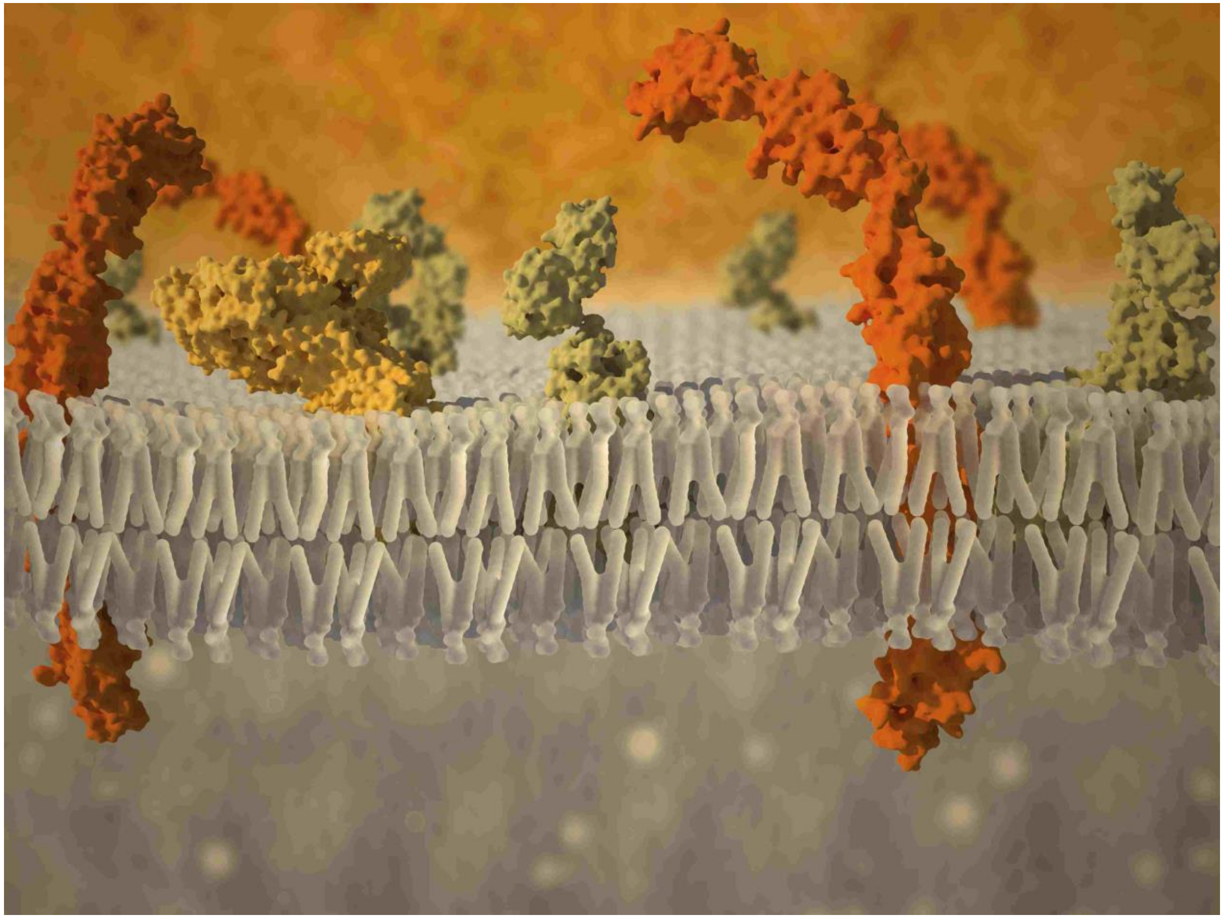
Cell membrane



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08/12/2016

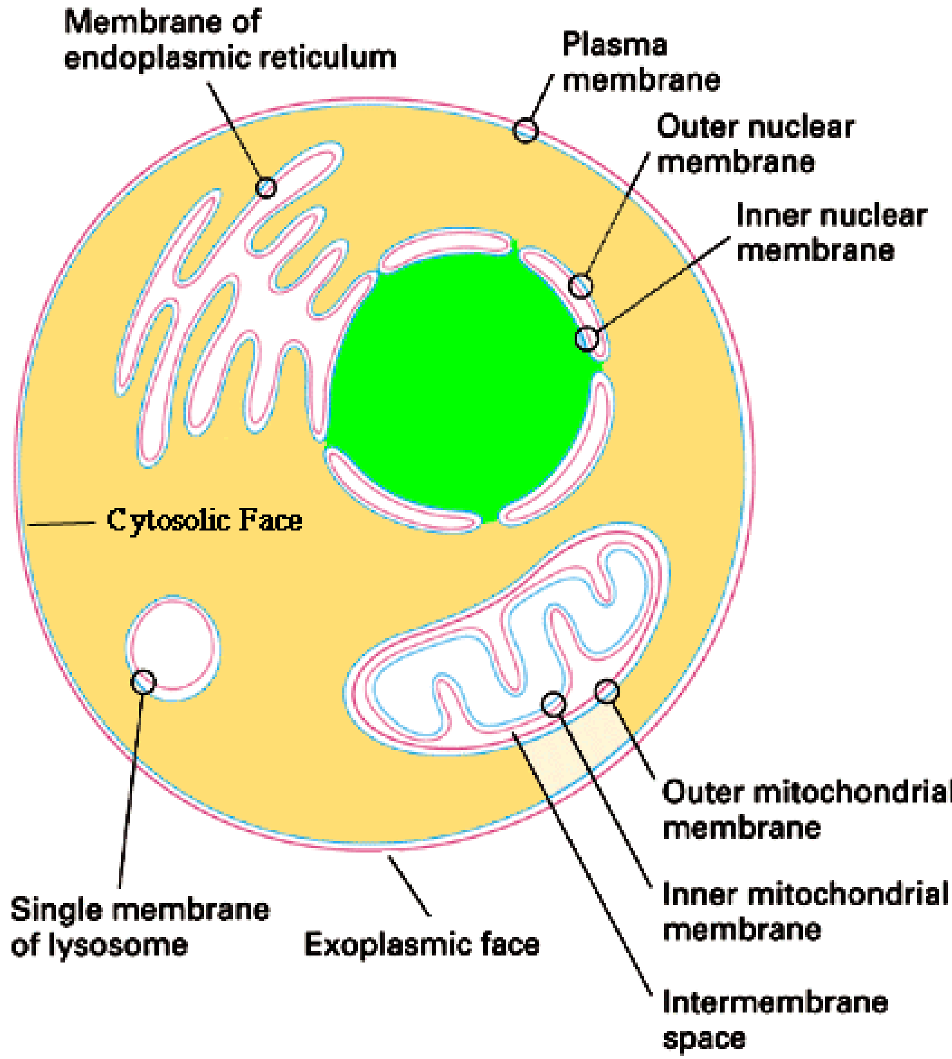
Objectives

1. Study the composition and organization of biological membrane
2. Study the importance of membrane fluidity and the factors important to maintain the fluidity
3. Study the functions of membranes
4. Outline the functional importance of major red cell membrane proteins
5. List selected disorders of red cell membrane and briefly explain the biochemical basis of them

Membranes of mammalian cells

1. Plasma membrane
2. Mitochondrial membrane
3. Endoplasmic reticulum
4. Golgi complex
5. Nuclear membrane
6. Lysosomes
7. Peroxisomes
8. Secretory vesicles

Provide regulated compartmentalization !!!



Components of cell membranes-I
Lipids

Classes of lipids:

1. Fatty acids
2. Triacylglycerol
3. Glycerophospholipids

e.g.: phosphatidylcholine (lecithin), phosphatidylserine,inositol

phosphatidylethanolamine, cardiolipin

4. Sphingolipids (glycosphingolipids)

e.g.: gangliosides, cerebrosides

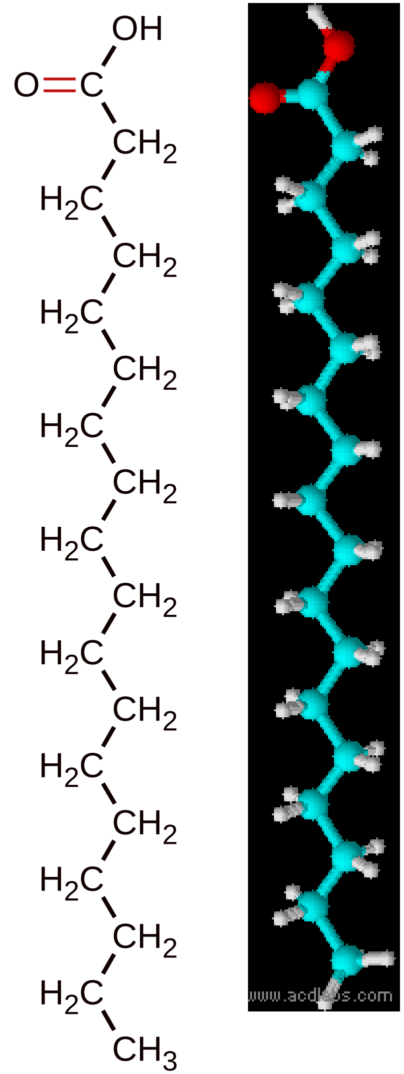
5. Sterols e.g.: cholesterol

Major lipid components in biological membranes

Lipids in plasma membranes are mostly amphipathic

Fatty acids

- Carboxylic acids with a long hydrocarbon chain
- Mostly associated with other chemical groups
- Diversity arise from
  - Chain length
  - Degree of unsaturation



