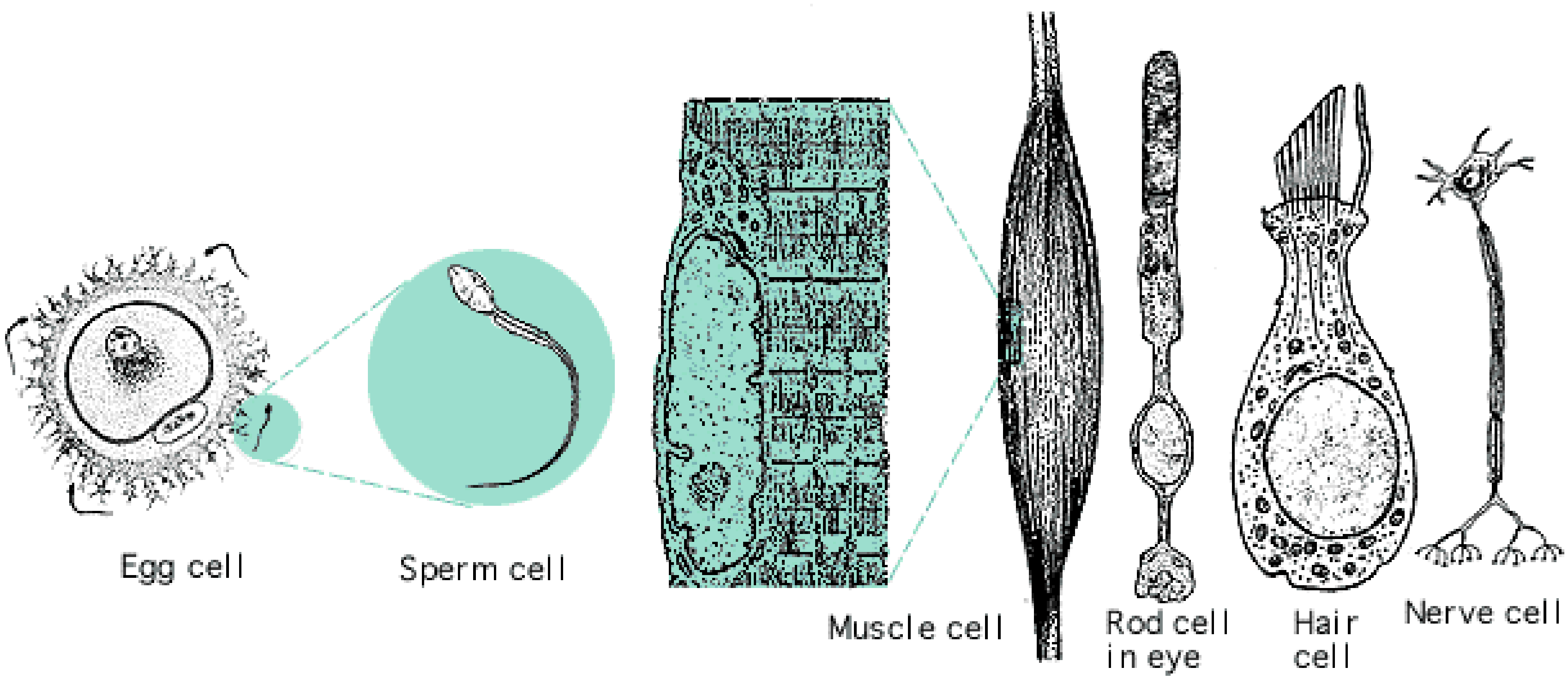
Lecture 13

Physics of Bio-membrane

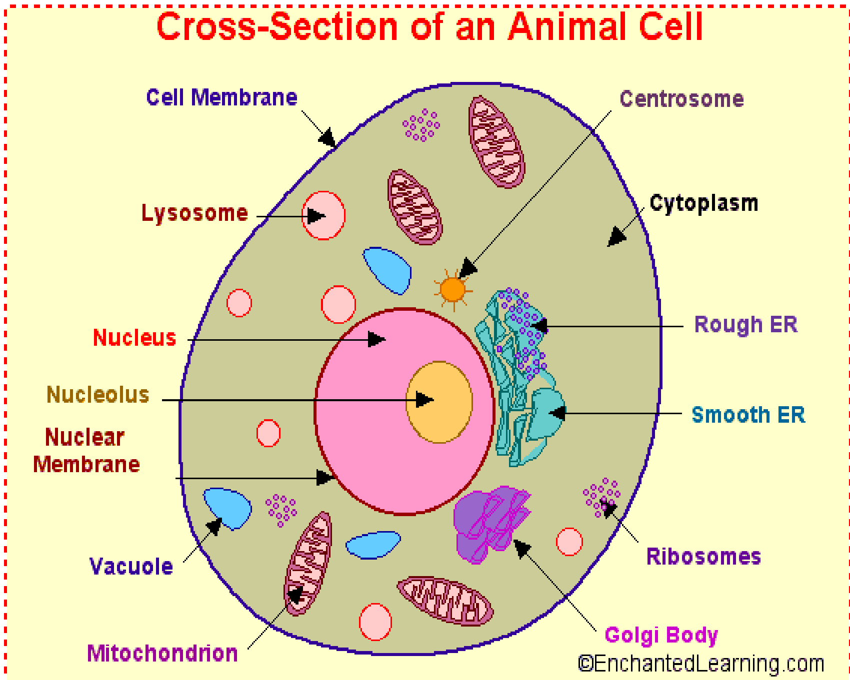
Part 1

All cells have a bio-membrane



All living cells and many of the tiny organelles internal to cells are bounded by thin membranes, called bio-membranes or plasma or cell membrane

Functions of bio-membrane:



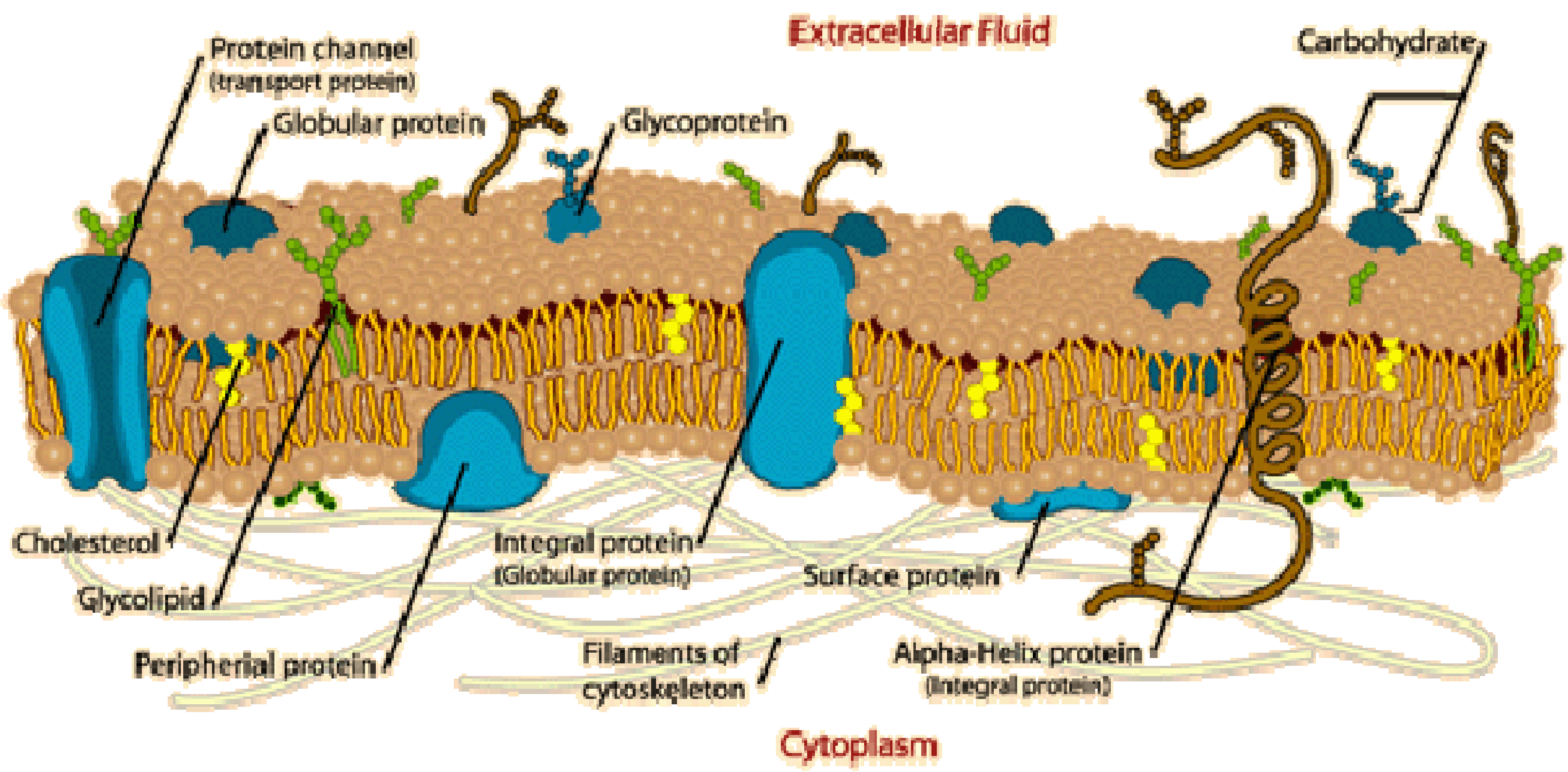
- **Separation** (separate cells, and organelles inside the cell)
- **Transport** (membrane is semi-permiable and regulates selective exchange of molecules and ions between the cell or organelle and its environment)
- **Energy transducer** (regulates energy conversion in biological systems, such as
- Photosynthesis (light to chemical energy),
- oxidative phosphorilation – (producing energy rich ATP)

