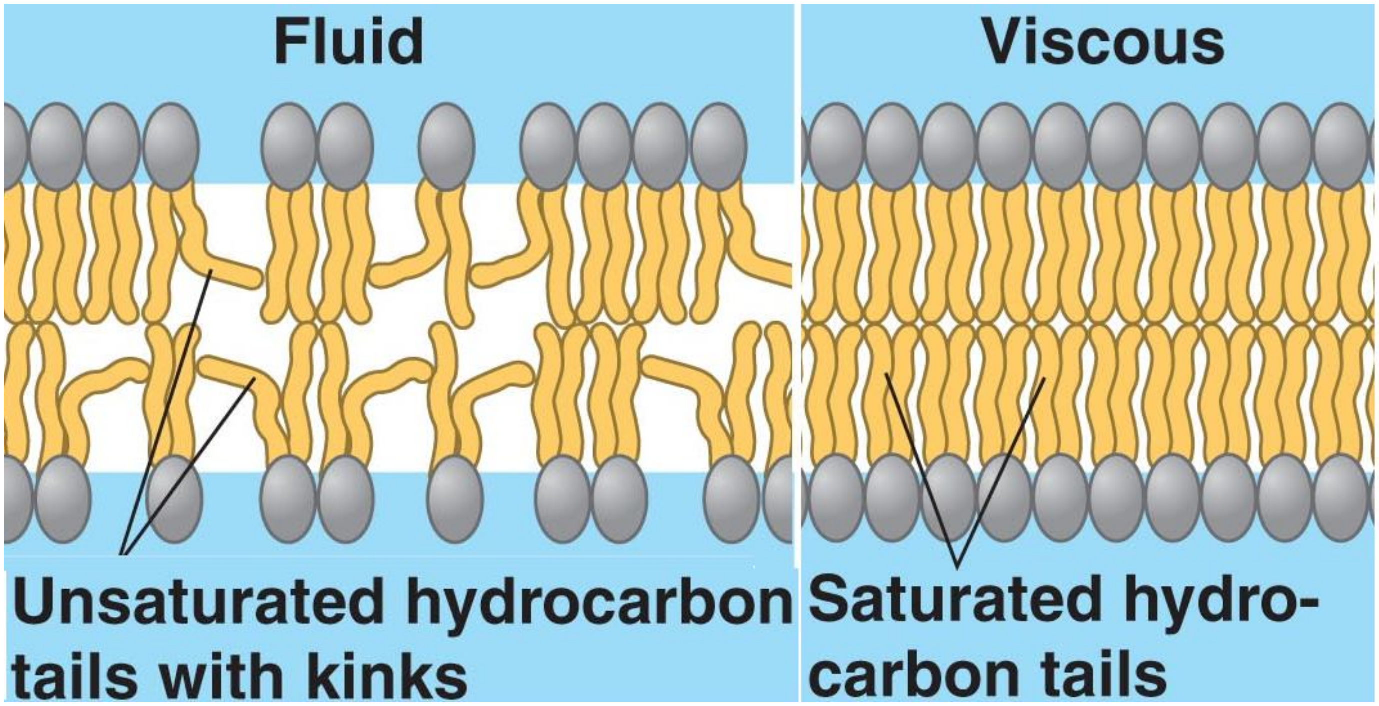




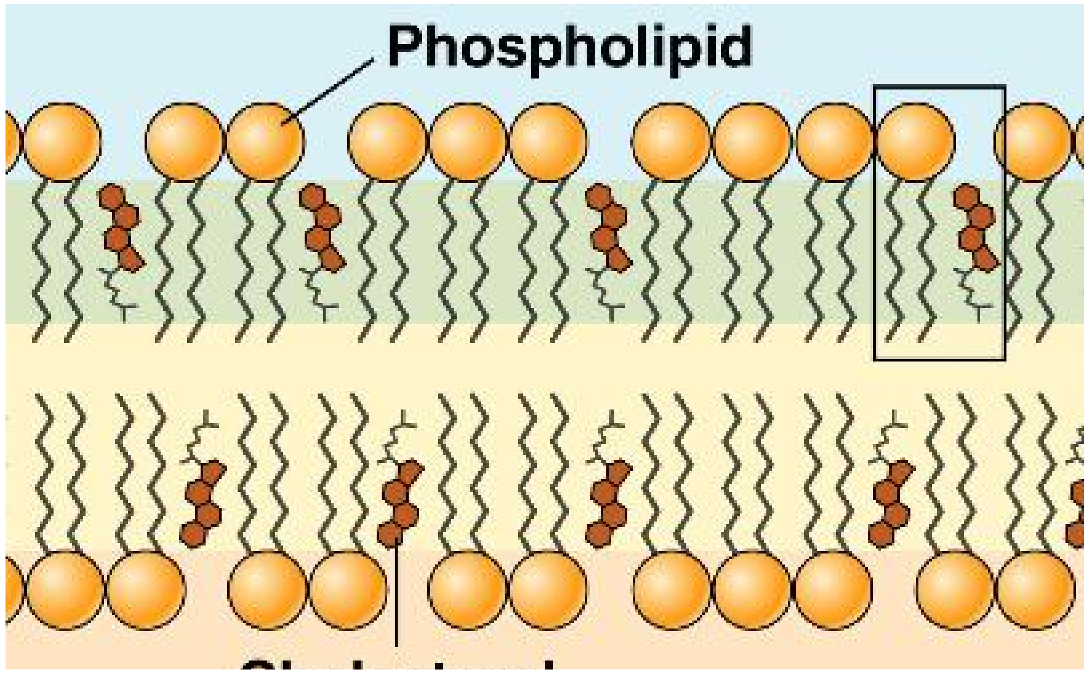


Phospholipids have the ability to move laterally but only upon a rare occasion are able to make a 180^{o} turn.





Membranes are more fluid when they contain more unsaturated fatty acids within their phospholipids. More unsaturated fatty acids result in increased distance between the lipids making the layer more fluid.



A word about cholesterol - It is found in the cell membranes of animals but not plants. It affects the fluidity of the membrane.

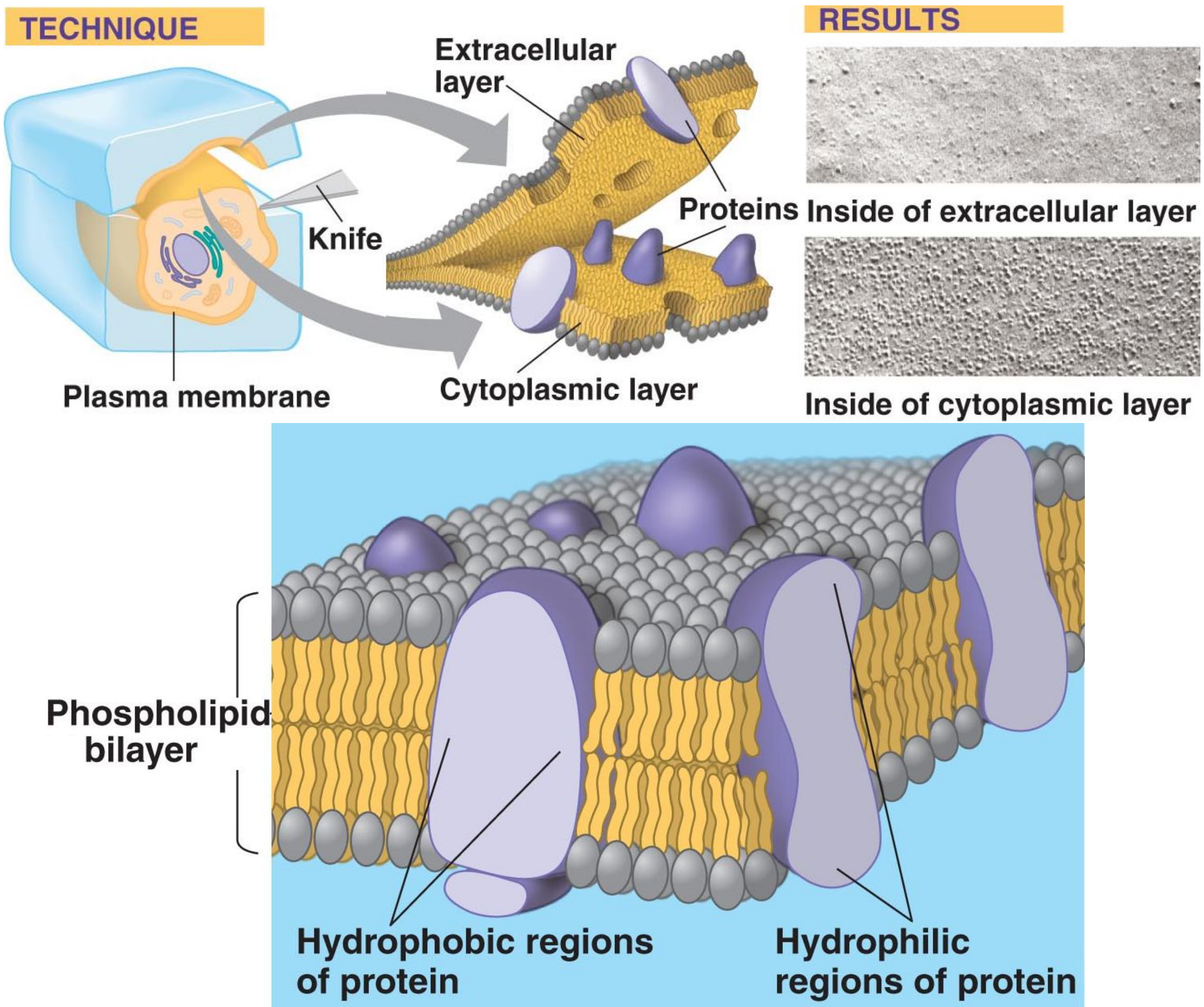
Cholesterol Functions in 3 ways

1. It can weakly bind to hydrocarbon tails making it more difficult for smaller molecules to cross membrane.
2. If the phospholipids are saturated, it prevents them from being packed too closely, making the membrane more fluid.
3. However - if the phospholipids are unsaturated there are kinks in the tails where the cholesterol molecules can fill in and anchor them making the membrane less fluid.

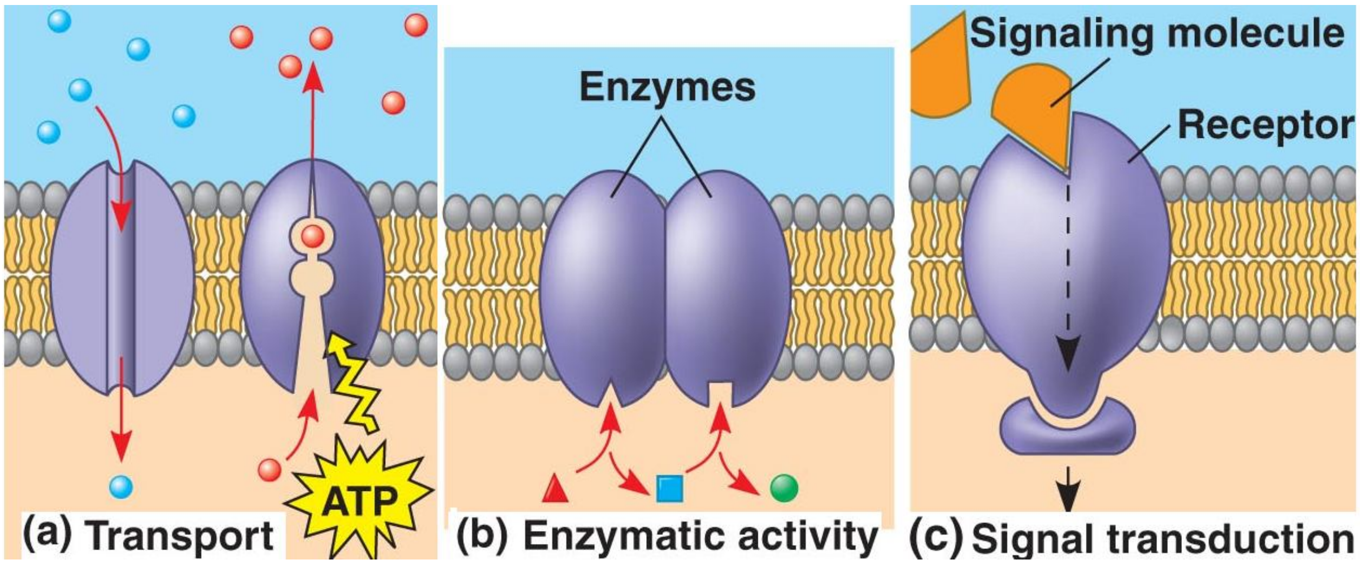
Fluid Mosaic Model

- Proteins are "stuck" in the membrane like a mosaic.
- Proteins can be on just the surface (peripheral) or embedded in the membrane (intrinsic).
  - Proteins that span the entire membrane are called “transmembrane”
- It is the different proteins that are responsible for the uniqueness of different membranes (plasma, eukaryotic, prokaryotic, organelle etc.)