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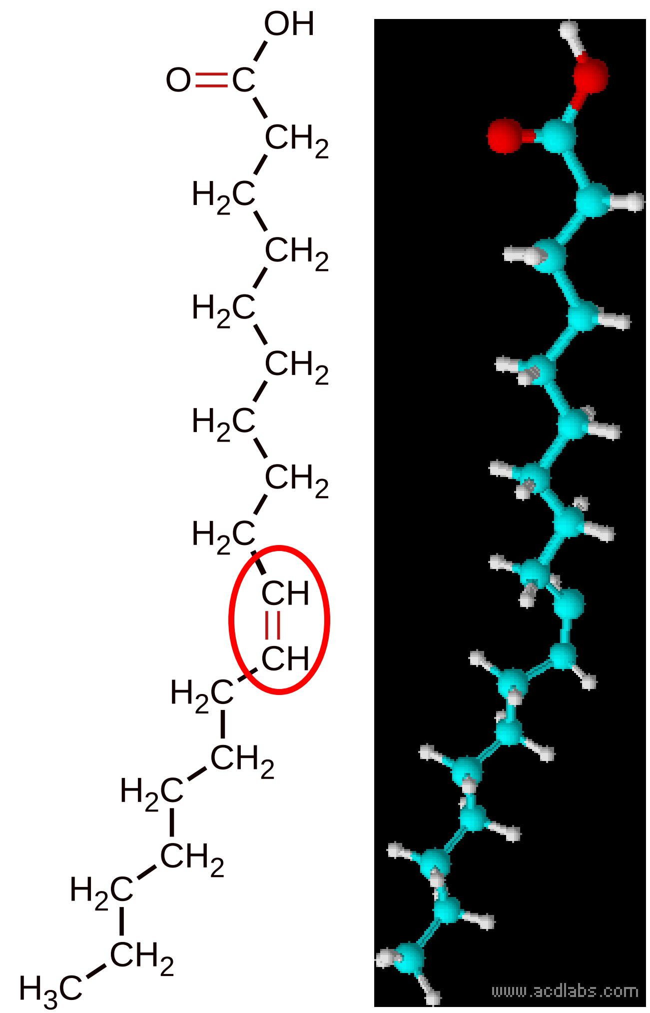
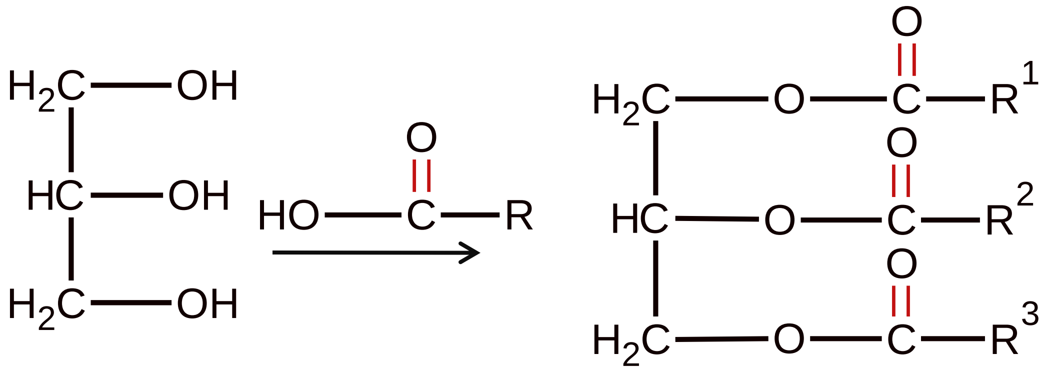


unsaturated

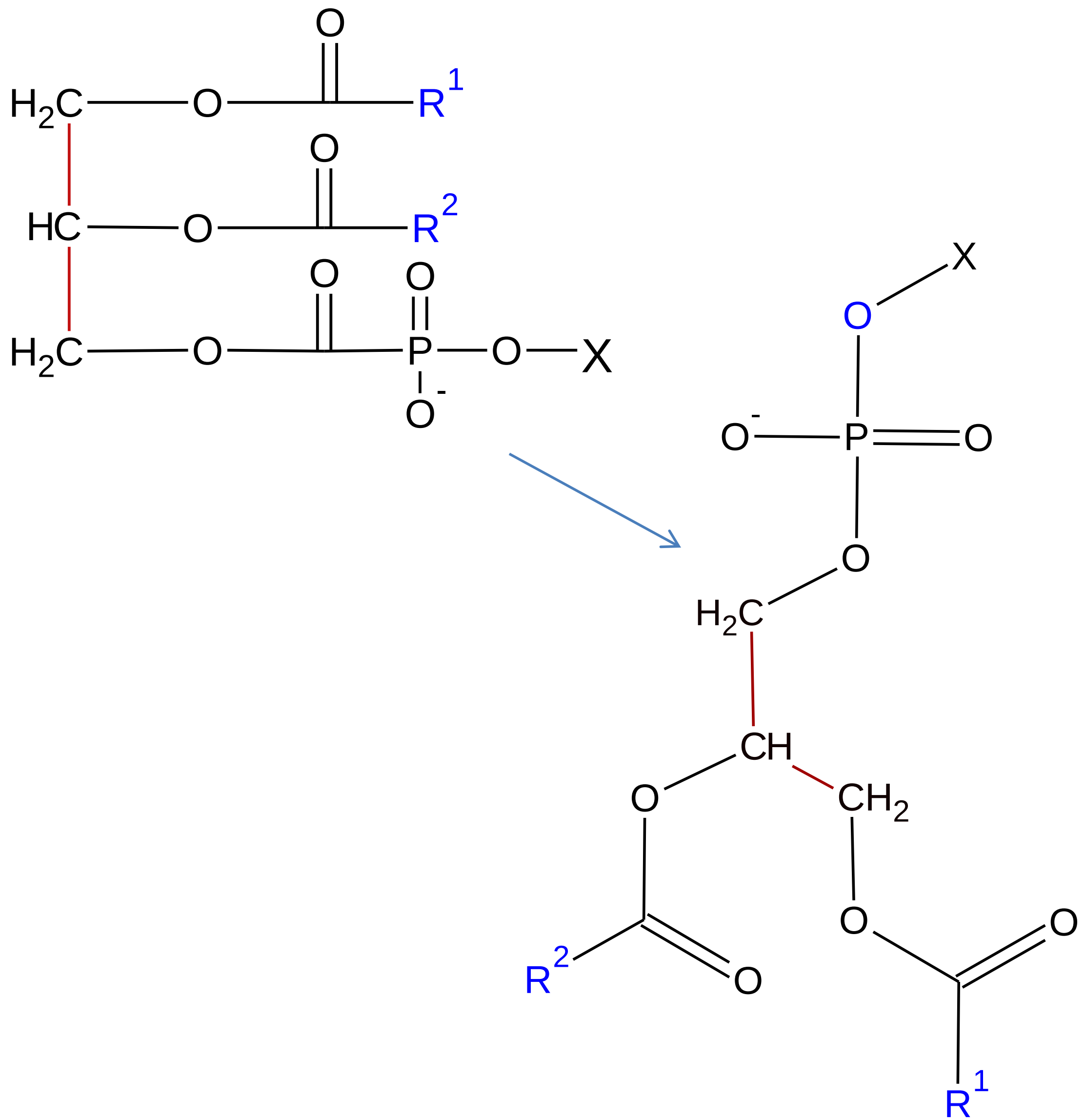
Triacylglycerols

- 3 Fatty acid chains +1 Glycerol
- Can contain more than type of fatty acids
- Found in fat deposits

