

Biological Membranes

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Objectives

After this session the student should be able to:

1. Explain the general structure of lipids found in biological membranes
2. Distinguish between intrinsic and extrinsic membrane proteins giving examples of each
3. Name the factors that increase and decrease membrane fluidity
4. Give examples of membrane asymmetry stating its importance
5. Explain how membranes can repair themselves when damaged
6. Give examples of different types of trans-membrane transport
7. Explain how ionic gradients are established across membranes and compartments

Recommended Reading

“The World of the Cell” Becker WM, Kleinsmith LJ, Hardin J

- Chapter 2:

- The importance of water; the importance of selectively permeable membranes

- Chapter 7: Membranes : Their Structure, Function and Chemistry

- Chapter 8: Transport across Membranes

Biological membranes

- Separate different compartments in the cell
- Are dynamic and fluid structures
- Consist of lipids and proteins.
- Vary in composition according to their site.

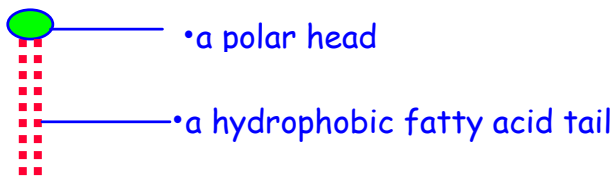
The relative amounts and chemical properties of lipid and protein molecules affect the properties of the membrane.

Lipids in Biological Membranes

- Phospholipids form the backbone of biological membranes
- The amount of lipid varies from 20% to 78% according to the site of the membrane.
- Phospholipid molecules can organize themselves to form stable membranes

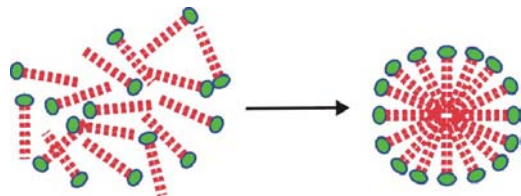
Amphipathic lipids

An amphipathic lipid molecule consists of:



Micelles

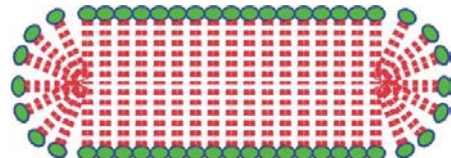
Amphipathic lipids suspended in an aqueous solution form micelles. The hydrophilic polar heads are at the periphery and the hydrophobic fatty acids tails at the centre. Micelles are stable structures.



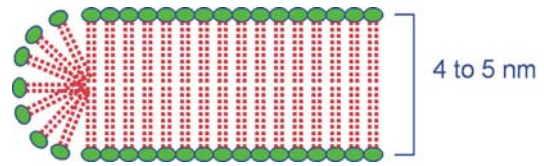
Membranes

The phospholipids of biological membranes are organised in the form of bi-layers with the polar hydrophilic heads in contact with the water and the hydrophobic tails associated with one another

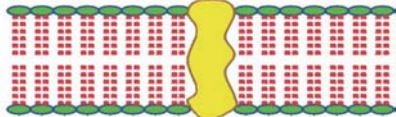
The two layers are continuous at their ends
The membrane is like a large, flattened micelle.



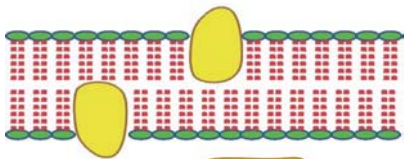
Phospholipid bi-layers are approximately 4 to 5 nanometers (nm) thick



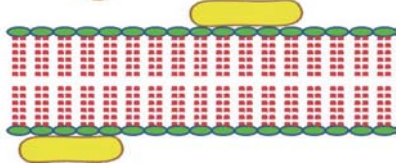
Biological membranes have **protein** associated with the phospholipid bilayer



Intrinsic membrane proteins are embedded within the membrane. They may extend through the membrane and project on both surfaces.