- **Transport of nerve impulses**
- plasma membrane in nerve cells transform external stimulus into the electric signal

Physics of cell membrane aims at understanding :

- Physical structure of cell membrane
- Dynamics of cell membrane
- The flow of matter across the membrane
- Energy transfer mechanisms

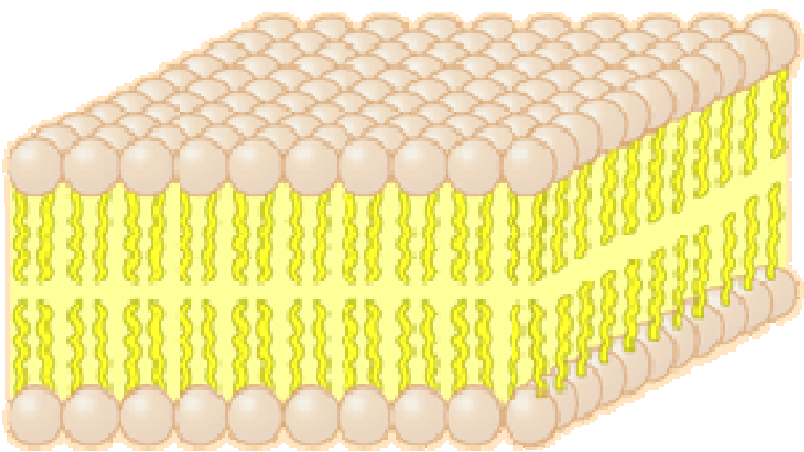
Structure of cell membrane



Cell membranes are composed of phospholipids and proteins (25-75%).