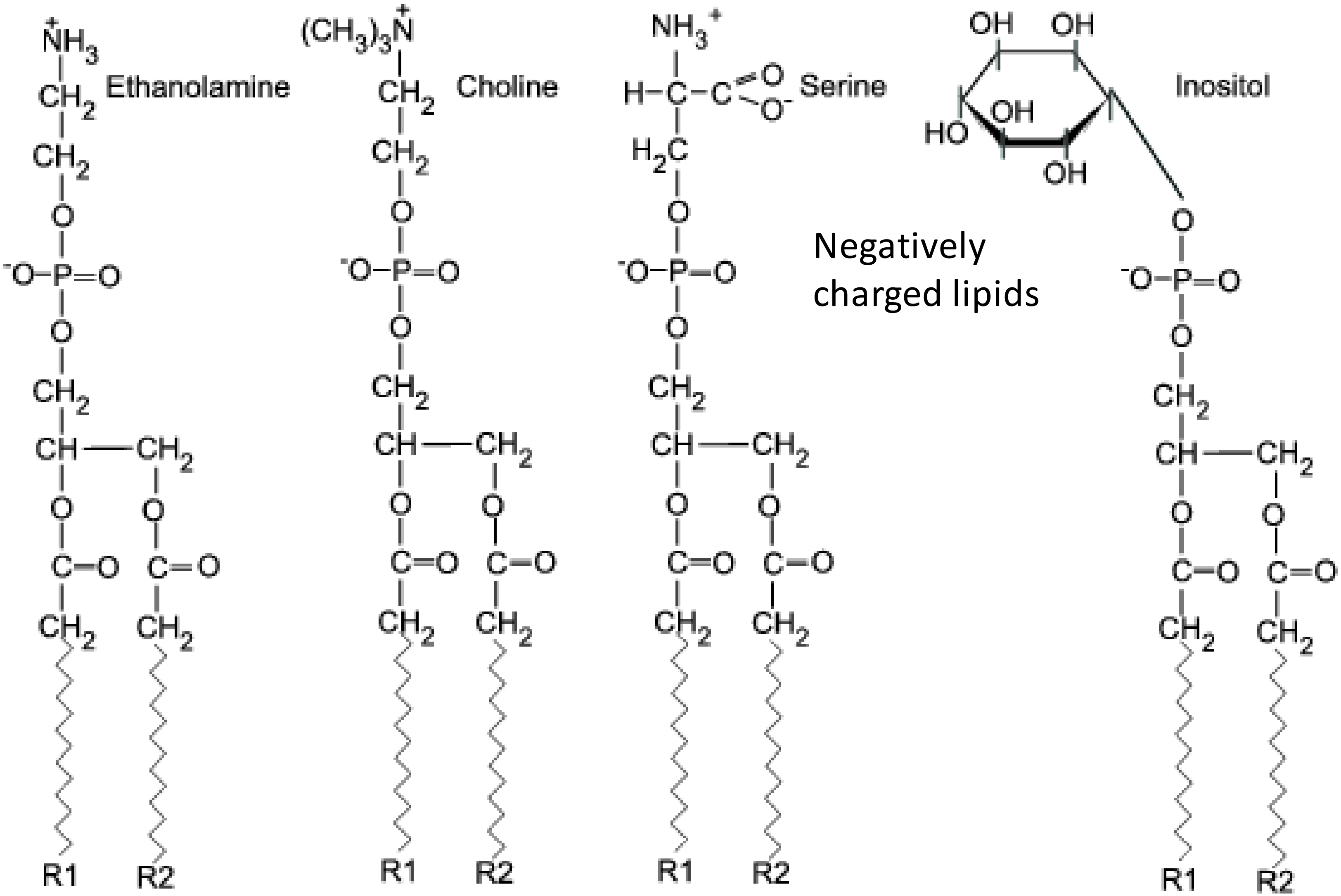


Glycerophospholipids

- The major lipid component
- Polar "head group" and nonpolar "tail" (amphipathic)
- Tail lengths vary
- Different head groups increase the diversity



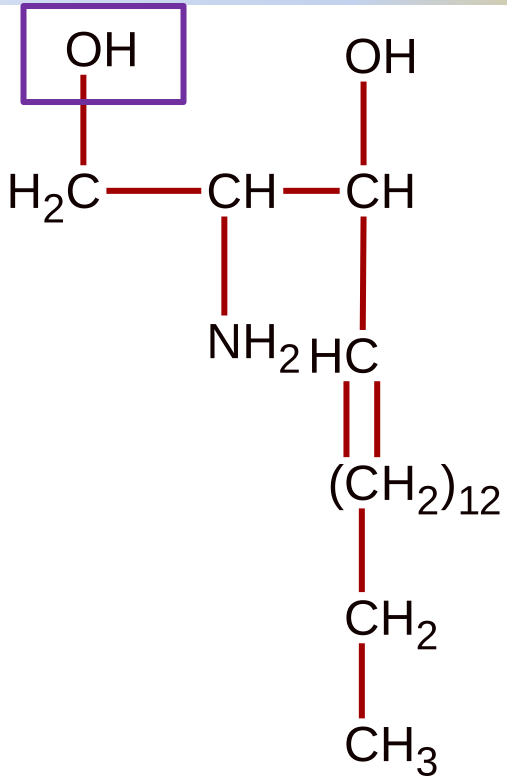
Head group diversity

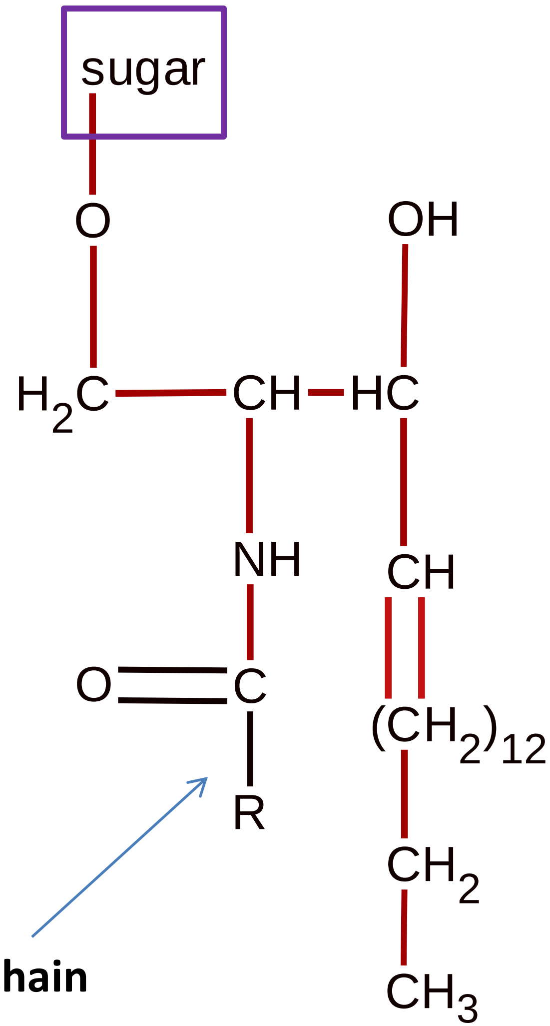


Negatively charged lipids

Sphingolipids

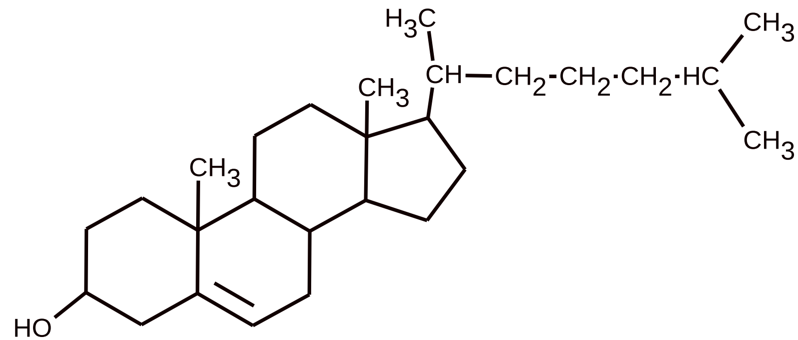
- Amino alcohol based
- Ceramides have a fatty acid chain (important in ABO blood group system)
- One alcohol group is modified (glycosphingolipids have sugar moieties)

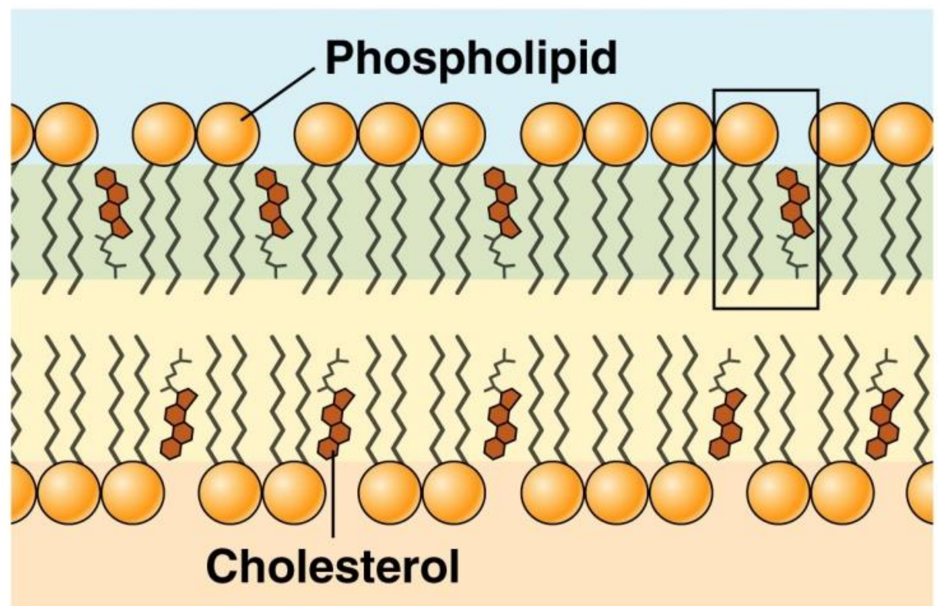




Sterols- e.g. cholesterol

- Mostly found in plasma membranes
- Very weakly amphipathic
- Structurally rigid due to fused rings
- Modulates membrane fluidity