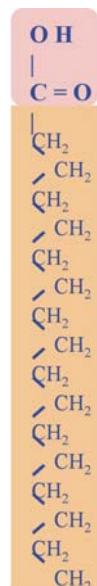
Some extend through one lipid layer and project on one surface.



Extrinsic membrane proteins are situated on the surface and are loosely bound to the membrane. They are easily removed by mild detergents

Fatty Acids form the backbone of phospholipids.

Fatty acids have two components:

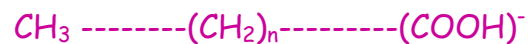


A carboxyl group (-COOH) Hydrophilic

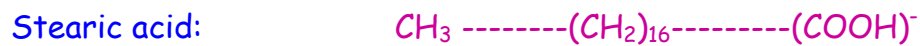
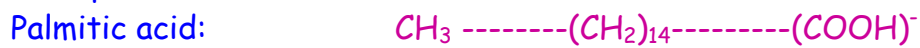
A Hydrocarbon chain (-CH₂-CH₂-) Hydrophobic

Saturated fatty acids have only saturated bonds (-CH₂-CH₂-).

They are represented by the formula:



Examples are:

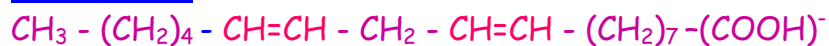


Unsaturated fatty acids contain unsaturated hydrocarbon bonds: (-CH₂-CH=CH-CH₂-).

Oleic acid has one unsaturated double bond



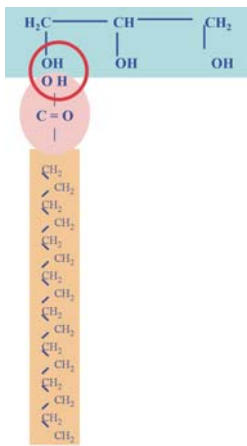
Linoleic acid has two unsaturated double bond



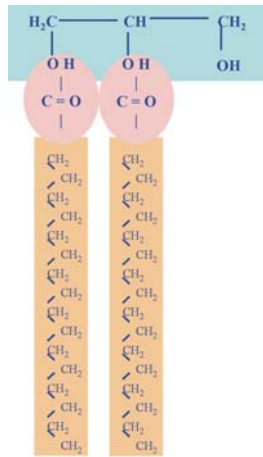
The three building blocks of phospholipids are:

- a) One or more fatty acid chains
- b) Glycerol $\text{CH}_2\text{OH} - \text{CH}_2\text{OH} - \text{CH}_2\text{OH}$
- c) A phosphate group - $(\text{PO}_4)^{-}$

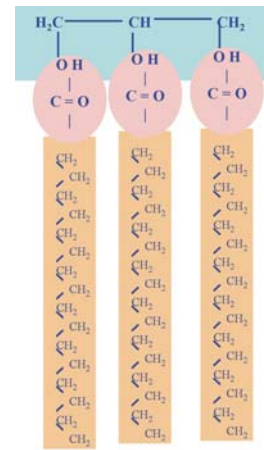
Esterification of a fatty acid with an alcohol group (OH) of glycerol forms a lipid. One two or three fatty acid chains may form ester bonds with glycerol