Evidence for the Fluid Mosaic Model



Proteins are Inserted into the Membrane



Function of Membrane Proteins

1. **Transport proteins**, or permeases, transport molecules across the membrane. Aquaporins are special protein channels used to move water across the membrane.

- Integral Membrane proteins

Span the phospholipid bilayer – usually a-helices

Why do proteins cross membranes as α-helices?

Must present hydrophobic surface

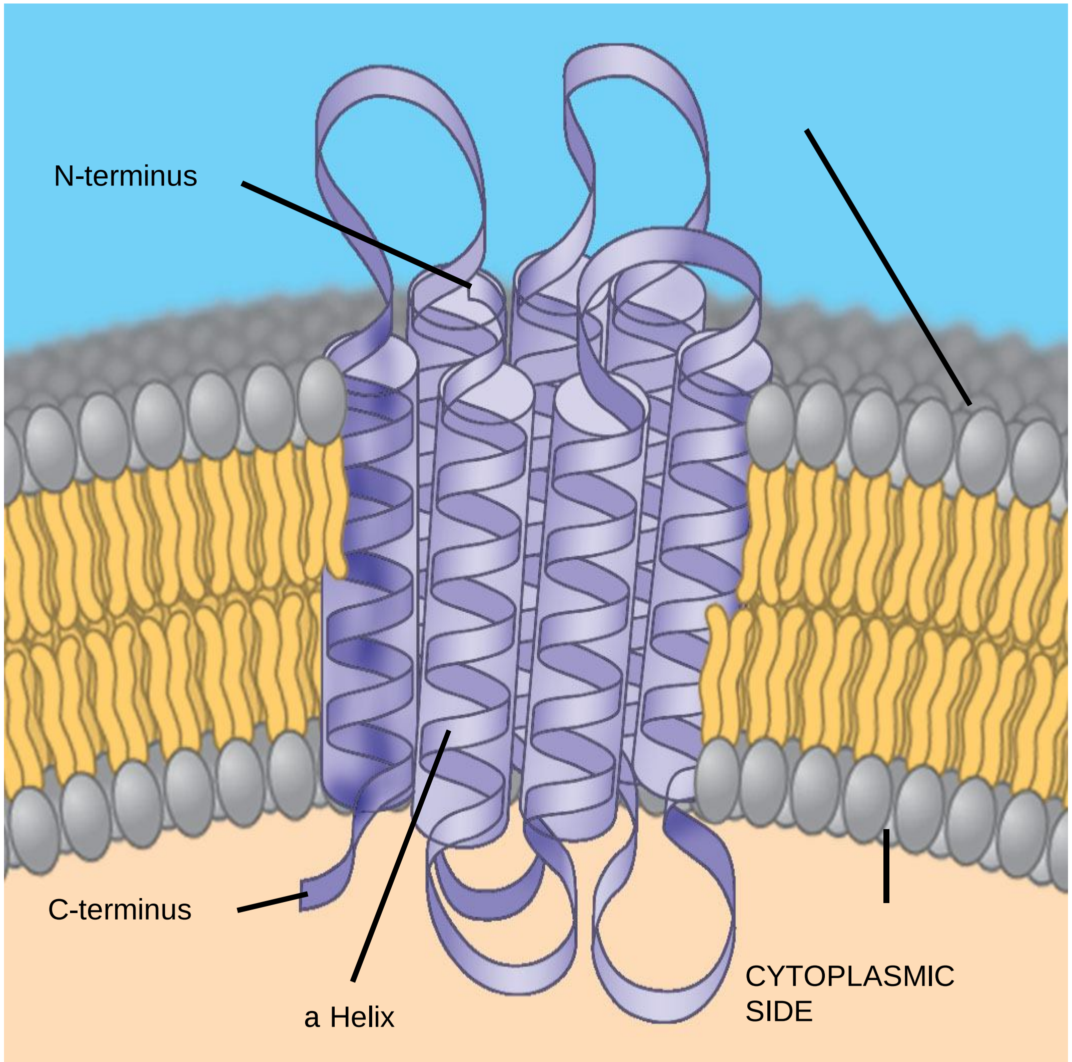
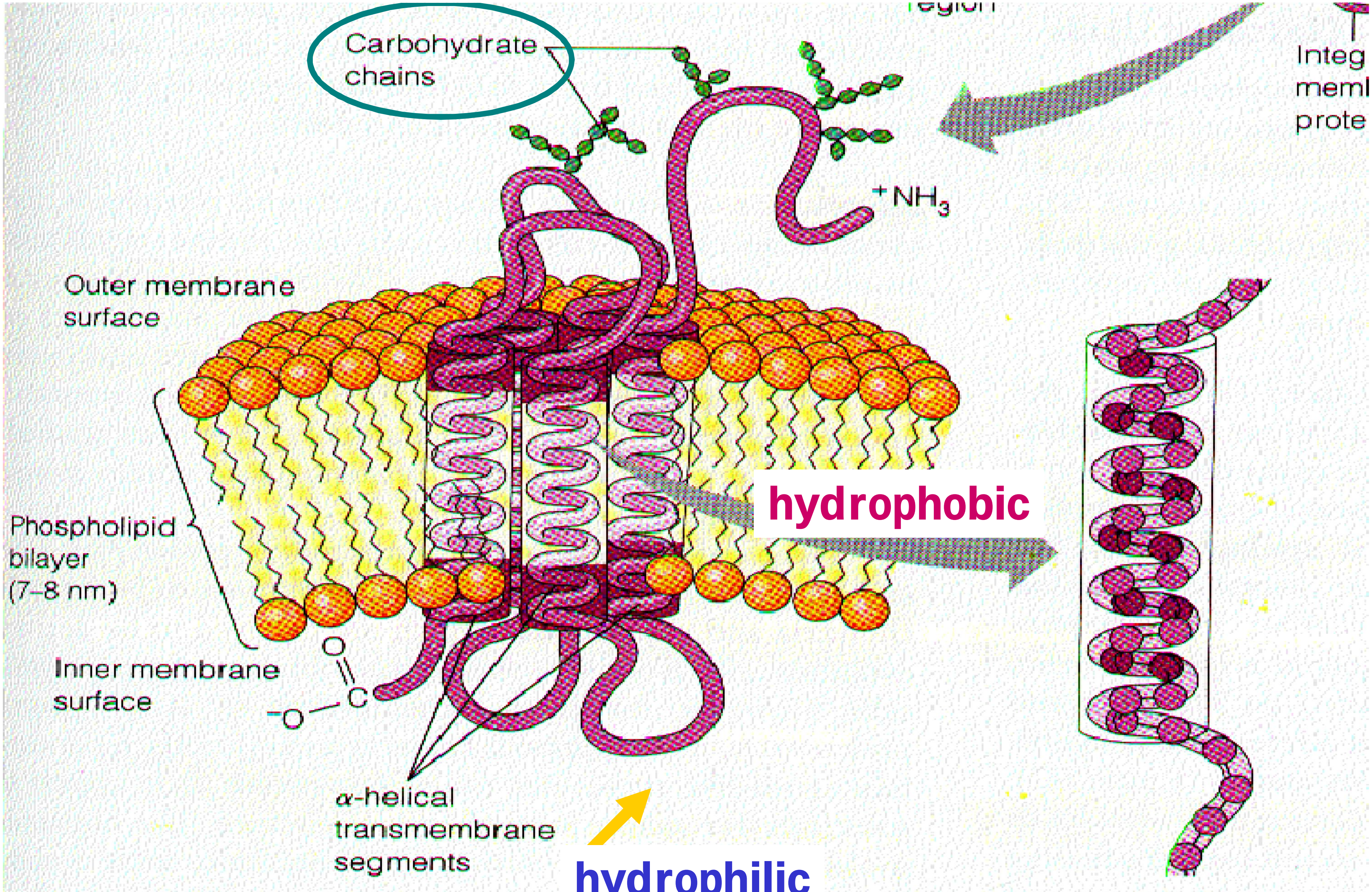


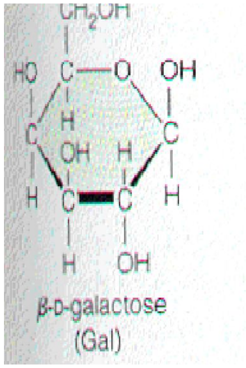
Figure 7.8



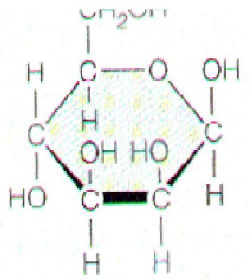
(b) An integral membrane protein

(c) An enlarged α-helical transmembrane segment (20–30 amino acids)