(a) Cholesterol in plasma membrane

Components of cell membranes-II Proteins

a. **Peripheral / Extrinsic proteins**

e.g.: enzymes located at membrane

b. **Intrinsic / Integral proteins**

spans either once or multiple times

e.g.: Low density lipoprotein receptor protein (once)

Band 3 protein of red cell (multiple times)

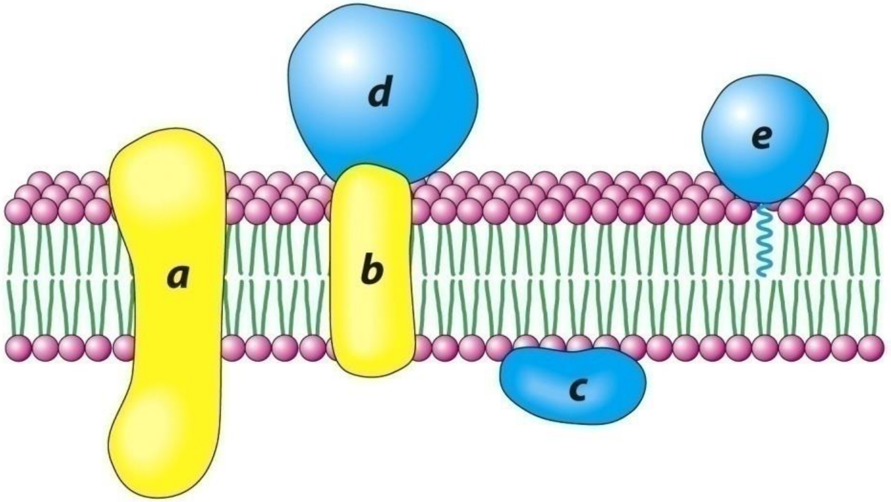
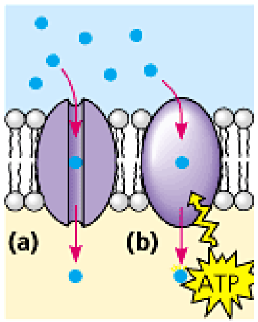
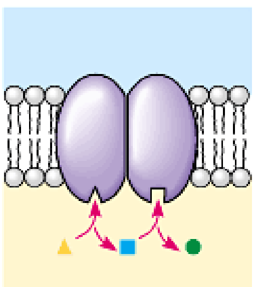


Figure 12.17
Biochemistry, Seventh Edition

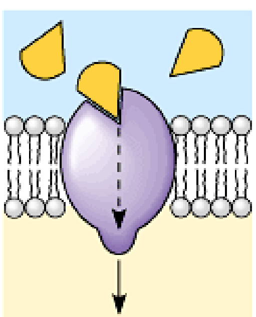
Functions of membrane proteins



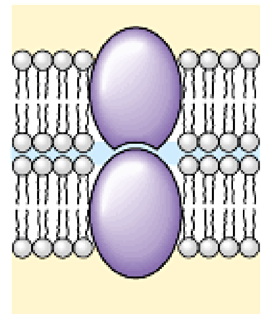
Transport



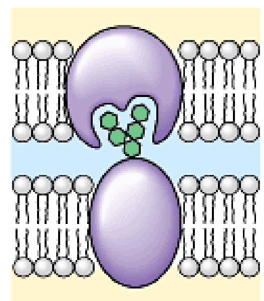
Enzymatic activity



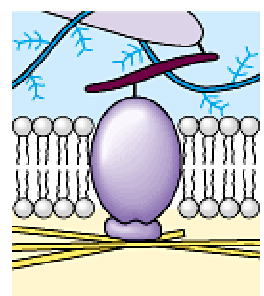
Signal transduction



Intercellular joining



Cell-cell recognition

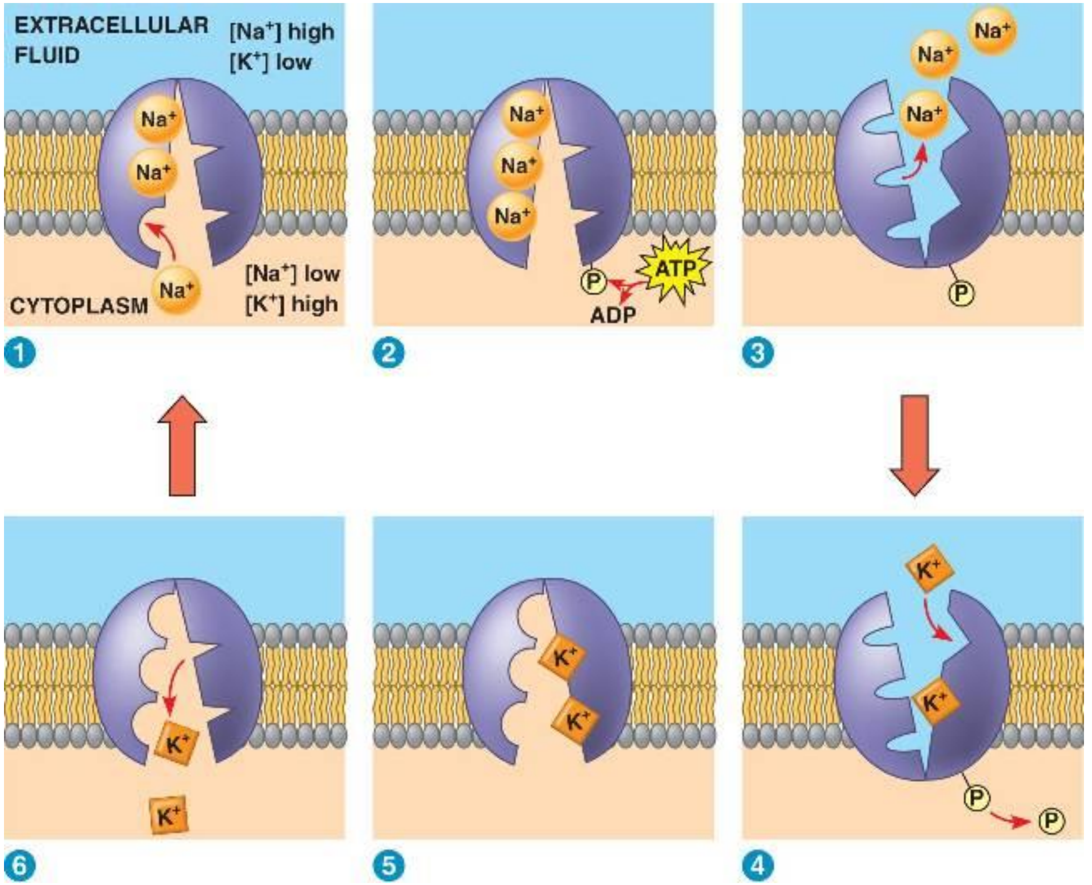


Attachment to the cytoskeleton and extracellular matrix (ECM)

Membrane proteins – Cont.

Na^+/K^+ ATPase

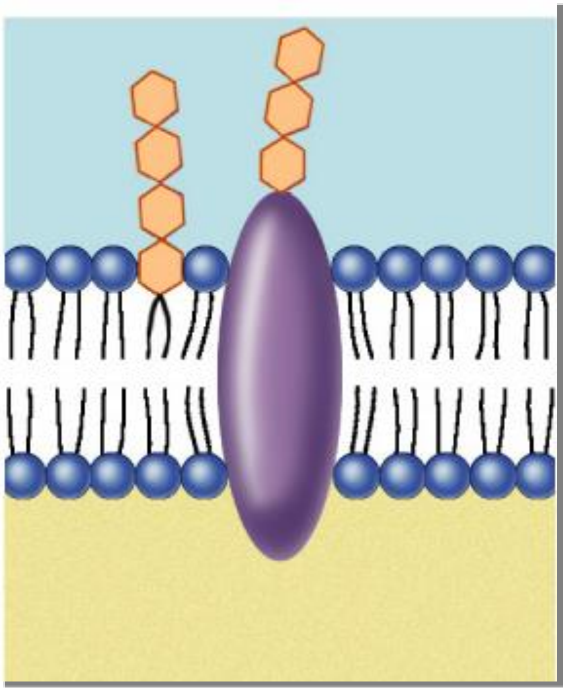
- This enzyme catalyses the hydrolysis of ATP to ADP, liberating energy in this process
- Each ATP molecule hydrolysed via this system results in the ejection of three Na^+ ions from the cell and the transport of two K^+ ions into the cell