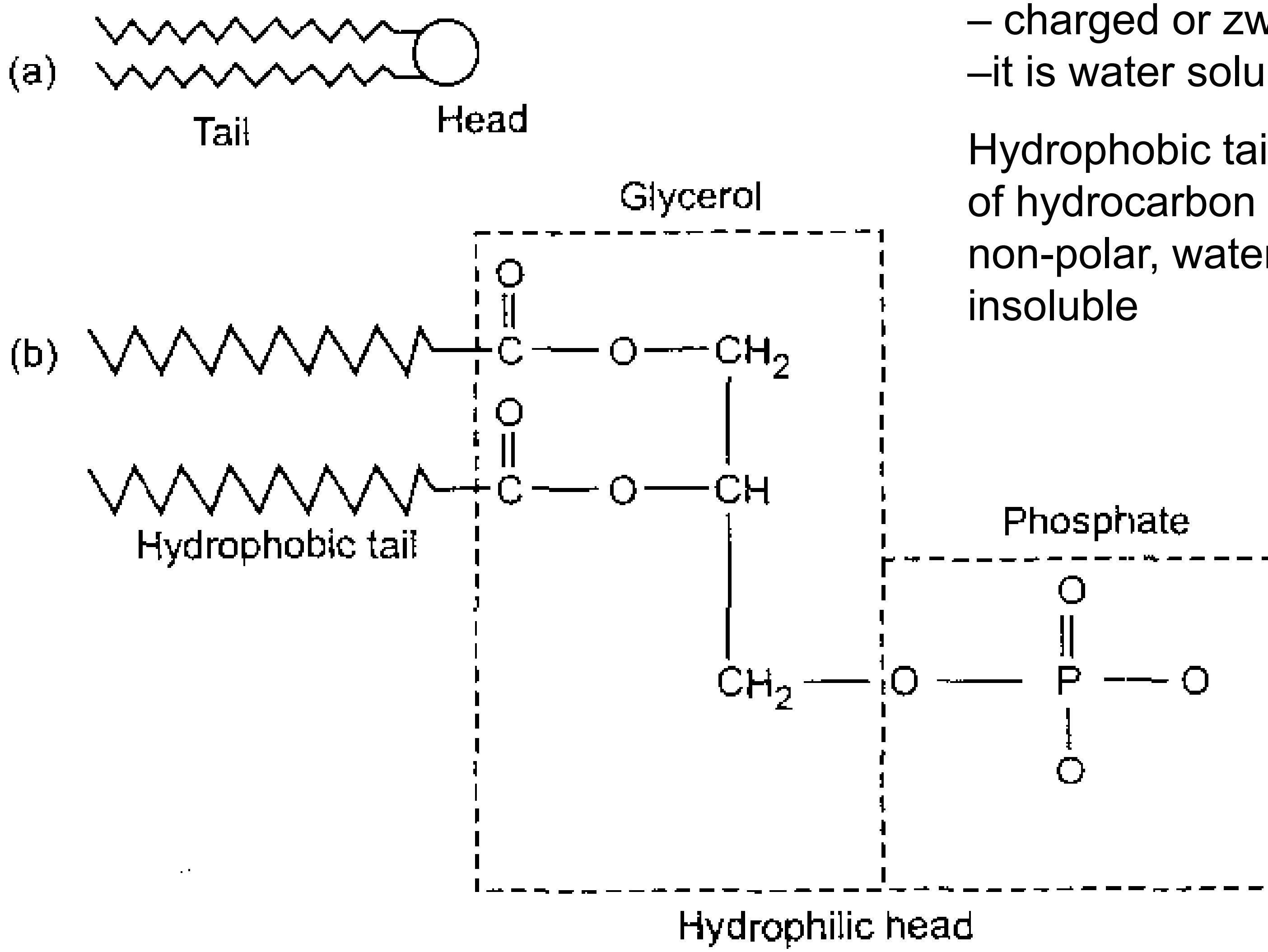
Structure of cell membrane

Cell membranes are thin sheet-like structures – only 6-10 nm thick.
Model membrane - phospholipid bilayers .



- the spheres represent the phosphate end, which is polar and water soluble (hydrophilic). The twin extensions represent the hydrophobic tails which are not water soluble (fatty acids).