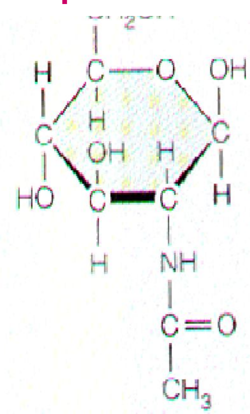
Sugars commonly found on glycoproteins



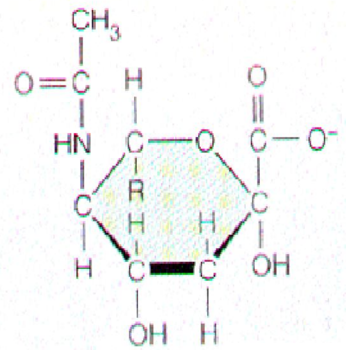
β-D-galactose



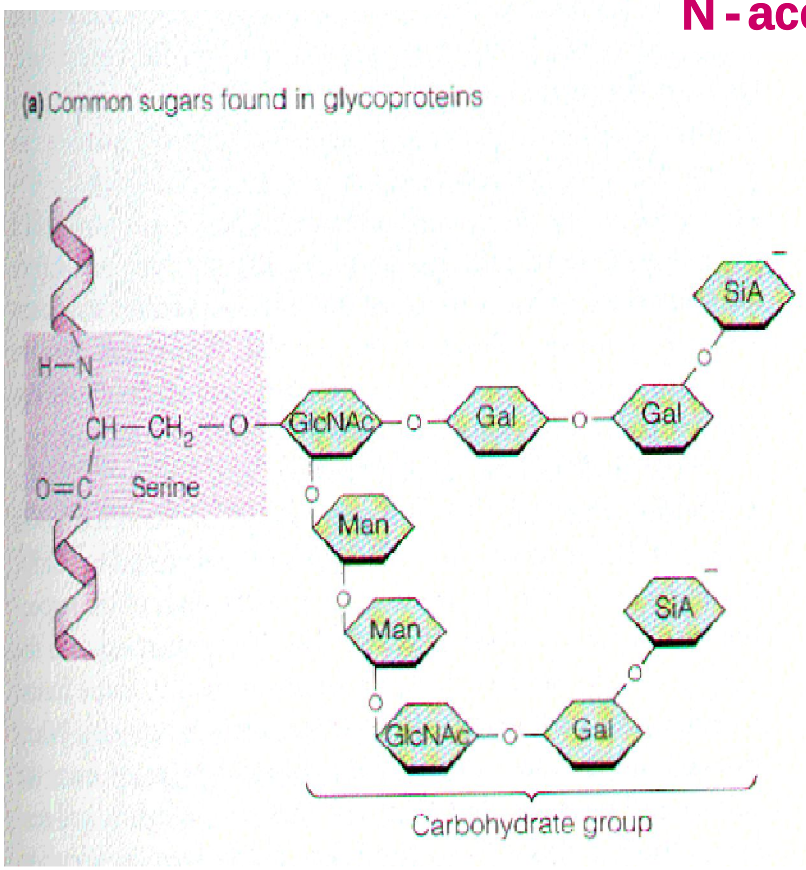
β-D-mannose



N-acetyl-β-D-glucosamine

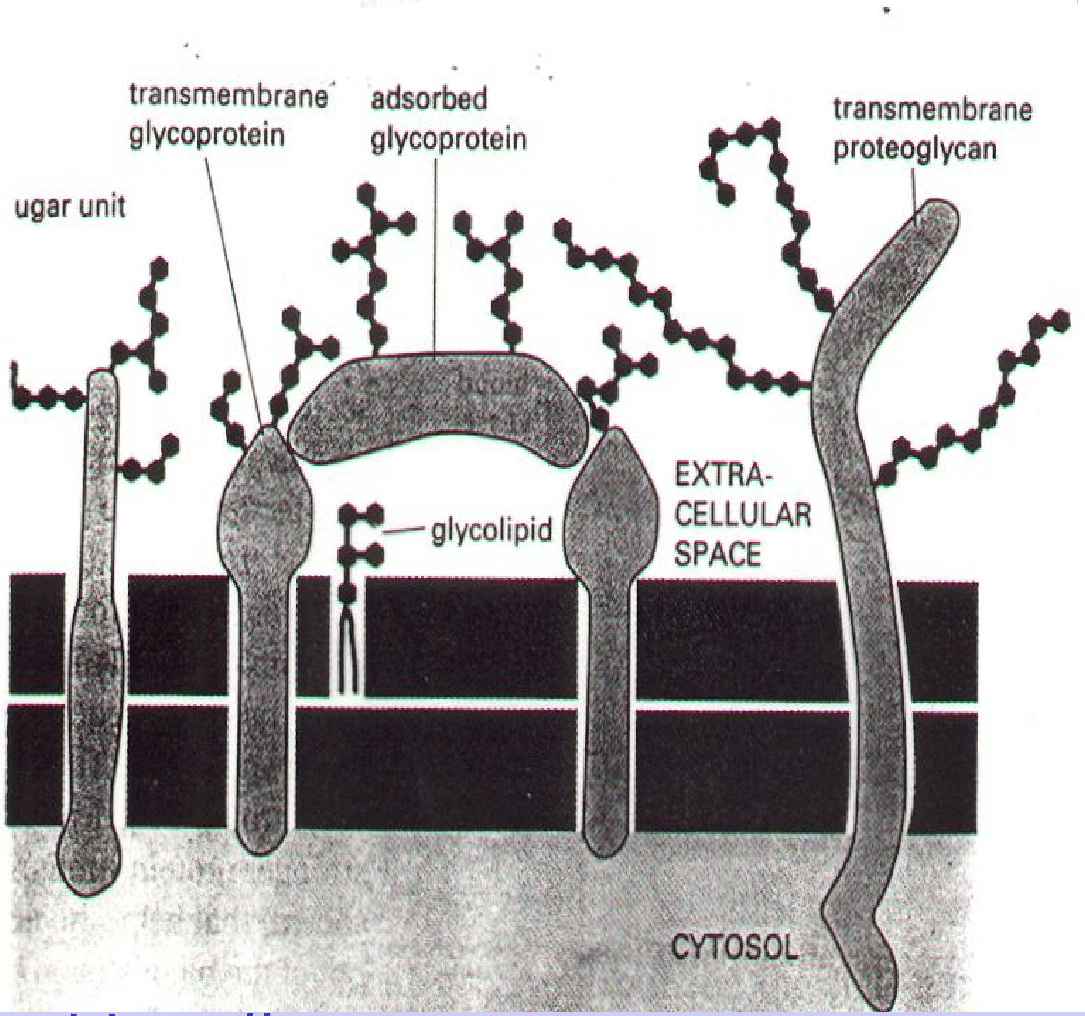


Sialic acid (SIA)
- charge

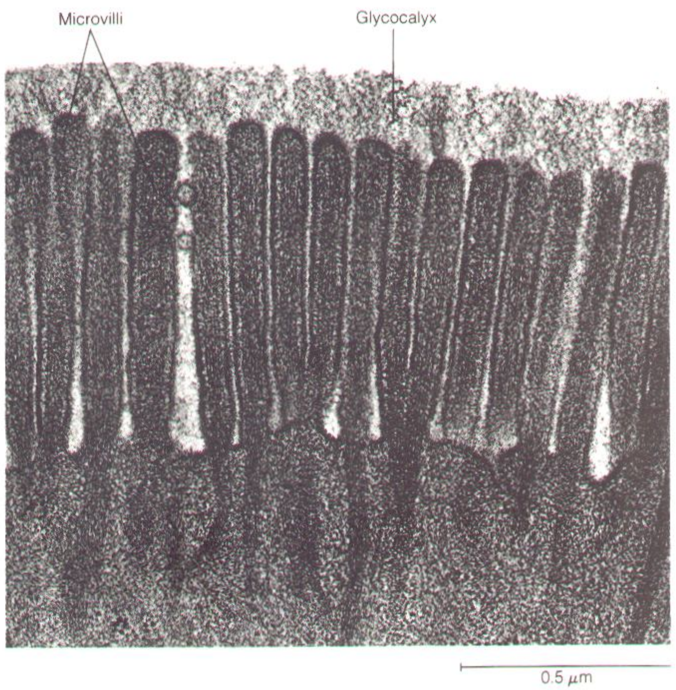


c. Carbohydrates – small amts often linked to proteins or lipids

Glycocalyx: *"sugar coat"*

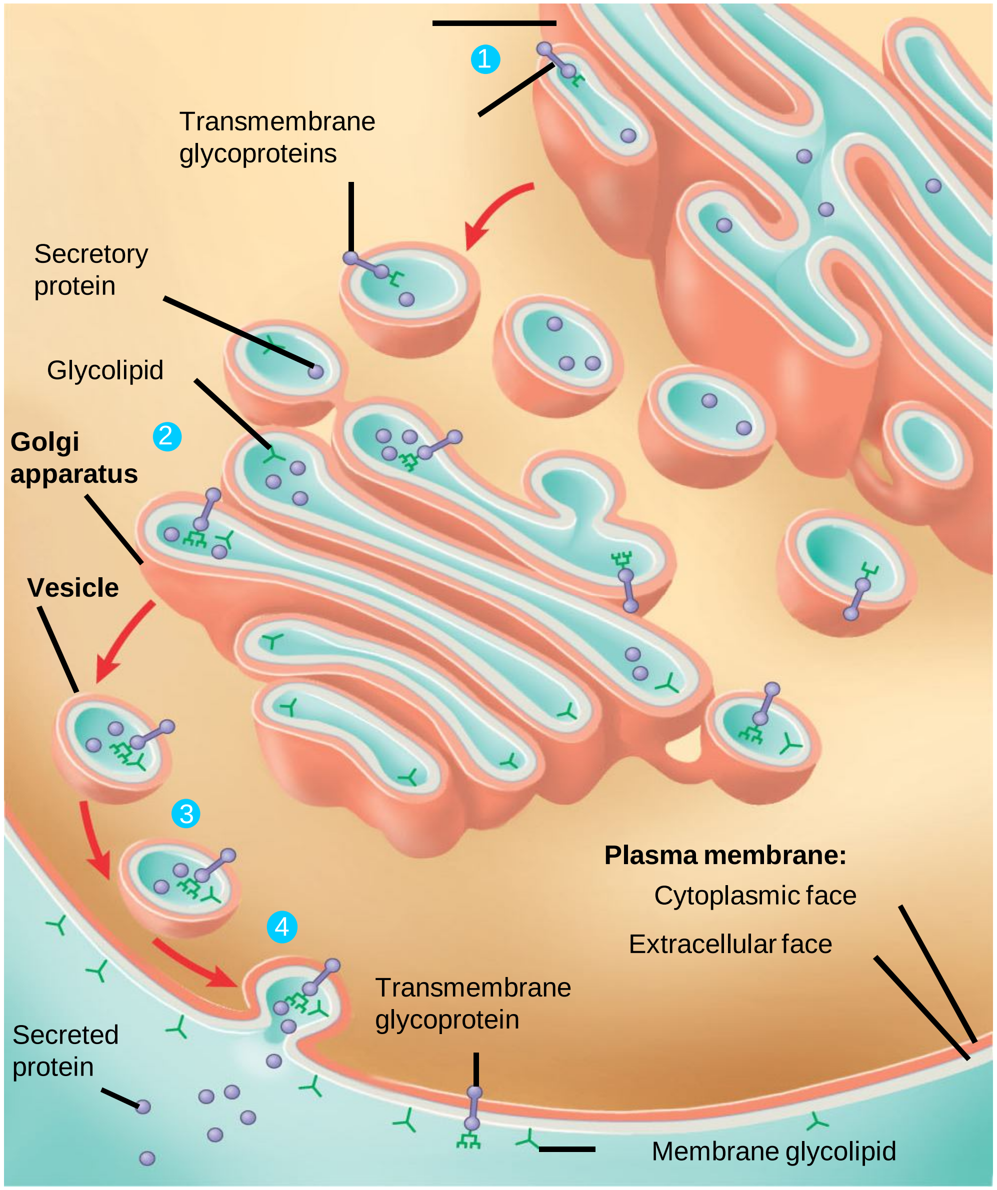


Outside cell



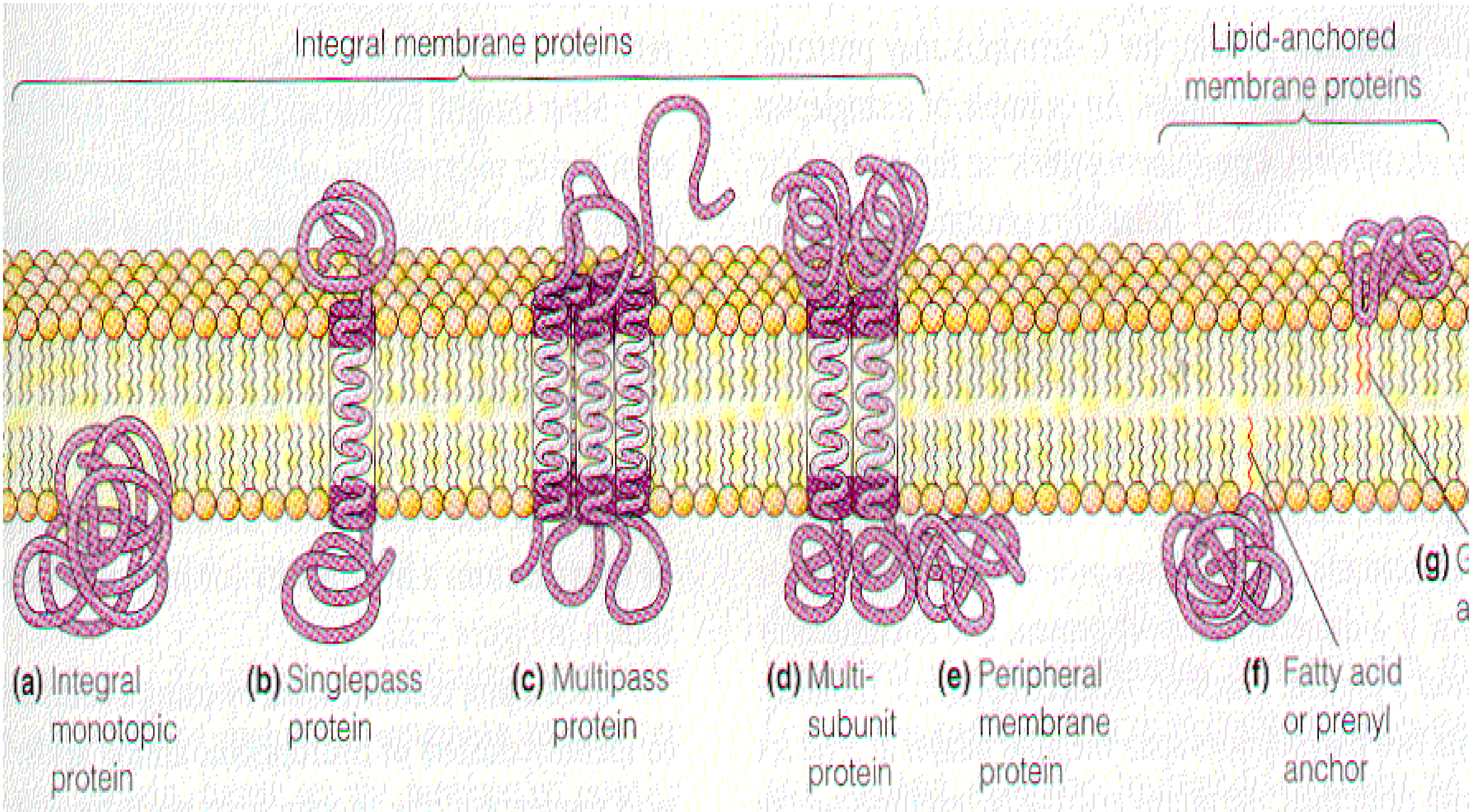
Inside cell

- Membrane proteins and lipids
  - Are synthesized in the ER and Golgi apparatus

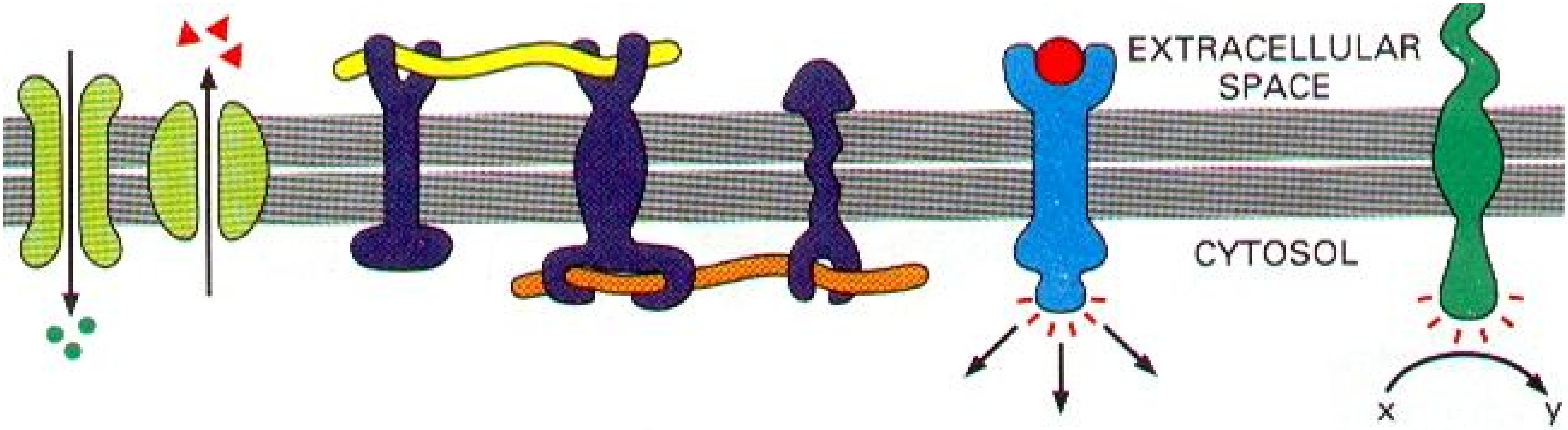


Membrane proteins

- Integral
  - Peripheral
    - Lipid-anchored



Roles of membrane proteins?