Components of cell membranes-III Carbohydrates

a. Glycoproteins: oligosaccharides covalently attached to proteins

b. Glycolipids: oligosaccharides covalently attached to lipids

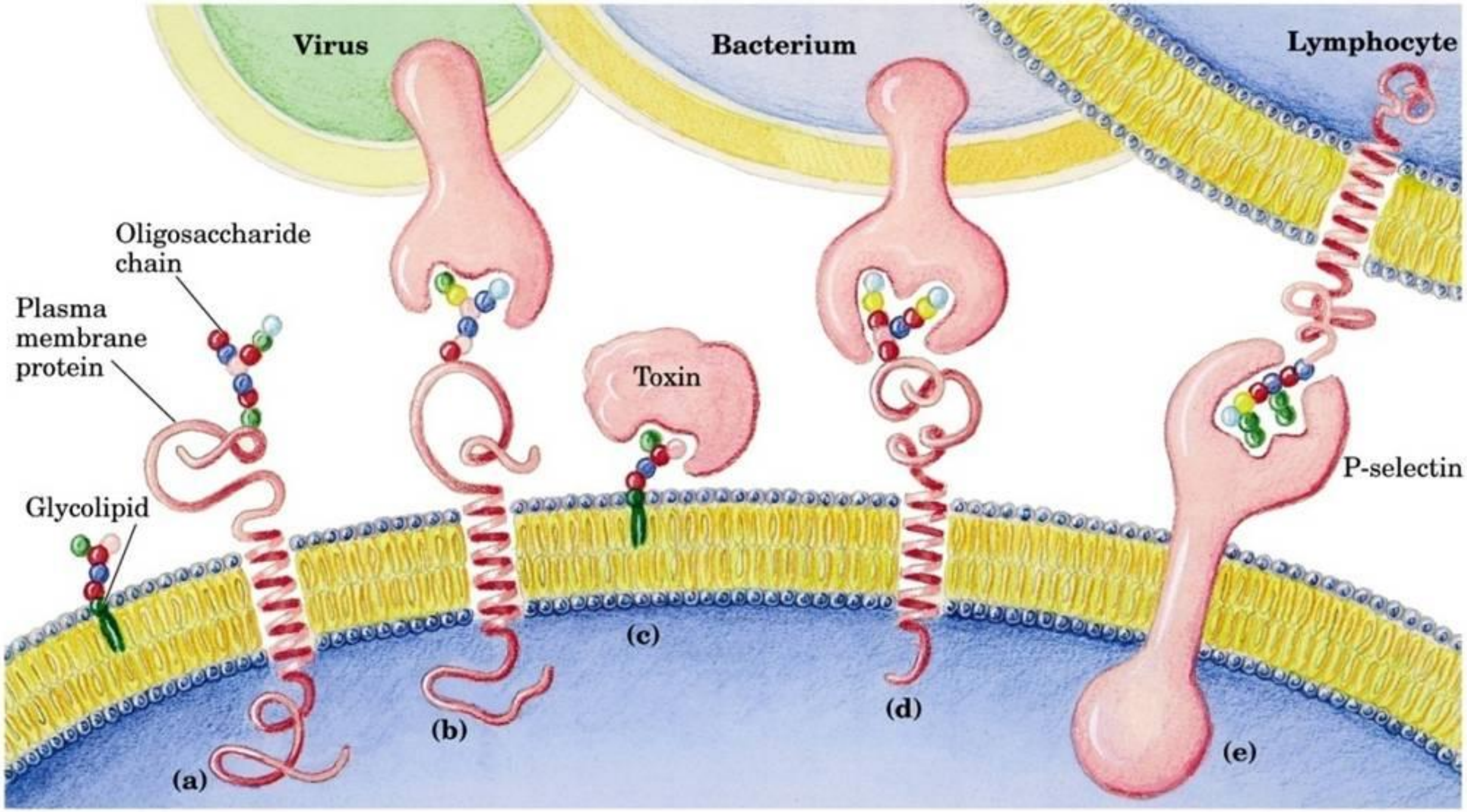


- Sugars are usually branched
- Up to 15 units

E.g. glucose, galactose, mannose, fucose, N-acetylgalactosamine, N-acetylglucosamine, and sialic acids

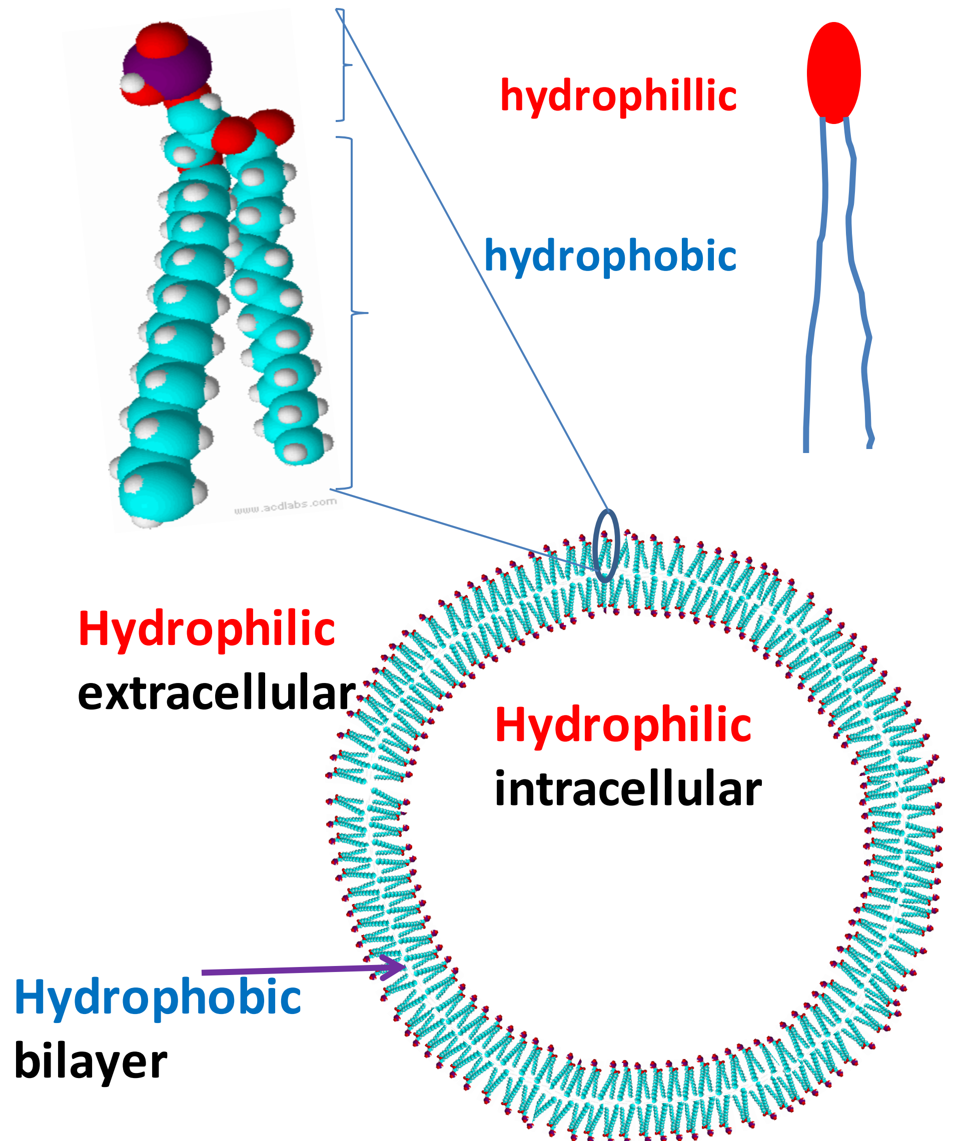
Functions of carbohydrates

- Cell to cell recognition-important for cell sorting and organization in development
- Basis of immune response-WBC and T-cell response