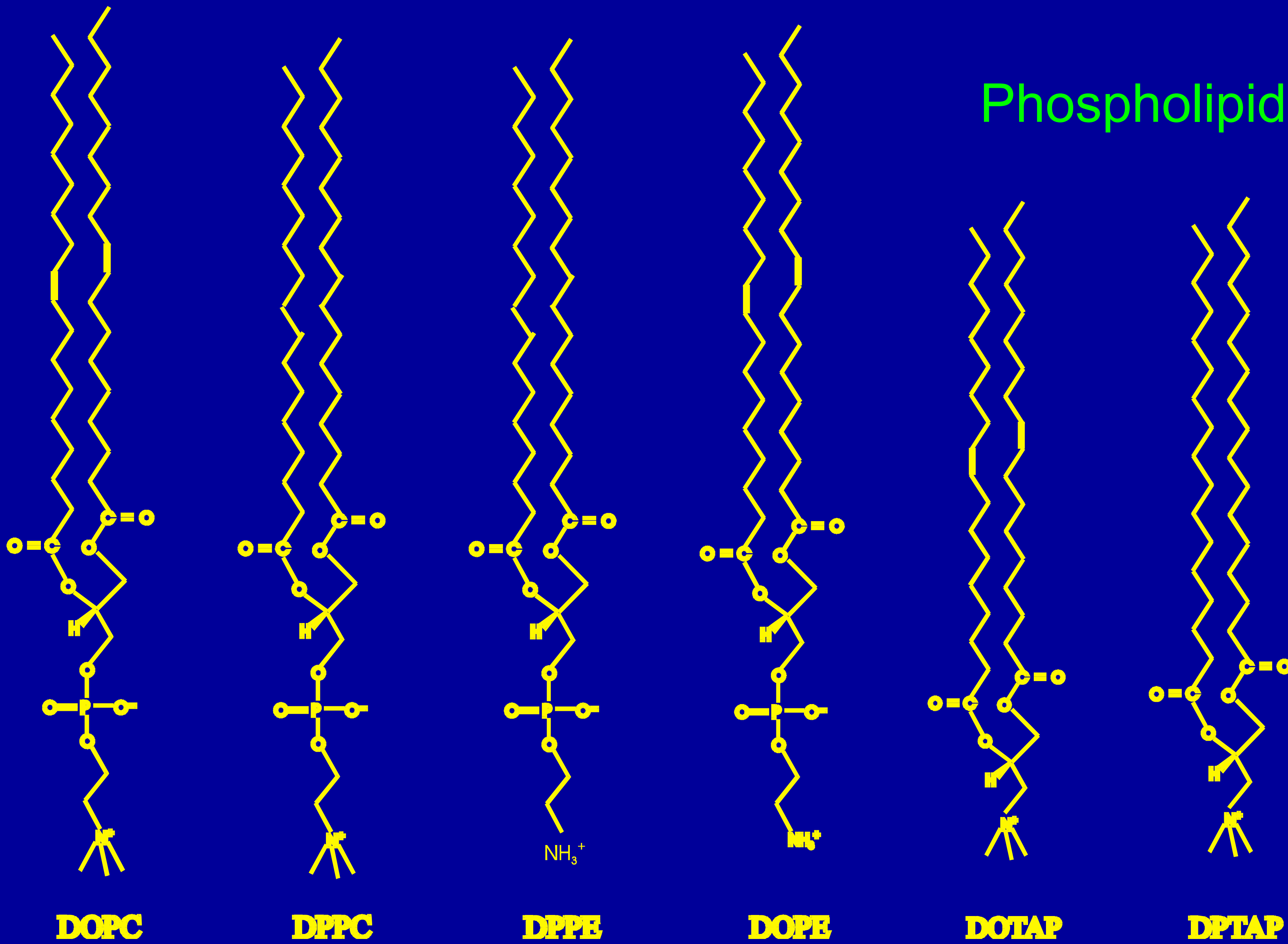
phospholipids

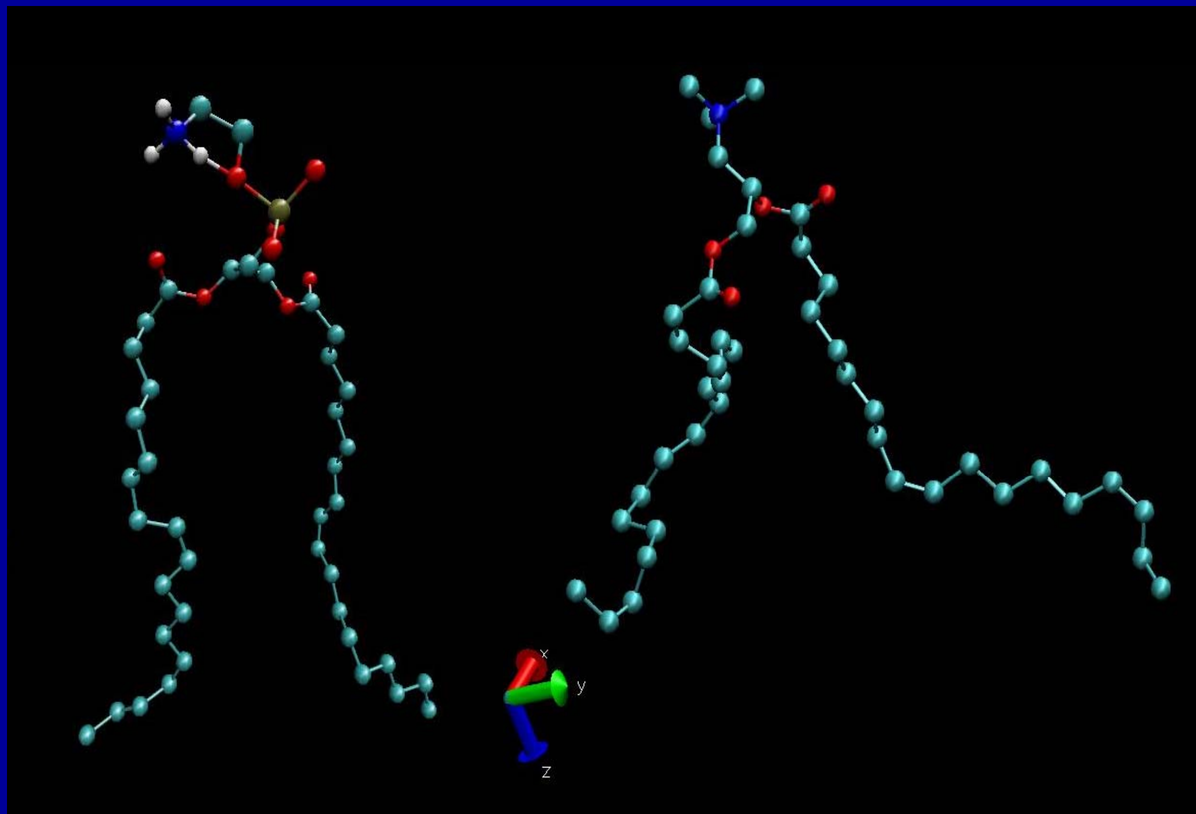


Hydrophilic head is polar – charged or zwitterionic –it is water soluble