Monoacyl glycerol
- one fatty acid

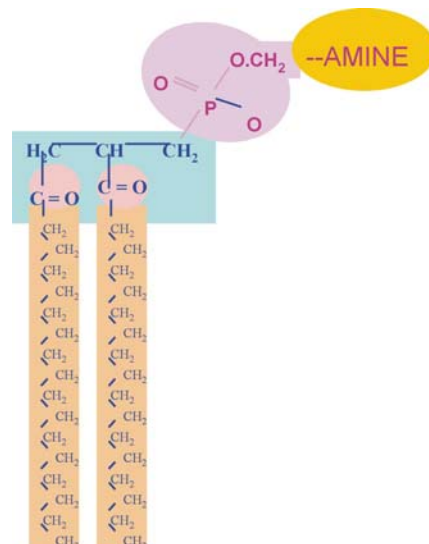


Diacyl glycerol
- two fatty acids



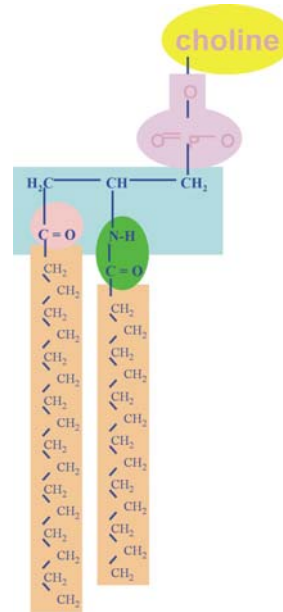
Triacyl glycerol
- three fatty acids

Phosphoglycerides are formed when one of the glycerol carbons is linked by a phosphate ester bond to an amine



Sphingolipids consist of:

1. A hydrocarbon chain attached to the first C of glycerol
2. A hydrocarbon chain attached to the 2nd C of glycerol by an **aminoacyl** linkage
3. A polar group on the 3rd C of glycerol. In sphingomyelin this is **choline** attached by a PO₄ linkage



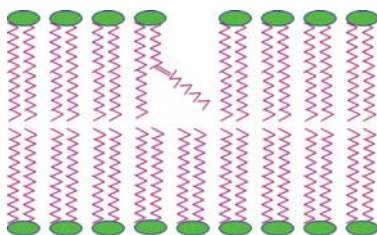
Phosphoglycerides are **amphipathic** lipids. They consist of a polar, **hydrophilic head** and a long fatty acid **hydrophobic tail**.



Unsaturated fatty acids have a double bond in the ***cis*** conformation

This alters the stereochemistry of the molecule

- The fatty acid is **bent** at the site of the unsaturated bond.



The stereochemistry has a profound effect on the lateral packing of lipids in the membrane. Unsaturated fatty acids decrease the close packing of molecules in the membrane

Other Membrane Lipids are:

Glycolipids contain sugar residues attached to a phospholipid or sphingolipid. They are common in myelin.

Cardiolipids are diphosphatidyl glycerols - they have two phosphatidyl groups. They are found in heart mitochondria.

Membrane Asymmetry

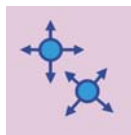
The inner and outer surfaces of all biological membranes are different. Asymmetry may be due to differences in:

1. **The polar head groups**
e.g. oligosaccharides are attached to the polar head on the outer surface of the plasma membrane.
2. **The lipid composition** of the inner and outer leaflets
e.g. in human erythrocytes the outer membrane contains mainly cholesterol, sphingomyelin and phosphatidylcholine, while the inner membrane is rich in phosphatidylserine
3. **The extrinsic membrane proteins**
e.g. cytochromes are found only on the inner surface of the inner mitochondrial membrane.
4. **Asymmetry of the integral proteins**
e.g. glycophorin has CHO groups on the external part of the protein and amino acid chains on the inner part

Membrane Fluidity

The molecules in biological membranes are not static but move around like corks floating on the surface of water.

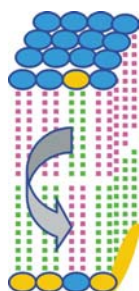
There are three types of movement:



1. **Lateral movement** in the plane of the lipid layer



2. **Rotational movement** around the longitudinal axis of the molecule



3. **Transversion** or "flip-flop" movement of phospholipids from one layer to the other. This movement is rare and requires energy.

Phase Transition Temperature

The fluidity of biological membranes is described by the rate of movement of lipid and protein molecules within the membrane.

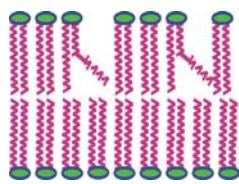
Temperature affects the tight packing of molecules.