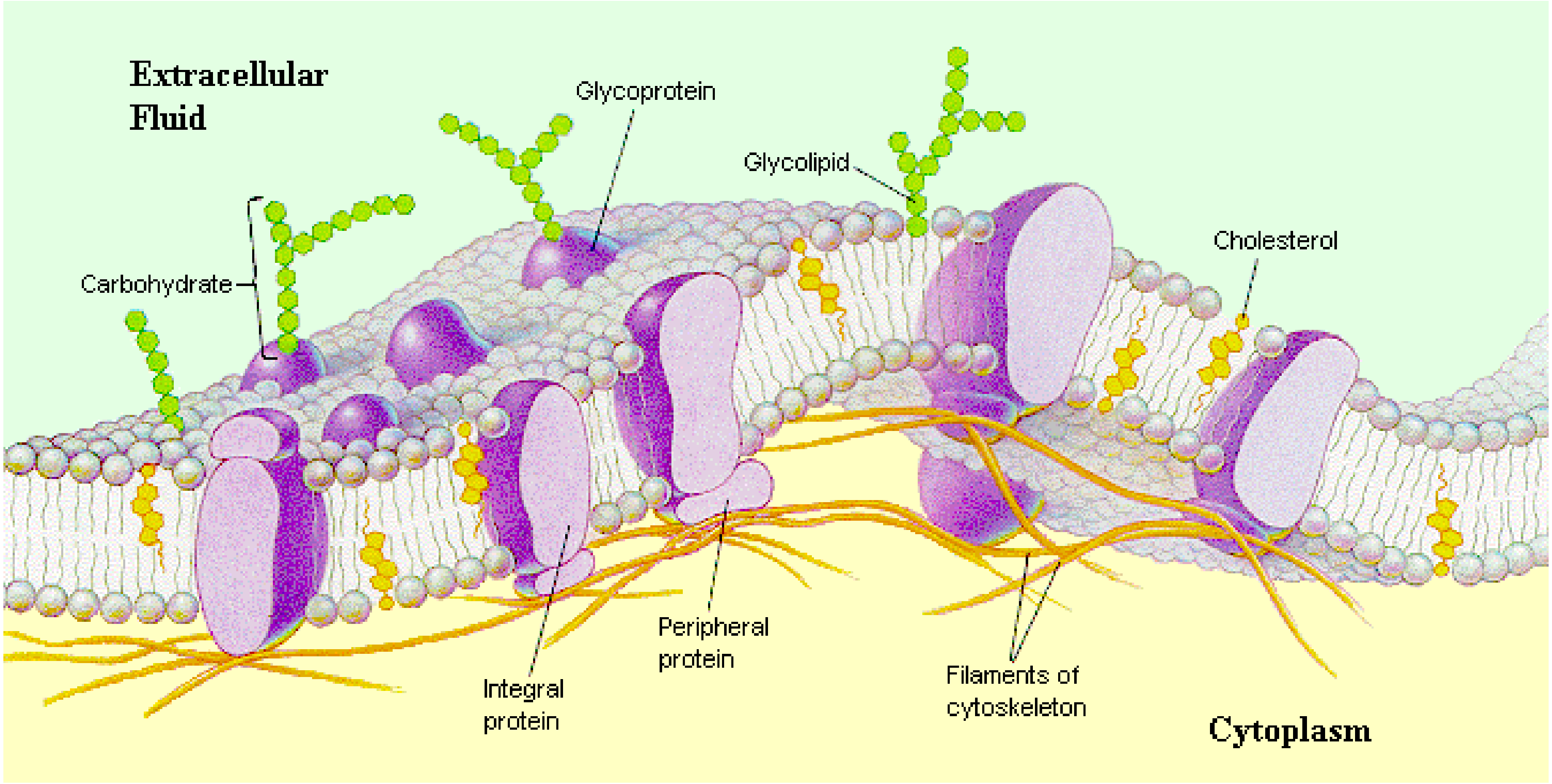


Membrane structure and organization

- Asymmetric enclosed structures
- Consists of two layers and primarily composed of glycerophospholipids (lipid component)
- Polar regions of glycerophospholipids are exposed to aqueous environment and tail regions are embedded in the interior

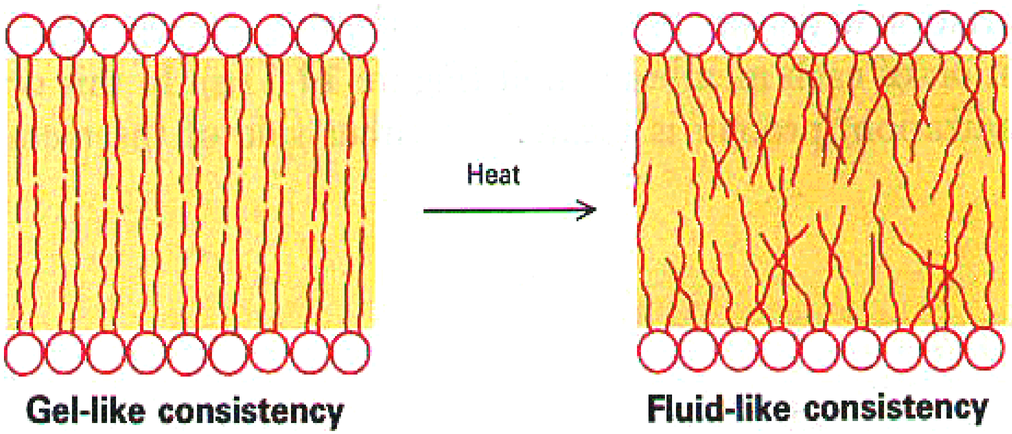


Fluid Mosaic model of biological membrane



Membrane fluidity

- Hydrophobic chains of the phospholipids are tightly aligned to provide a stiff structure
- As the temperature is increased these hydrophobic side chains undergo a transition from an ordered to a disordered state (transition temperature)
- Membrane becomes more fluid-like



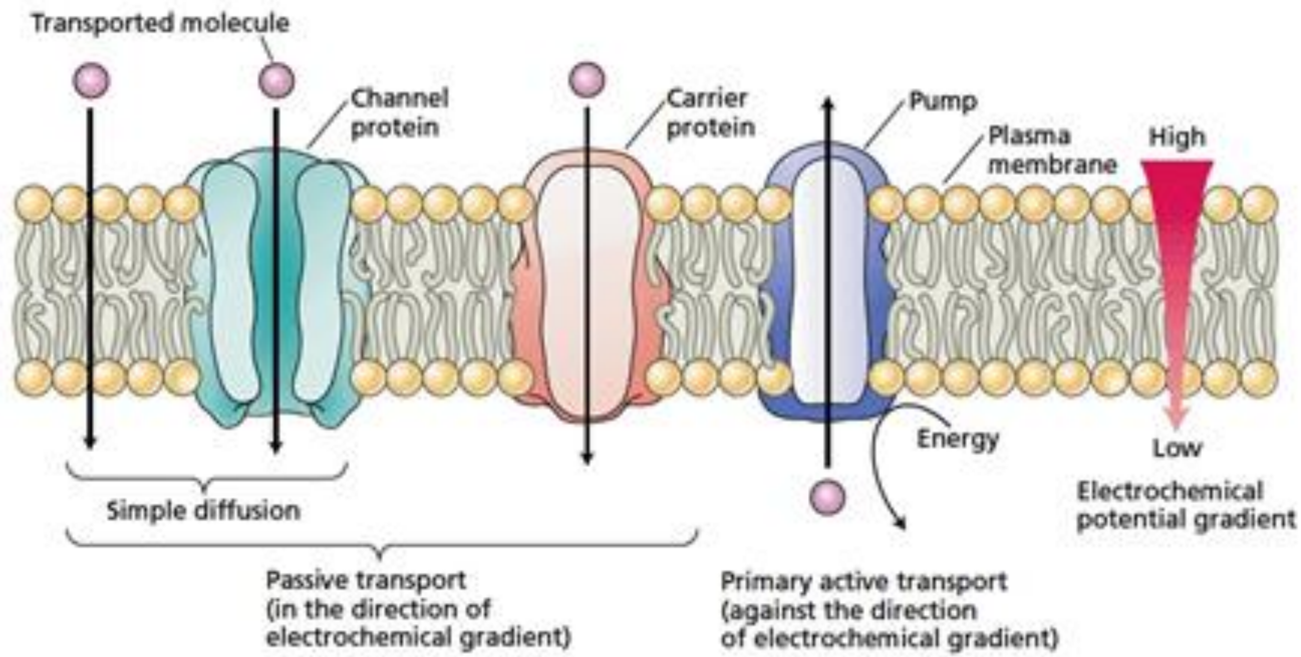
At 37 °C biological membranes are more fluid-like

Factors that influence membrane fluidity

1. Length and degree of unsaturation of the fatty acyl chain
   - Saturated fatty acids decreases membrane fluidity and vise versa
2. Cholesterol modulates the membrane fluidity in two different ways
   - Increase fluidity in the regions containing saturated fatty acids
   - Decrease fluidity in the regions containing unsaturated fatty acids

Membrane permeability

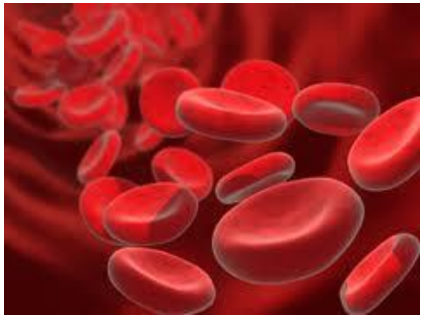
- Lipid soluble substances are transported via simple diffusion
- Non-lipid soluble substances are transported via protein channels present in the membrane as integral proteins



Red blood cell membrane

The red cell membrane consists of:

- Proteins ~50% - Integral / Peripheral proteins
- Lipids ~40% - Mainly phospholipids / cholesterol
- Carbohydrates ~10% - glycolipids / glycoproteins



Maintaining the biconcave disc-like shape is crucial for function

Red blood cell membrane proteins

PERIPHERAL PROTEINS

- Structural proteins-Interact to form a cytoskeleton.
- Cytoskeleton acts as a tough supporting framework for the lipid bilayer
- Four peripheral proteins play a key role in the structure of the red cell cytoskeleton, these are :

  -Spectrin, which is the most abundant and

  consists of two chains α and β spectrin

  - Ankyrin

  - Actin

- Non-structural proteins– Glyceraldehyde 3- phosphate dehydrogenase

RBC membrane proteins – Cont.

INTEGRAL PROTEINS

- These penetrate the lipid bilayer and are firmly anchored within it via interactions with the core.