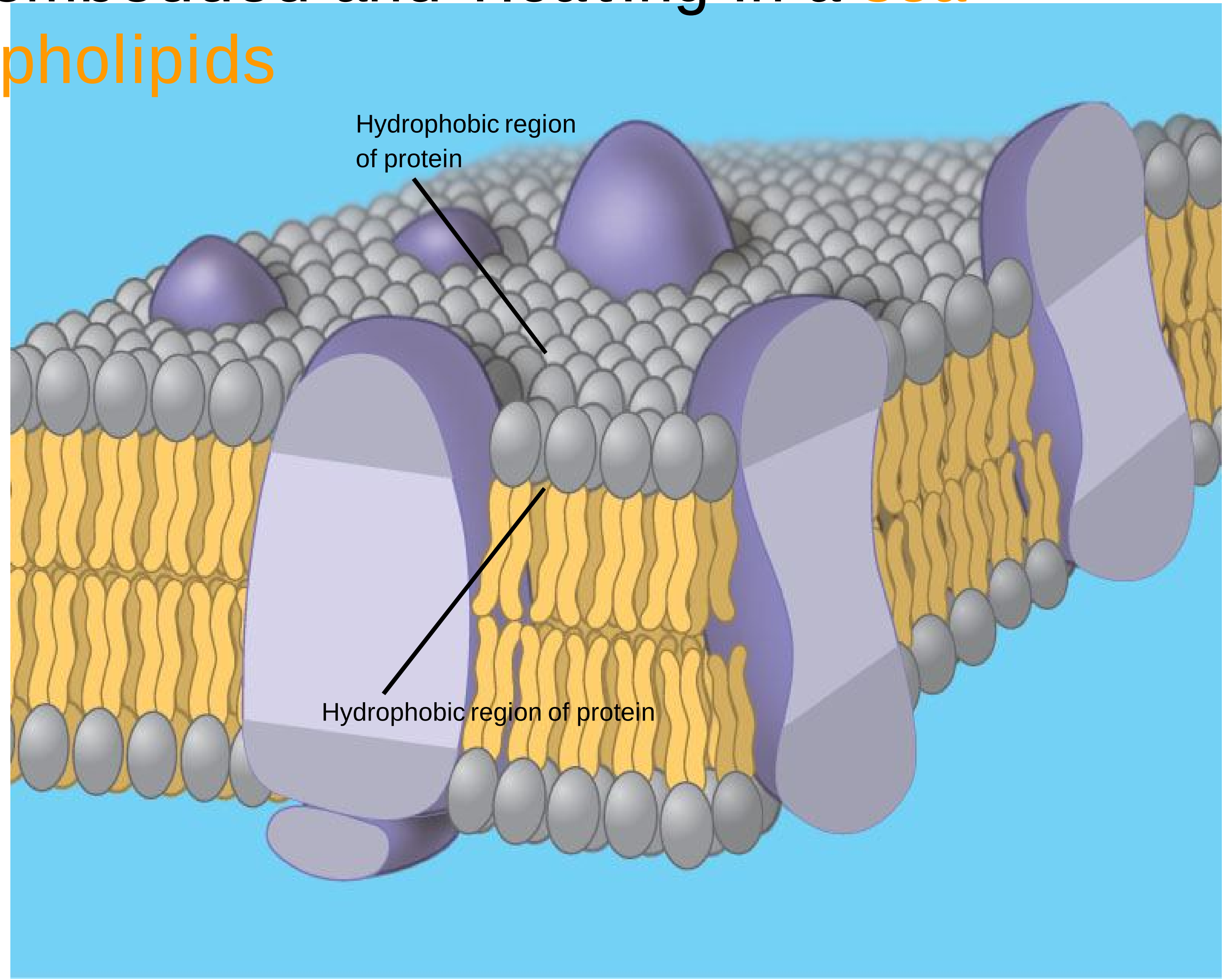


A. Transport – channels and pumps
B. Links to structural proteins
C. Receptors - doorbells
D. Enzymes – localized biochemical rxns
E. Energy Generation – utilize gradient

Fluid Mosaic Model

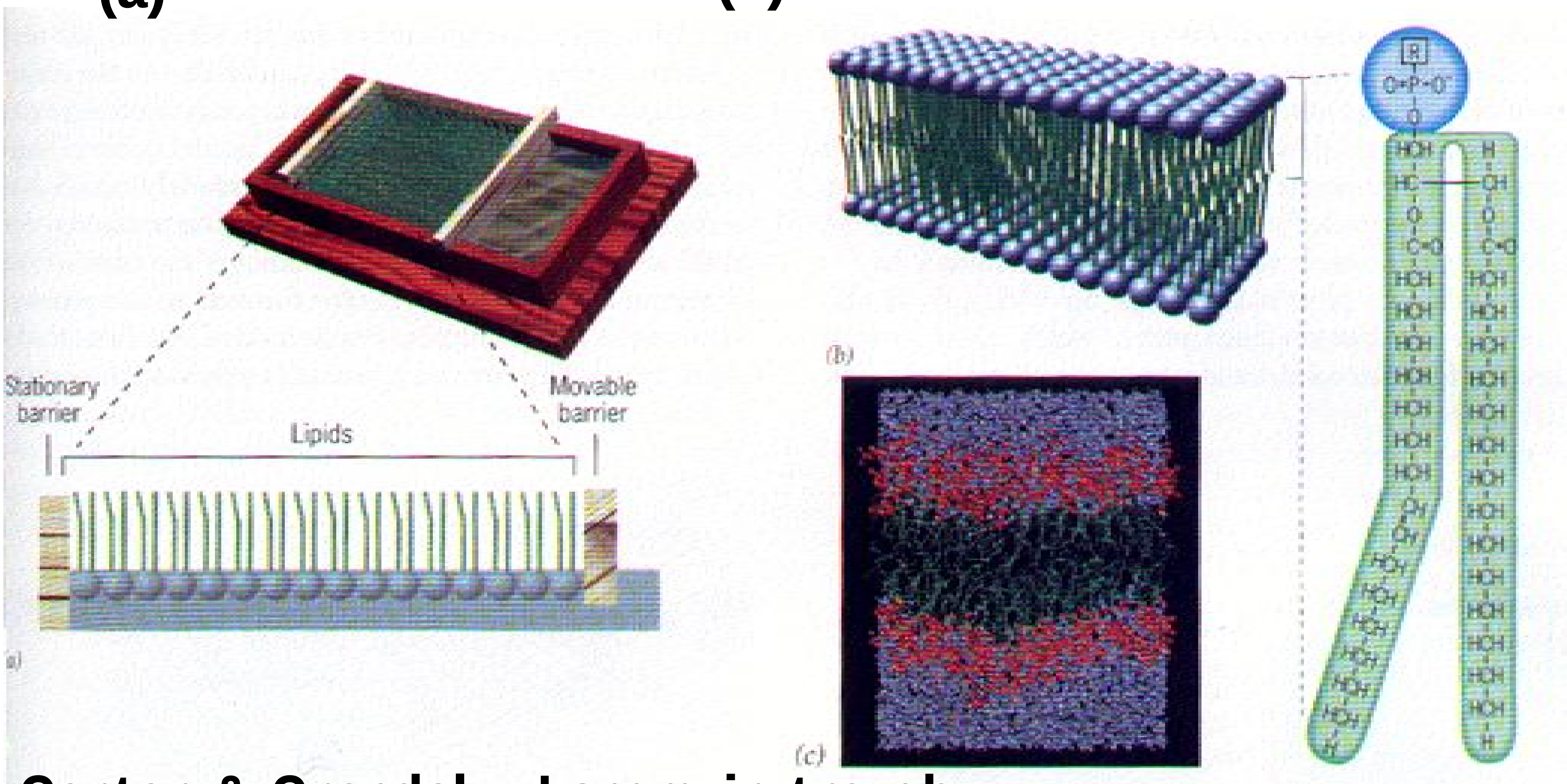
Proteins embedded and floating in a sea of phospholipids

Evidence?



Evidence for Phospholipid

(a) **(b)**

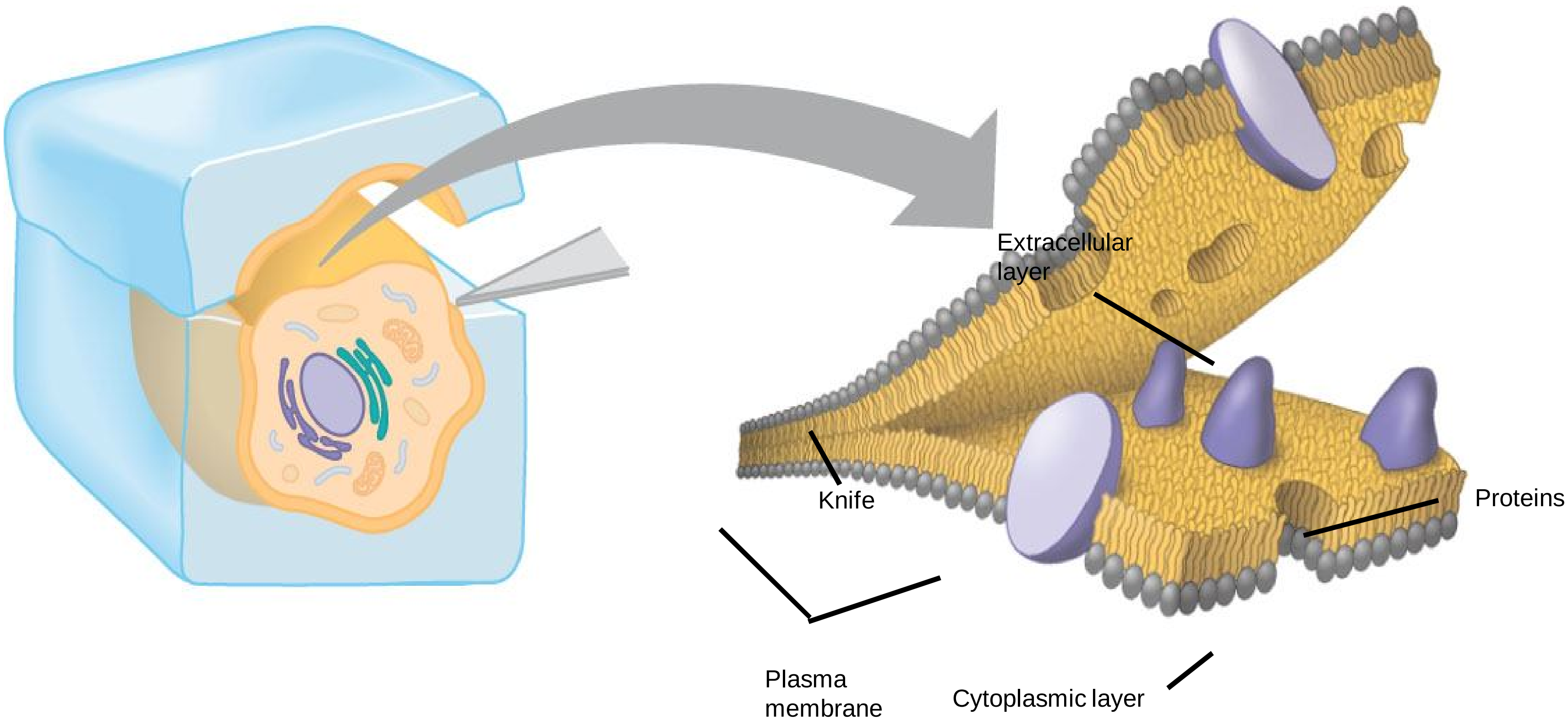


Gorter & Grendel – Langmuir trough

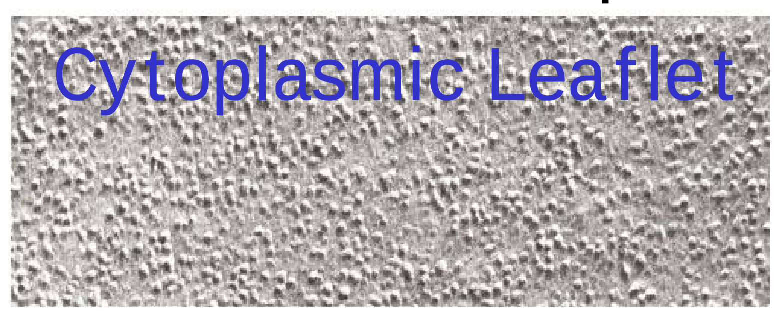
Red blood cells had enough lipid to <u>twice</u> cover their surface