- At a certain temperature the membrane changes from the solid (gel) phase to the liquid phase and vice-versa.
- This is the **phase transition temperature** (or melting point) of the membrane



Membrane fluidity is affected by various factors

1. A **higher temperature** increases membrane fluidity
 - Membranes in vivo must be **above** the phase transition temperature
2. The **phase transition temperature** of membranes varies according to their lipid composition
 - Some poikilothermic (cold blooded) animals alter their membrane composition according to the ambient temperature.
 - Hibernating animals change their membrane lipid composition to maintain membrane fluidity during the cold season.

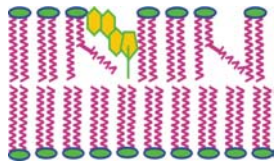


3. **Unsaturated fatty acids** increase membrane fluidity and lower its phase transition temperature
Double bonds(=) cause bending of fatty acid molecules and looser packing



4. **Cholesterol** has a variable effect on membrane fluidity. Cholesterol has an irregular flat ring structure.

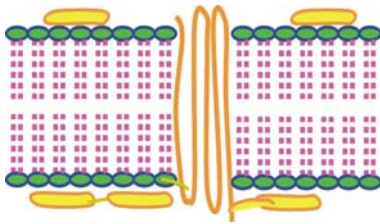
If the membrane consists mainly of saturated fatty acid chains, it interdigitates with the hydrocarbon chains making them more loosely packed, thus **increasing fluidity**.



If the membrane contains several unsaturated fatty acids, it fits into the gaps caused by bending at the double bonds and thus **stabilizes** the membrane.

Cholesterol occurs commonly in the outer leaflet of animal plasma membranes.

5. Protein interactions affect membrane fluidity



a. Lipid-protein interactions

- trans-membrane proteins have hydrophobic domains that interact with the lipid molecules

b. Protein - protein interactions

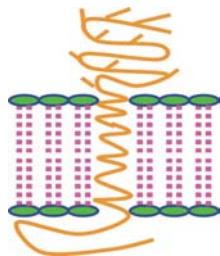
- peripheral proteins form a stabilising

meshwork that binds with integral proteins

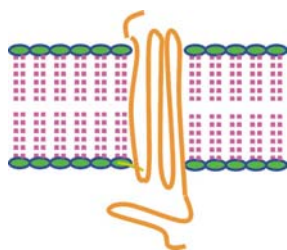
c. Number of membrane proteins

- more proteins impose more restrictions on membrane mobility

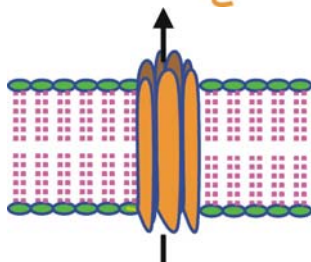
Examples of membrane proteins



Glycophorin - a glycoprotein with branched oligosaccharide residues on the part of the protein projecting on the outer surface of the plasma membrane. It is responsible for the MN blood group on red blood cells



"Band 3" Protein - consists of loops of protein chains in the lipid bilayer. It acts as a transporter of the anions Cl^- and HCO_3^-



Bacteriorhodopsin - consists of 7 closely packed alpha-helical chain loops enclosing a central channel. It pumps H^+ ions across bacterial membranes.

Transport Across Membranes

1. **Diffusion** is the movement of solutes along a concentration gradient. It is a passive process.

- Lipid-soluble substances e.g. alcohol diffuse readily through the lipid membrane.
- A limited amount of diffusion of small polar molecules is also possible.

2. **Osmosis** is the passive movement of water across a semipermeable membrane from a solution of low concentration to a solution of high concentration, until equilibrium is reached. The osmolarity is the measure of the concentration of solutes in a solution. Plasma membranes are semipermeable. It is important that the osmolarity of the solutions inside and outside the cells are equal.