    -Band 3 (acts as anion transport channel)

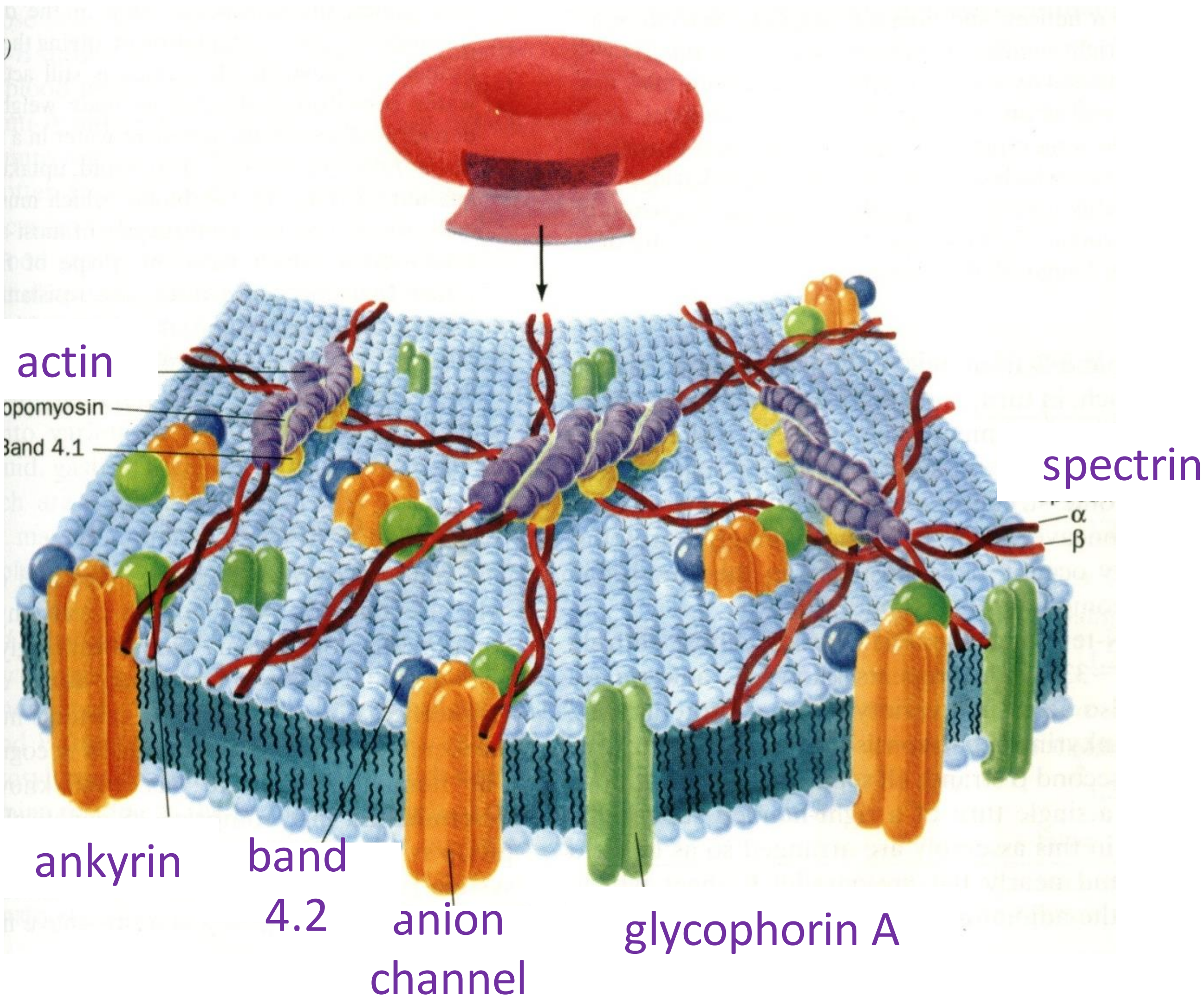
    -Glycophorins A, B, and C

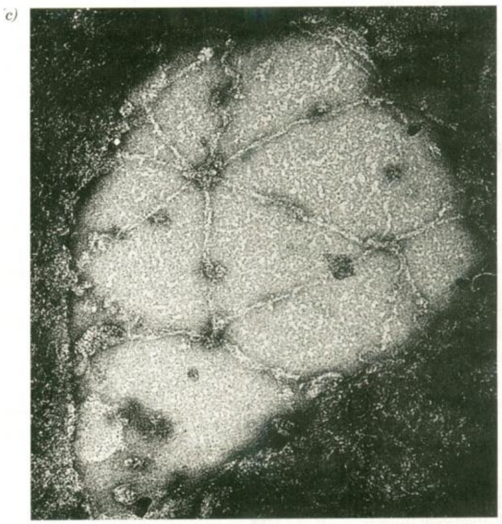
    -Na+/K+ ATPase

    -glucose transport protein

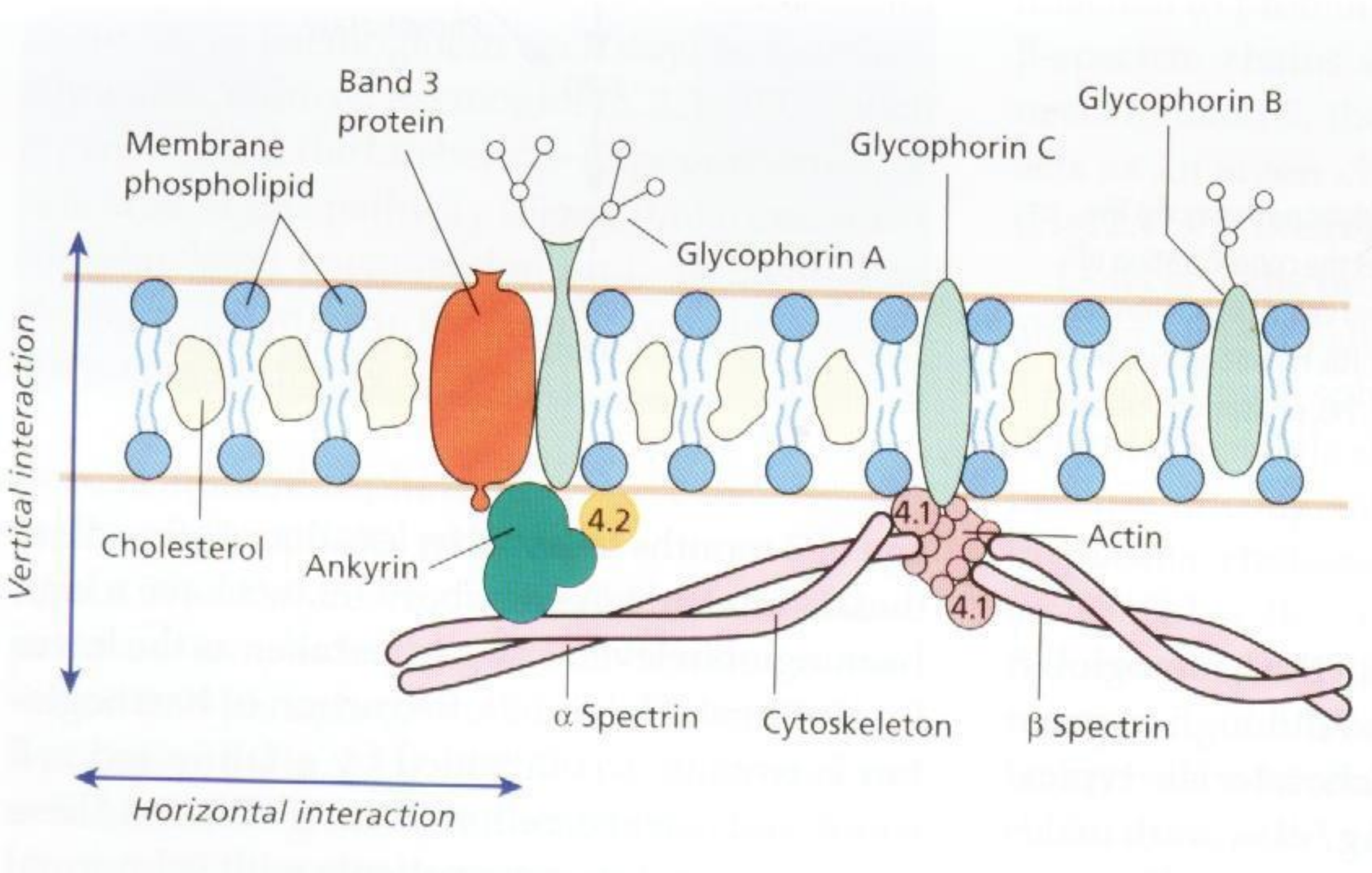
    -surface receptors (e.g. transferrin receptors for iron transport).