Conclude lipid is a <u>bilayer</u> – hydrophilic heads faced aqueous environment

Evidence for integral membrane proteins: Freeze-Fracture Electron Microscopy



Illustrates: asymmetry of membrane componets



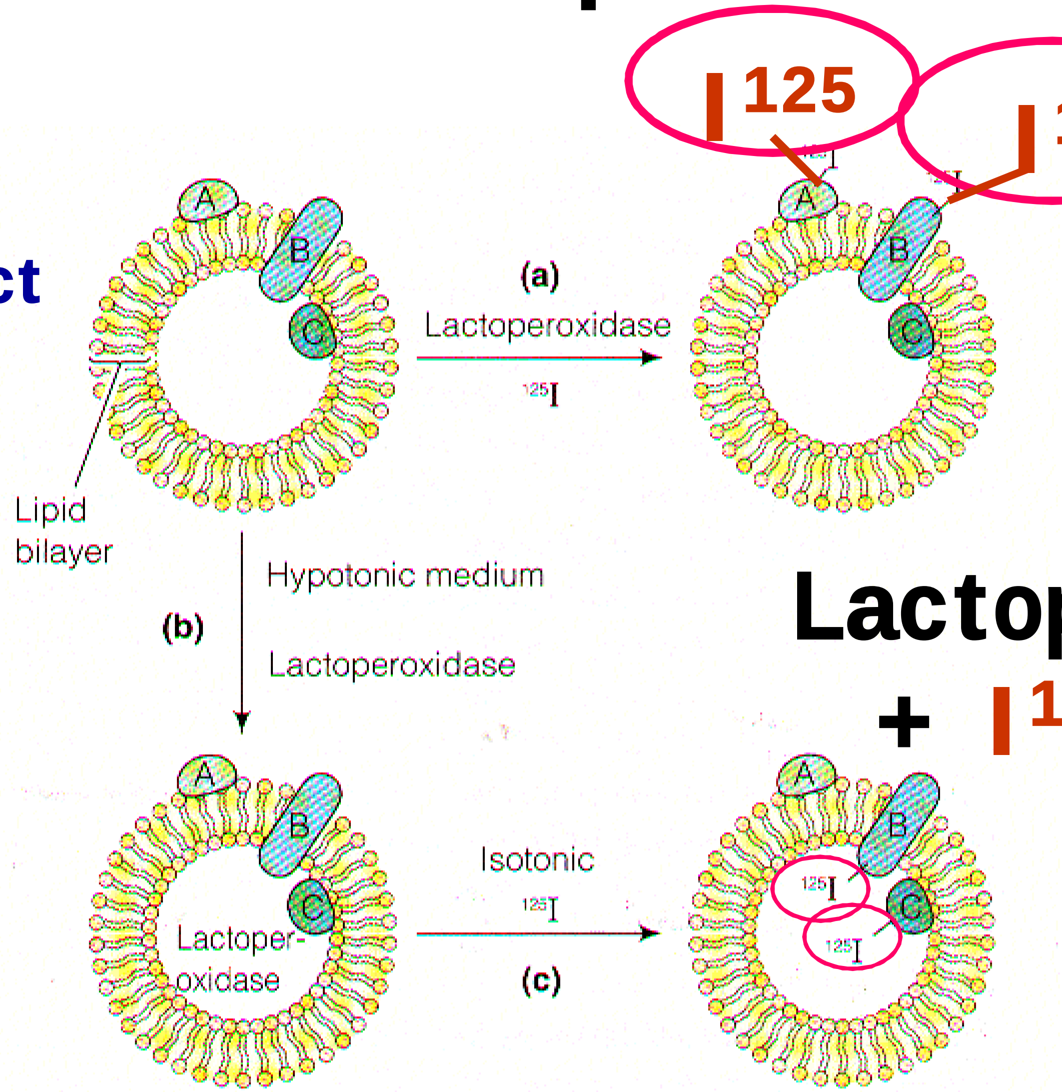
Fluid Mosaic Model predicts:

*A. Membranes are **fluid**: lipids & proteins move in the plane of the bilayer*

*B. Proteins and lipids are **asymmetrically** distributed in the bilayers*

Evidence for protein asymmetry

intact



LP adds I to protein
LP can't pass thru
intact membrane

Lactoperoxidase (LP)

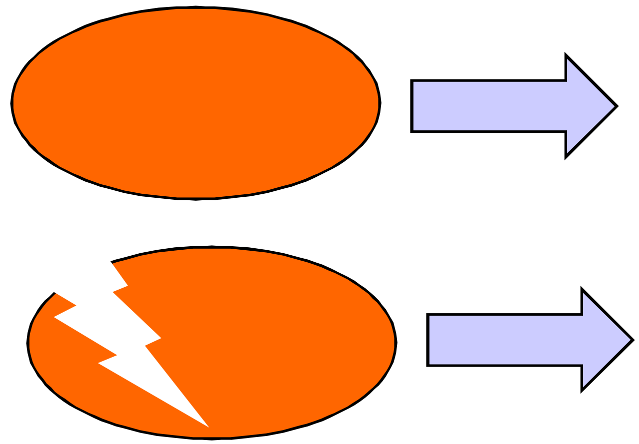
+ I 125

permeable

Evidence for lipid asymmetry?

Cut off head groups off of exposed lipids

Digested them with phospholipase



Intact red blood cells → **SM, PC**

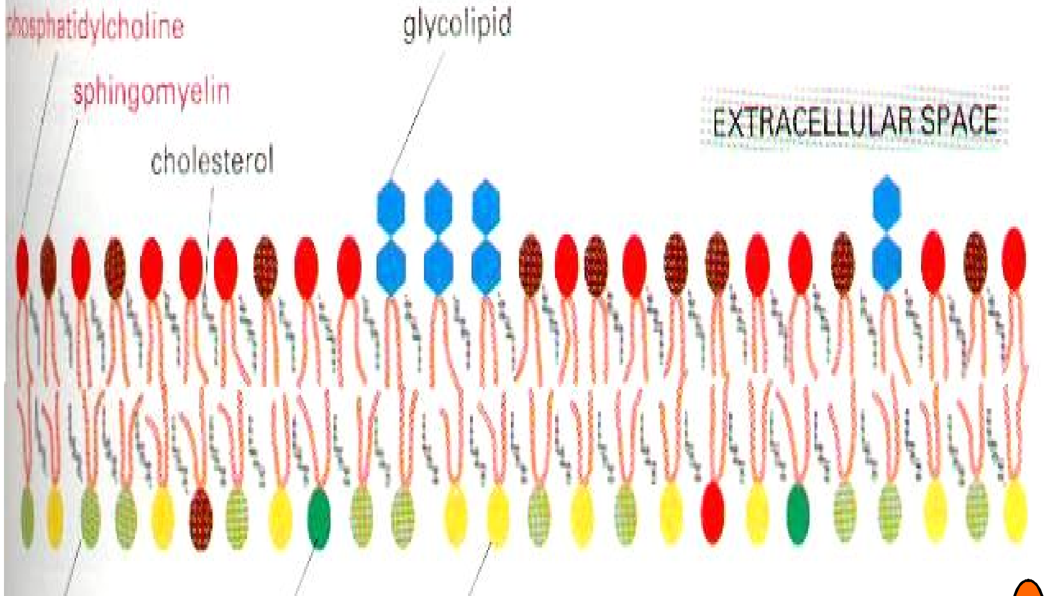
Broken red blood cells → **PE, PS SM & PC**

Results: ***isolated different types of phospholipids suggesting lipids were distributed <u>differently</u> in the inner and out parts of the bilayer***

SM, sphingomyelin; PC, phosphatidylcholine;
PE, phosphatidylcholine; PS phosphatidylserine

Mosaic: Lipids are asymmetrically distributed

Extracellular space



Cytosol

- phosphatidylcholine
- sphingomyelin
- glycolipid
- cholesterol

- phosphatidylinositol
- phosphatidylserine
- phosphatidylethanolamine

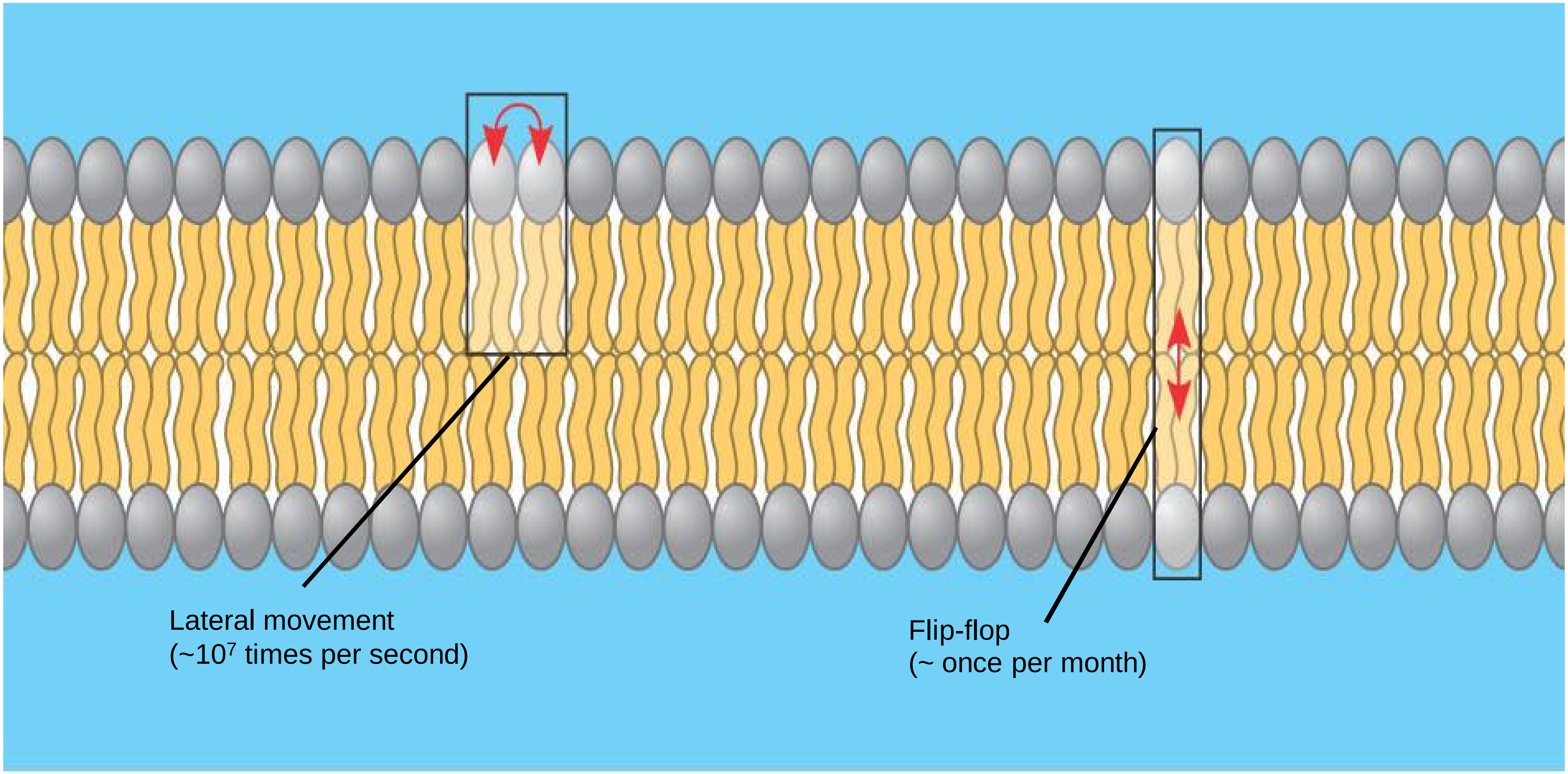
Fluid Mosaic Model predicts:

A. Membranes are fluid: lipids & proteins move in the plane of the bilayer

B. Proteins and lipids are asymmetrically distributed in the bilayers

The Fluidity of Membranes

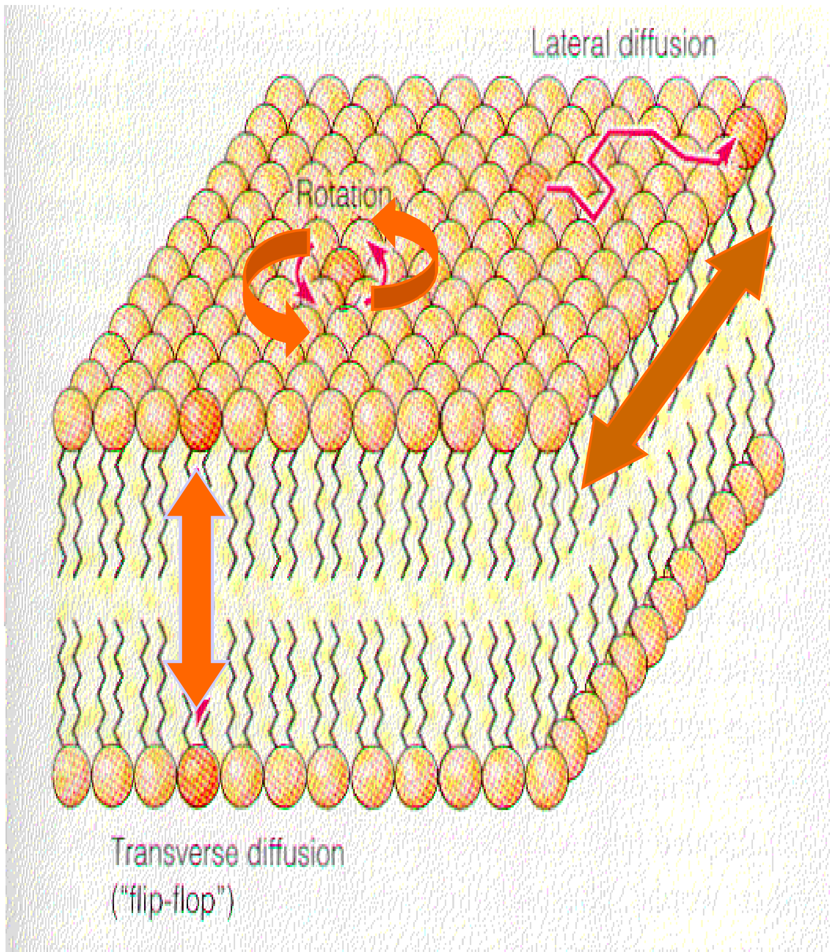
- Phospholipids can move ***laterally*** within the



(a) Movement of phospholipids

Movement of membrane phospholipids

1. Rotation about long axis



2. Lateral exchanges $1 \times 10^{7 \text{ times}}$/sec.

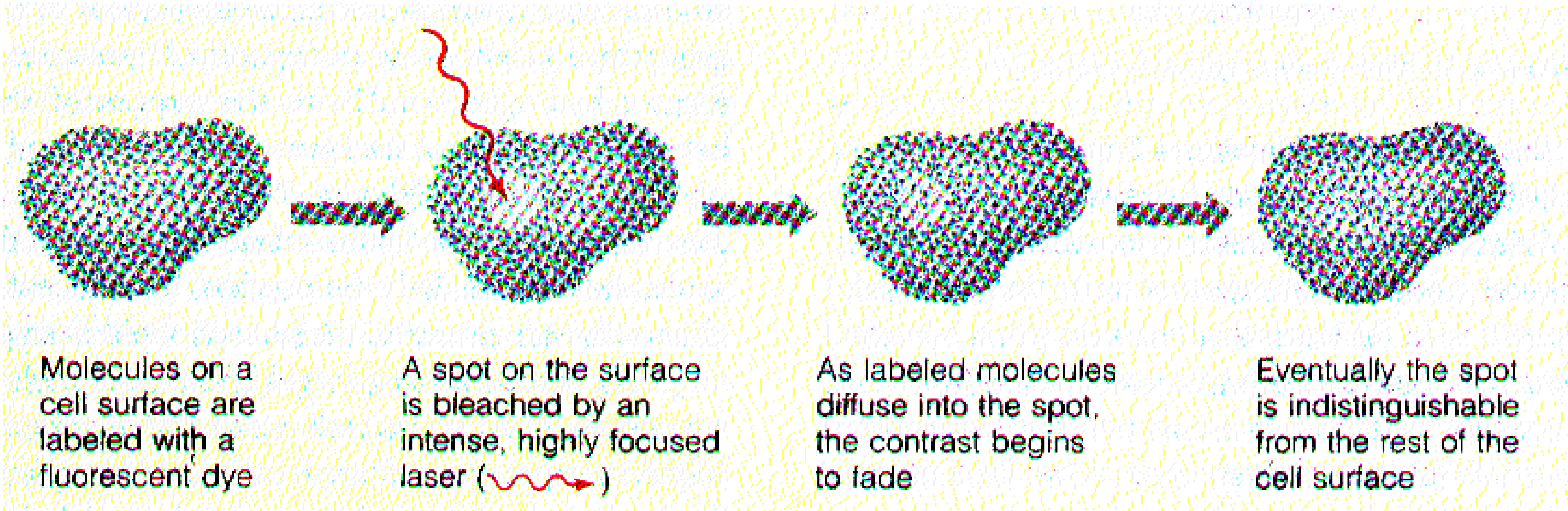
moves several μm/sec

3. Flip-flop – *rare*

<1 time/wk to 1 time/few hrs

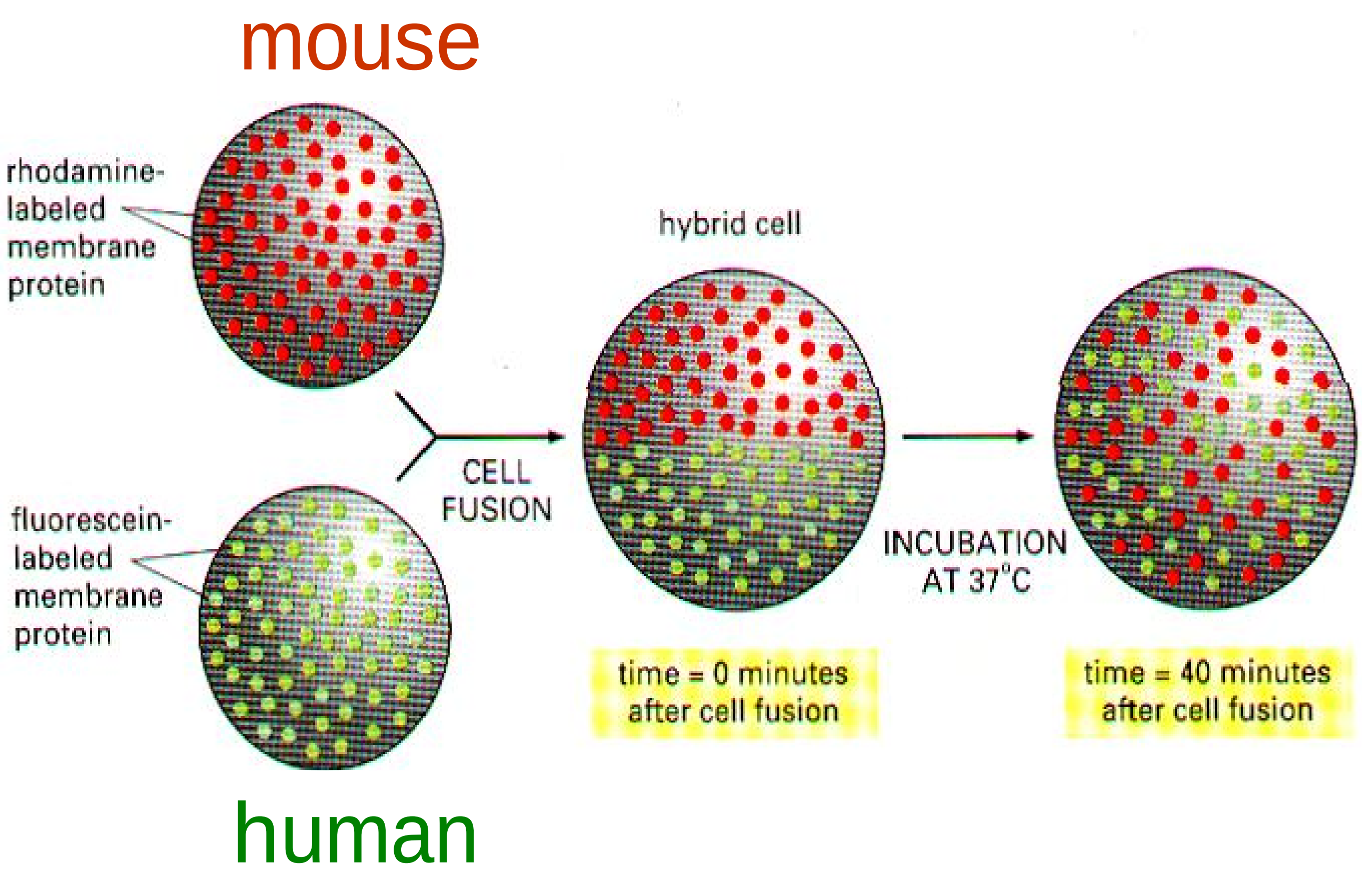
"*flippases*"

Evidence for lipid fluidity: Photobleaching



Evidence for membrane protein fluidity?