3. **Facilitated transport** requires the presence of special protein carriers or channels that allow the easy passage of molecules across a membrane. They are specific for facilitating the passage of particular molecules.

There are several types of carriers:

(i) **Ionophores** - These are channels that transport ions across the membrane. They consist of:

- a. A hydrophobic outer region to interact with lipid
- b. A pore or channel with a hydrophilic lining

Each ionophore is specific for one ion

For example: Valinomycin carries K^+ ions;

Monesin carries Na^+ ions

Proton carriers transport H^+ ions

(ii) **Gated Channels** are specific ion channels that open only in response to a particular stimulus.

- **Electrically gated channels** open in response to electrical changes.

Examples:

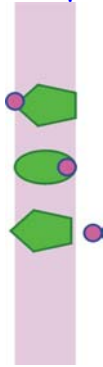
- Voltage gated Na^+ channels in axons open in response to an electrical impulse in the axon

- Voltage gated Ca^{2+} channels in muscle SER open in response to an electrical impulse in the muscle membrane

- **Chemically gated channels** open up in the presence of a particular molecule. Examples are:

- Acetylcholine-gated Na^+ channels open up to allow the passage of Na^+ when acetylcholine is released at the synapse
- Chloride channels open up in response to c-AMP

(iii) **Carriers** are integral membrane proteins that bind to a specific molecule and transport it across the membrane. Carriers operate in the presence of a concentration gradient.



Facilitated transport by carriers involves:

- Binding of the molecule to the carrier at one surface
- A conformational change (change in shape) in the carrier
- Release of the molecule at the other surface and return of the carrier to its original conformation

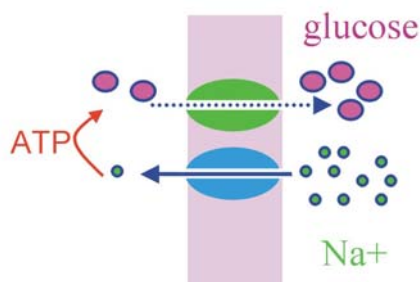
Example: Glucose cannot diffuse through membranes. It requires a glucose transporters. Glucose carriers are found in the membranes of erythrocytes, adipocytes and hepatocytes, and allow the passage of glucose into these cells. The number of glucose carriers is reduced in diabetes.

4. **Active transport** is the transport of molecules against a concentration gradient. This requires energy, usually provided by ATP. Most of these are ion pumps.

Examples:

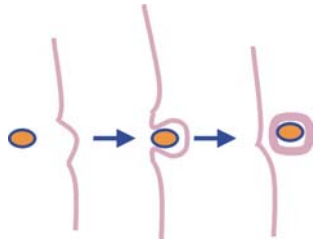
- Na^+ pump - pumps Na^+ ions against a concentration gradient to establish a voltage potential across membranes
- Ca^{2+} pump in muscle SER pumps calcium ions from the cytosol into the SER
- Proton pump in mitochondria pumps H^+ ions to establish a high concentration gradient across the inner mitochondrial membrane

5. **Co-transport** is the transport of one molecule against a concentration gradient in exchange for the diffusion of another type of molecule in the opposite direction.



This process couples an energy-utilising transport to an energy-releasing transport. Example: Co-transport of glucose. Glucose may be transported into a cell against a concentration gradient utilising the energy generated by the flow of Na^+ ions along a concentration gradient.

6. **Bulk transport** is the transport of macromolecules or complex particles across a membrane



Examples:

- **Pinocytosis** is the internalisation of a macromolecule

- **Reverse pinocytosis** is the externalisation of a macromolecule

- **Phagocytosis** is the internalisation of a complex particle e.g bacterium or a cell fragment into a cell

- **Receptor mediated endocytosis** is internalisation of large molecules after their attachment to a specific membrane receptor. The receptors bound to the molecules to be transported gather in one area of the membrane and form a coated pit, which is then internalised into the cell. Example: The hormone insulin enters cells in this way. It can enter only those cells that have the insulin receptor.