Structural details of RBC membrane





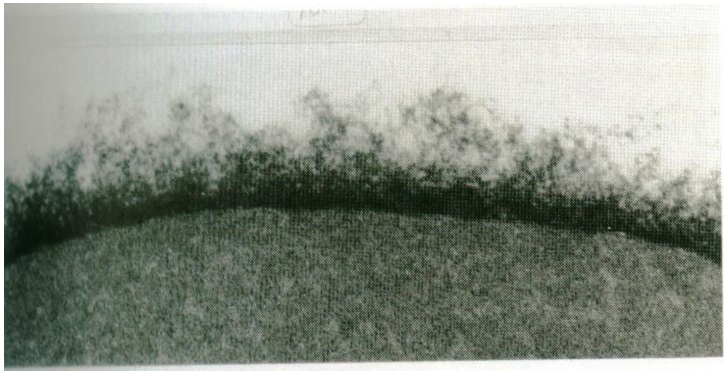
Horizontal and vertical interactions



Blood group antigens

- Found on the red cell membrane
- Responsible for the determination of the blood group of the individual
- Blood group antigens are found on both lipid and protein components of the red blood cell membrane

**Antigens are also present in other tissues

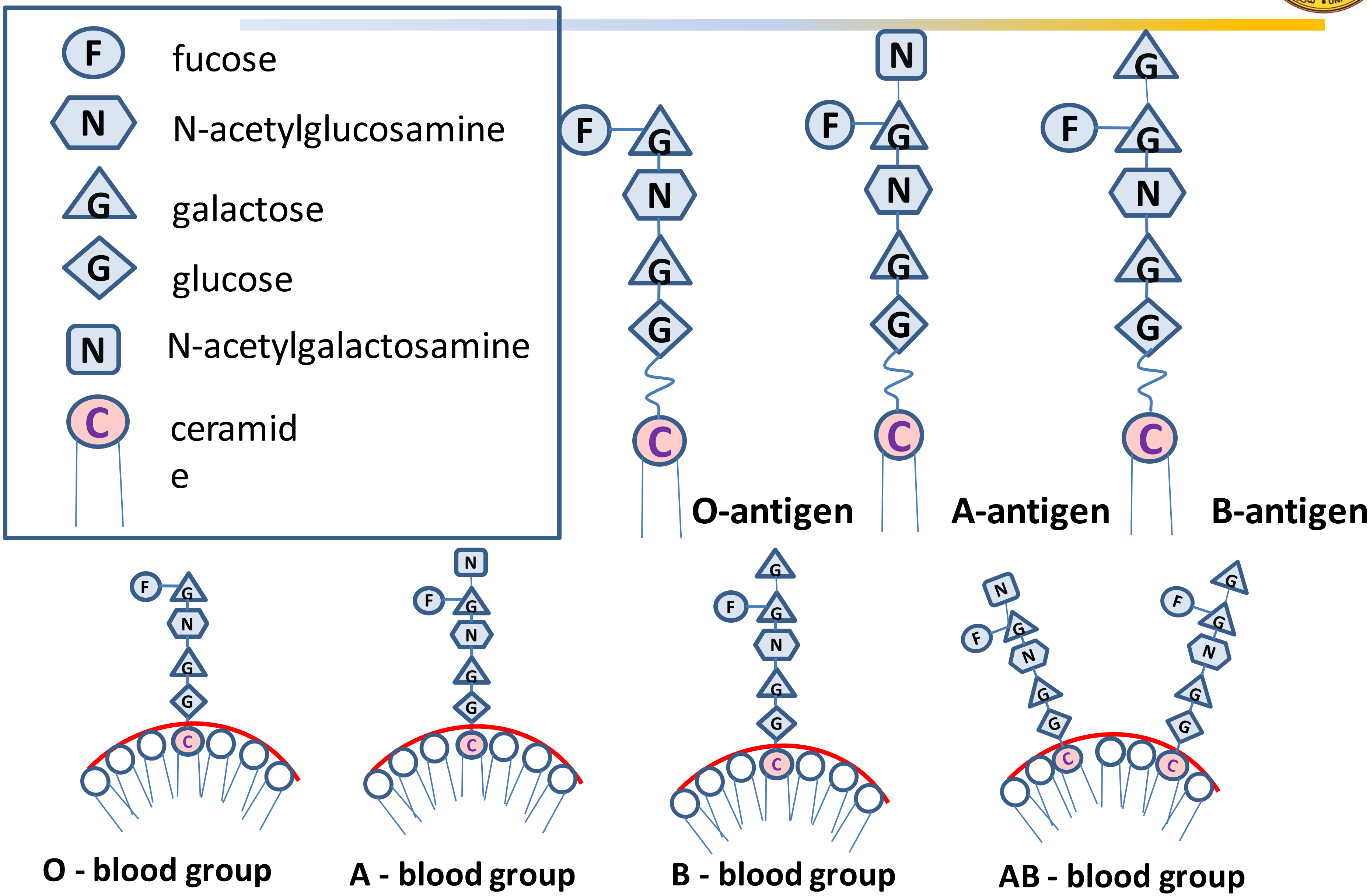


RBC glycocalyx

ABO blood group system

- **Genetically determined**
- A and B genes do not directly produce antigens → produce an enzyme called *transferase* → attaches a sugar molecule to the chemical structure of the antigen → sugar molecule responsible for specificity
- A antigen → N-acetylgalactosamine transferase
- B antigen → galactosyl transferase
- O antigen → no transferase (also called H antigen)

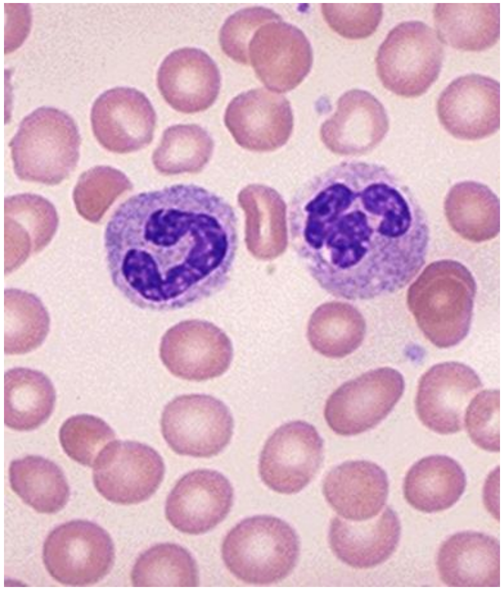
Details of ABO antigens

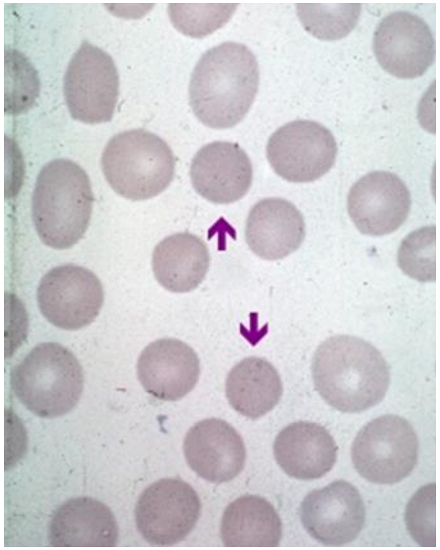


Defects of Proteins in the RBC membrane-

- Defects of the proteins may explain some of the abnormalities of the shape of the red cell membrane, e.g. hereditary spherocytosis and elliptocytosis.
- Spherocytosis- defective vertical interactions
  - E.g. Ankyrin, spectrin
- Elliptocytosis-defective horizontal interactions
  - E.g. spectrin-actin interactions

Spherocytosis and Elliptocytosis

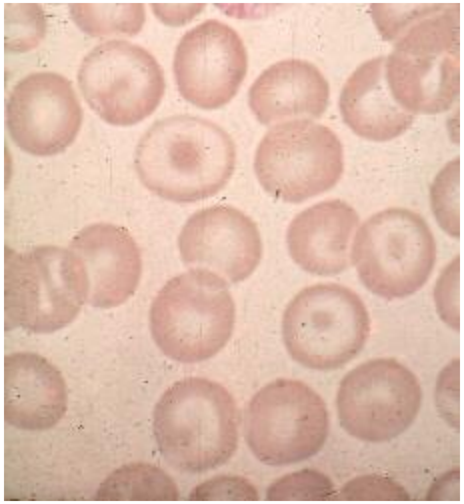


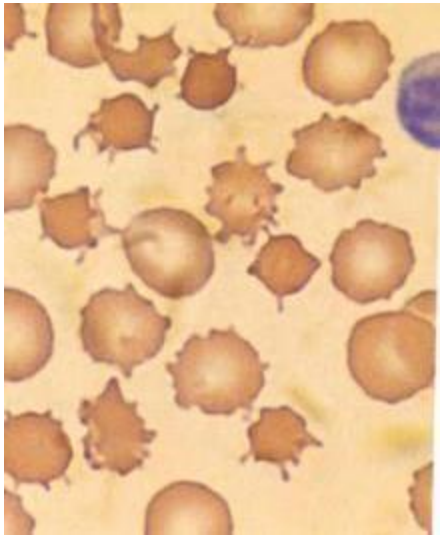


Defects of Lipids in the RBC membrane-

- Alterations in lipid composition because of congenital or acquired abnormalities in plasma cholesterol or phospholipids
  - e.g. target cells and acanthocytes.
- Observed in some liver diseases and abnormalities in lipid absorption

Target cells and Acanthocytes





Summary

Thank you!!

Questions?