Cell fusion: 1970 D. Frye & M. Edidin



Lipids: critical role in maintaining membrane fluidity

•Saturated fatty acids stack nicely

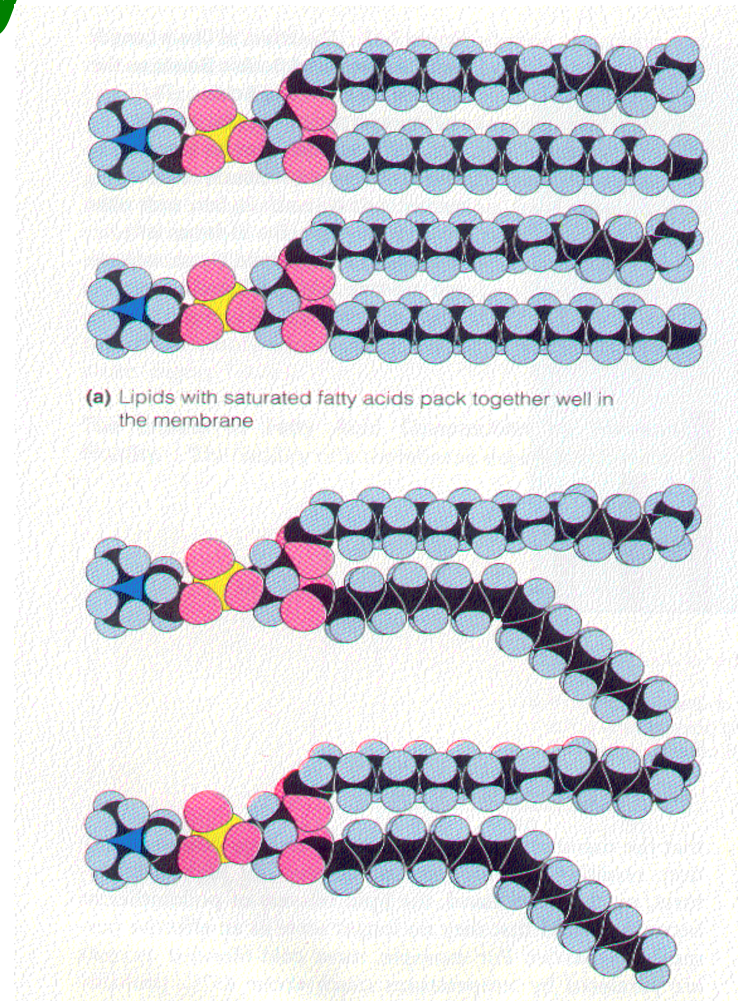
stiffer

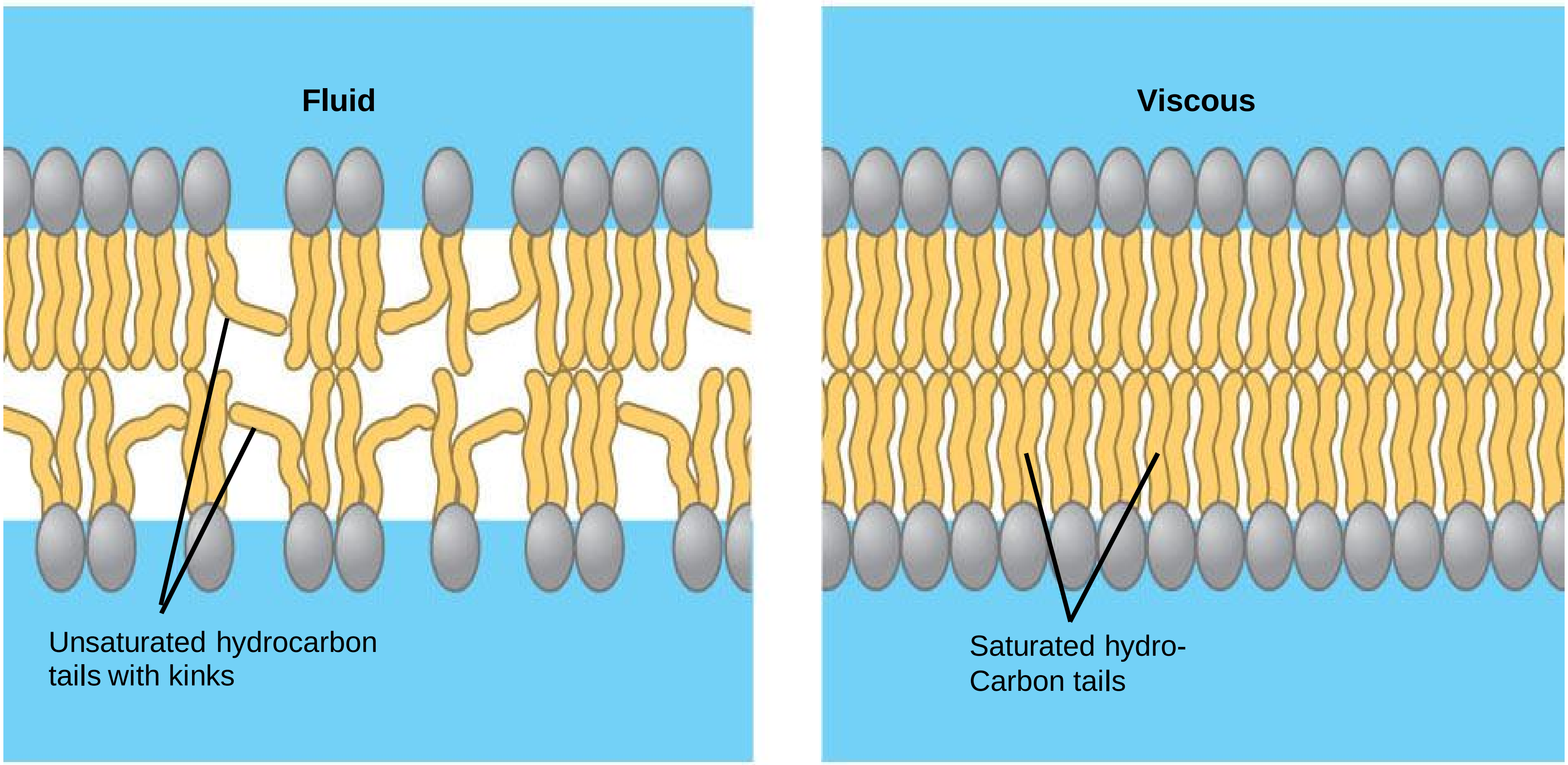
•Unsaturated fatty acids – more fluid; double bond causes kinks
Stacks poorly

More fluid

Shorter chains – stack poorly; More movement

Length & saturation of hydrocarbon tails affect packing & membrane fluidity

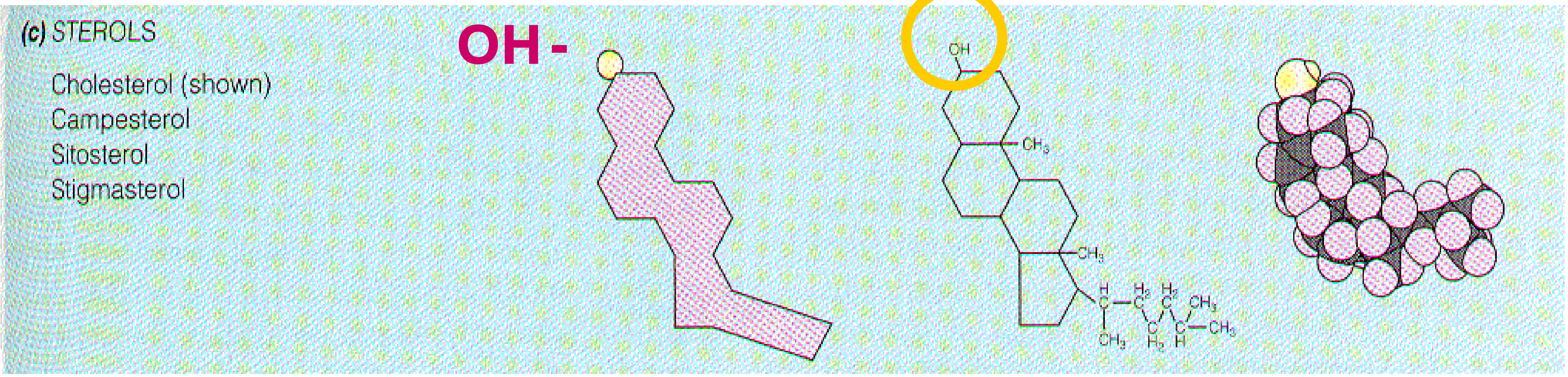


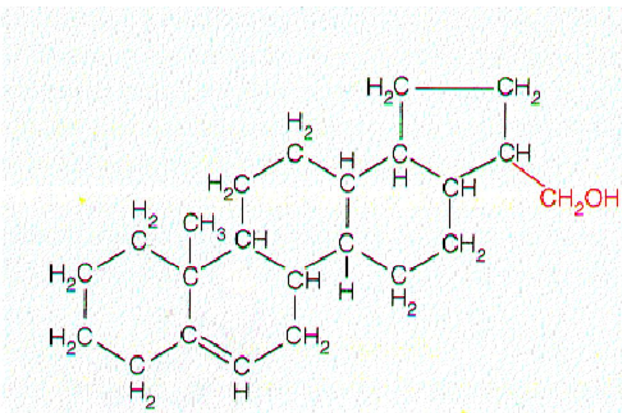


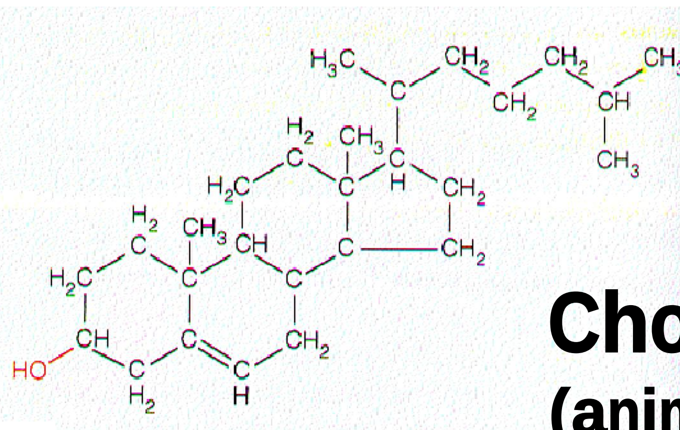
(b) Membrane fluidity

Figure 7.5 B

Sterols – affect membrane fluidity





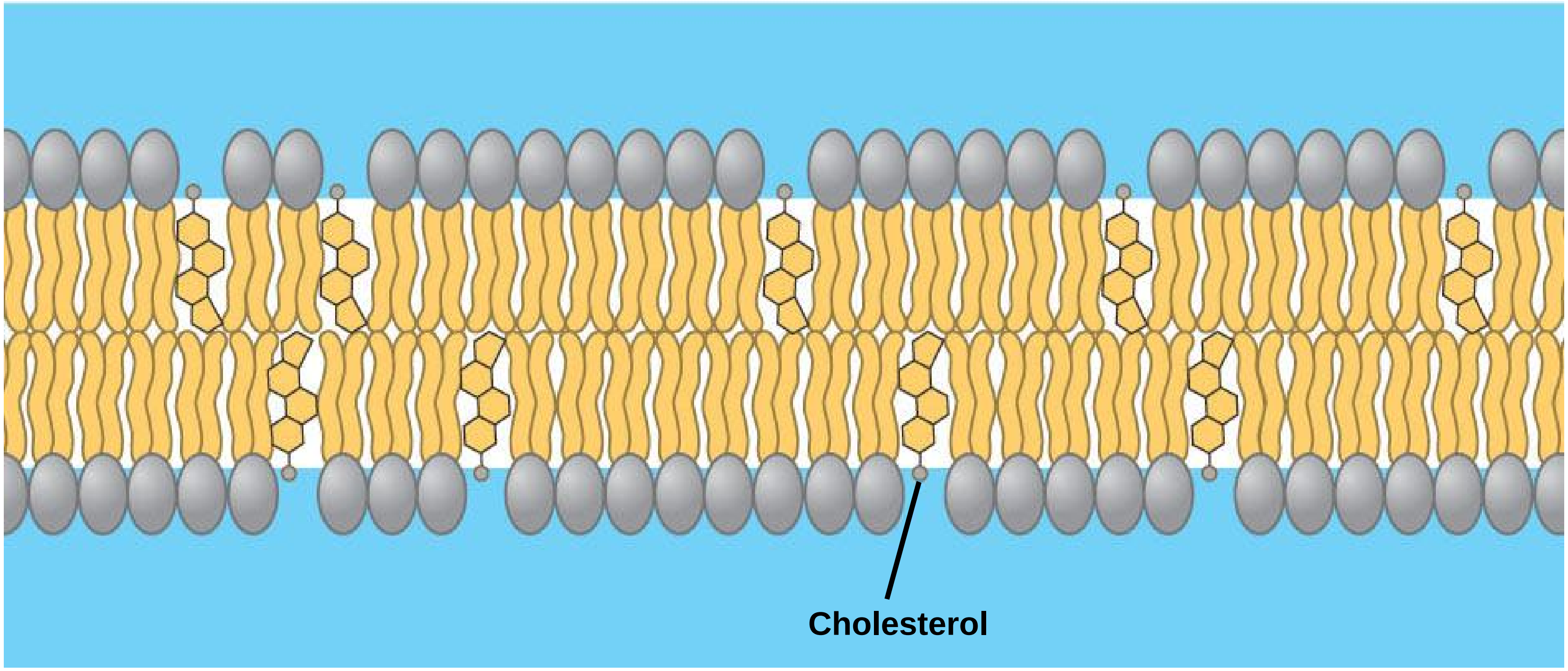


Cholesterol (animal)

Hopanoid (prokaryotes)

cholesterol

- At high temperature has a loosening effect
- At low temperature has a stiffening effect



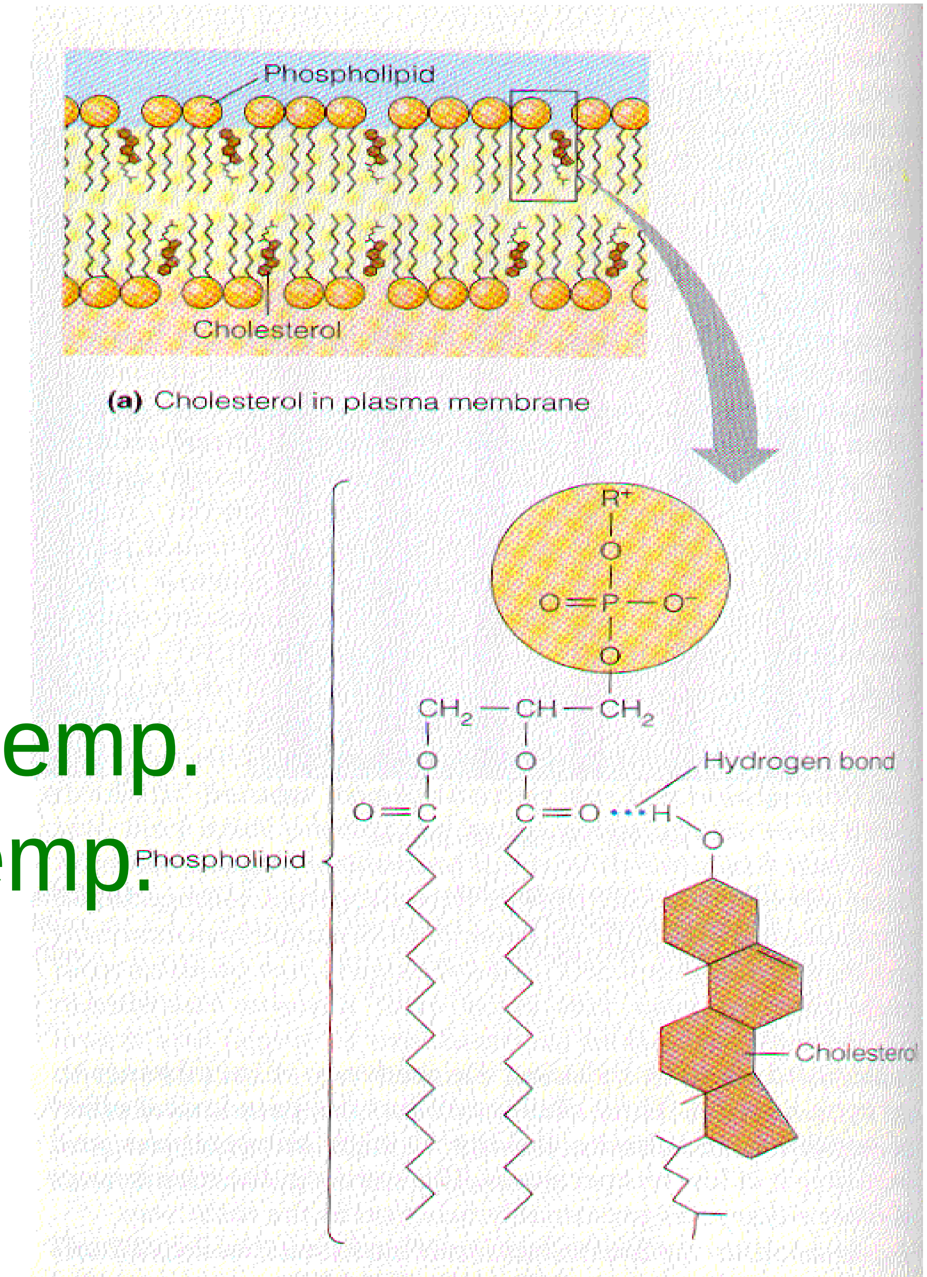
(c) Cholesterol within the animal cell membrane

Cholesterol is common in animal cells

Paradox:

a) ↓ fluidity at high temp.

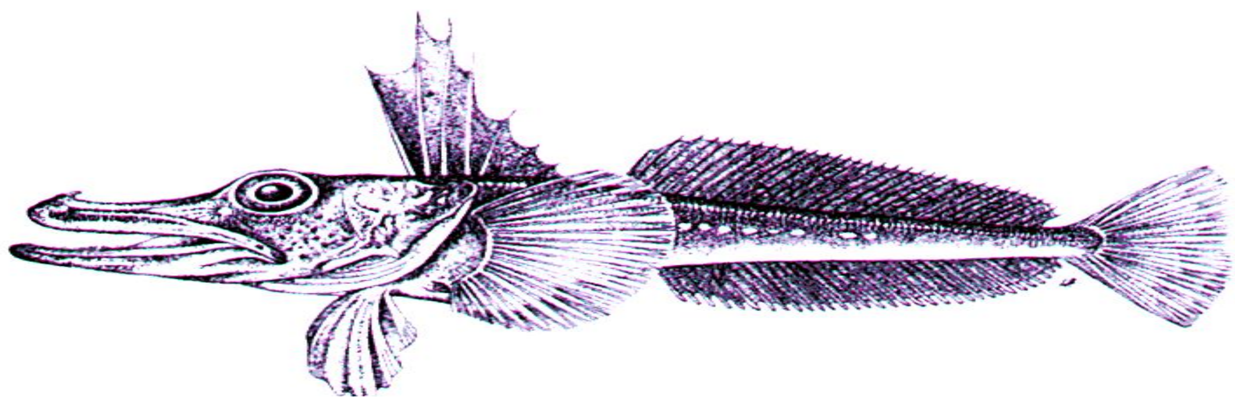
b) ↑ fluidity at low temp.



(a) Cholesterol in plasma membrane

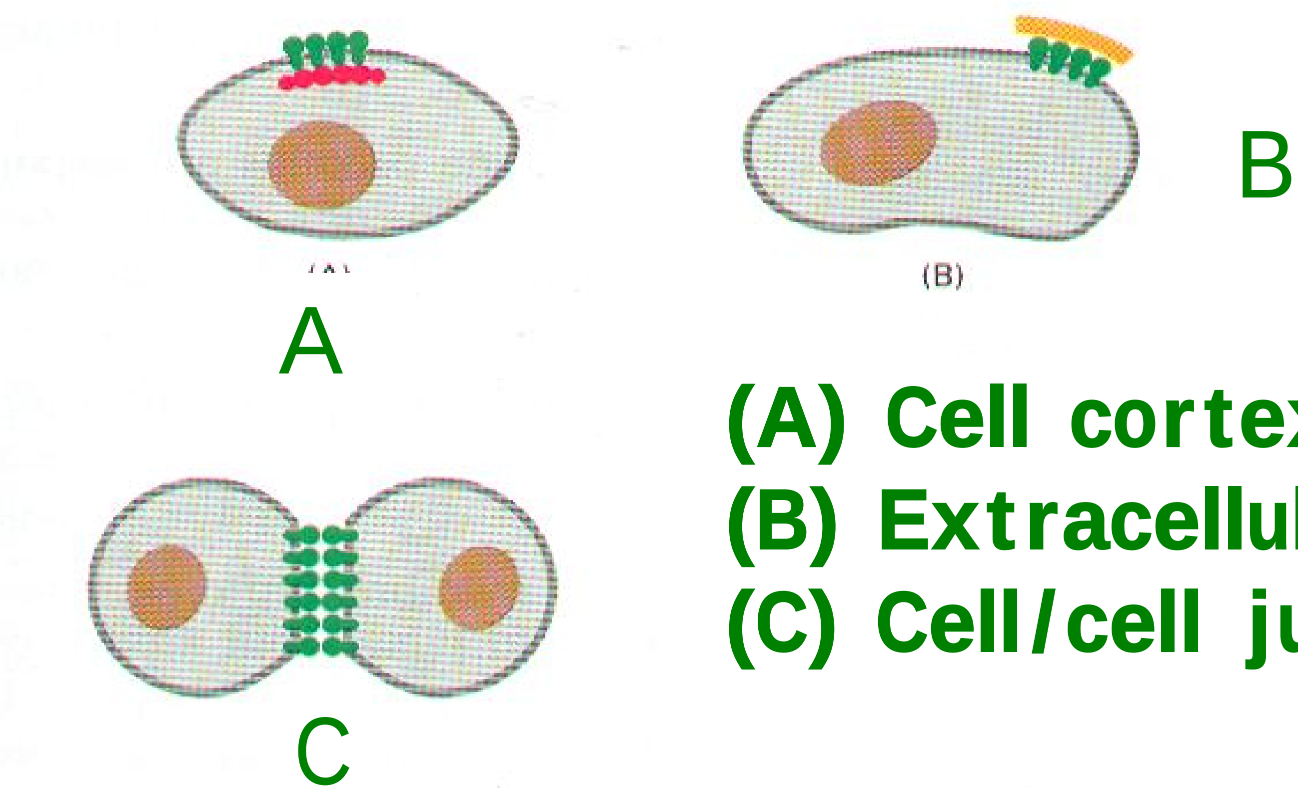
Most organisms regulate membrane fluidity

“Homeoviscous adaptation”



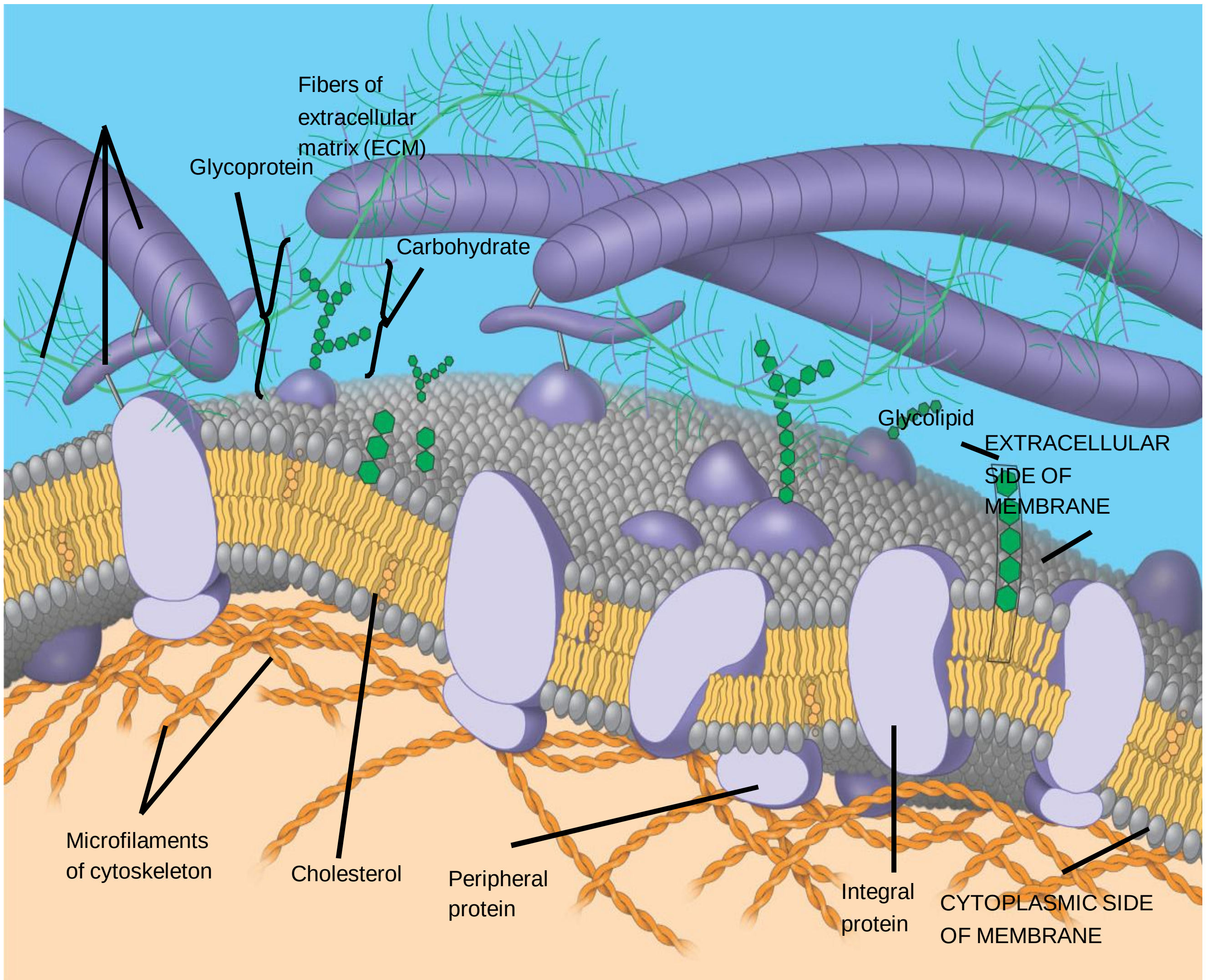
Fish, plants	**Mammals, palm trees**
0-20ºC	30-37ºC
Polyunsaturated F.A.	Saturated F.A.
Shorter chains	Longer chains
Cholesterol	cholesterol

Restricting movement of membrane proteins -> Membrane Domains



(A) Cell cortex
(B) Extracellular matrix
(C) Cell/cell junctions

Tethering of membrane proteins to the Extracellular Matrix or The Cytoskeleton



Summary: Membranes

1. **Fluid Mosaic Model**: **fluid** nature & **asymmetric** distribution of components

2. Components:
   - **Lipids** – phospholipids, sterols, glycolipids
   - Fluidity

   - **Proteins** – integral, peripheral, lipid-linked
   - transport, receptors, enzymes, structural support, electron transport, specialized functional domains

   - **Carbohydrates** – as glycolipids & glycoproteins external glycocalyx

Thanks for Your Patience

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14.02.2019