Hydrophobic tail consists of hydrocarbon chains – non-polar, water insoluble

Phospholipids




x
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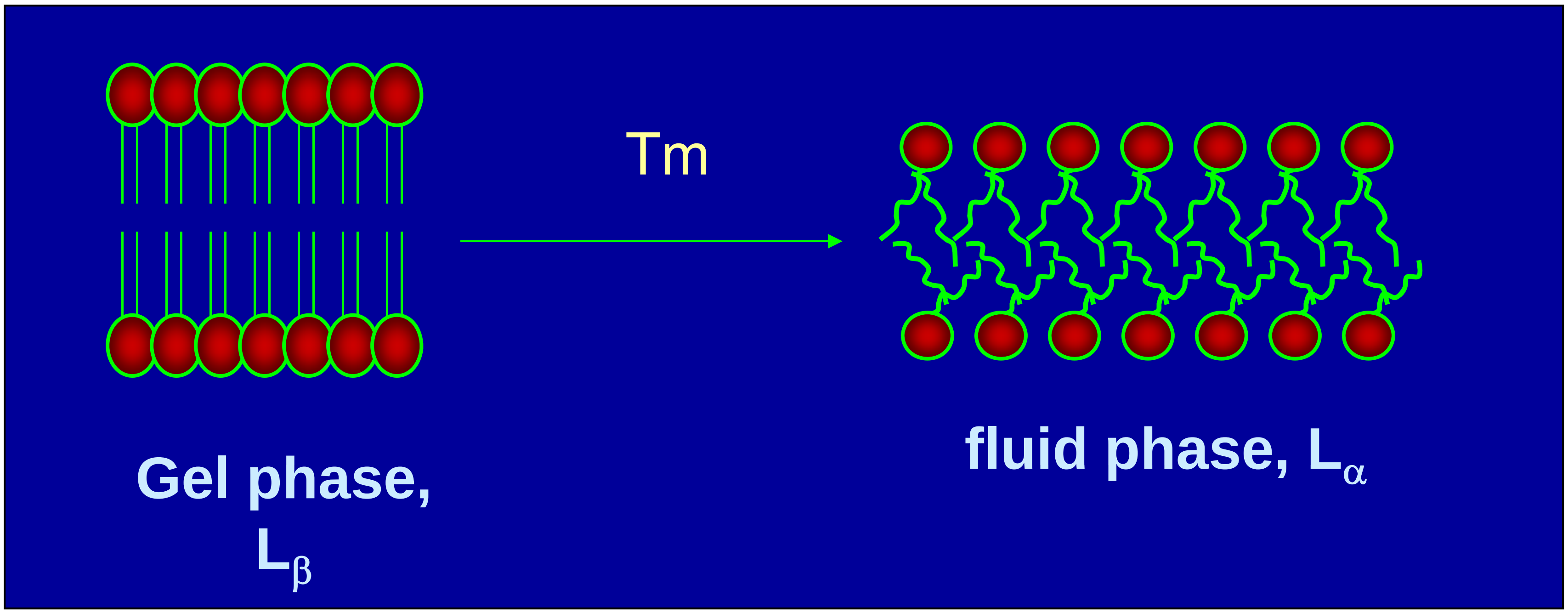
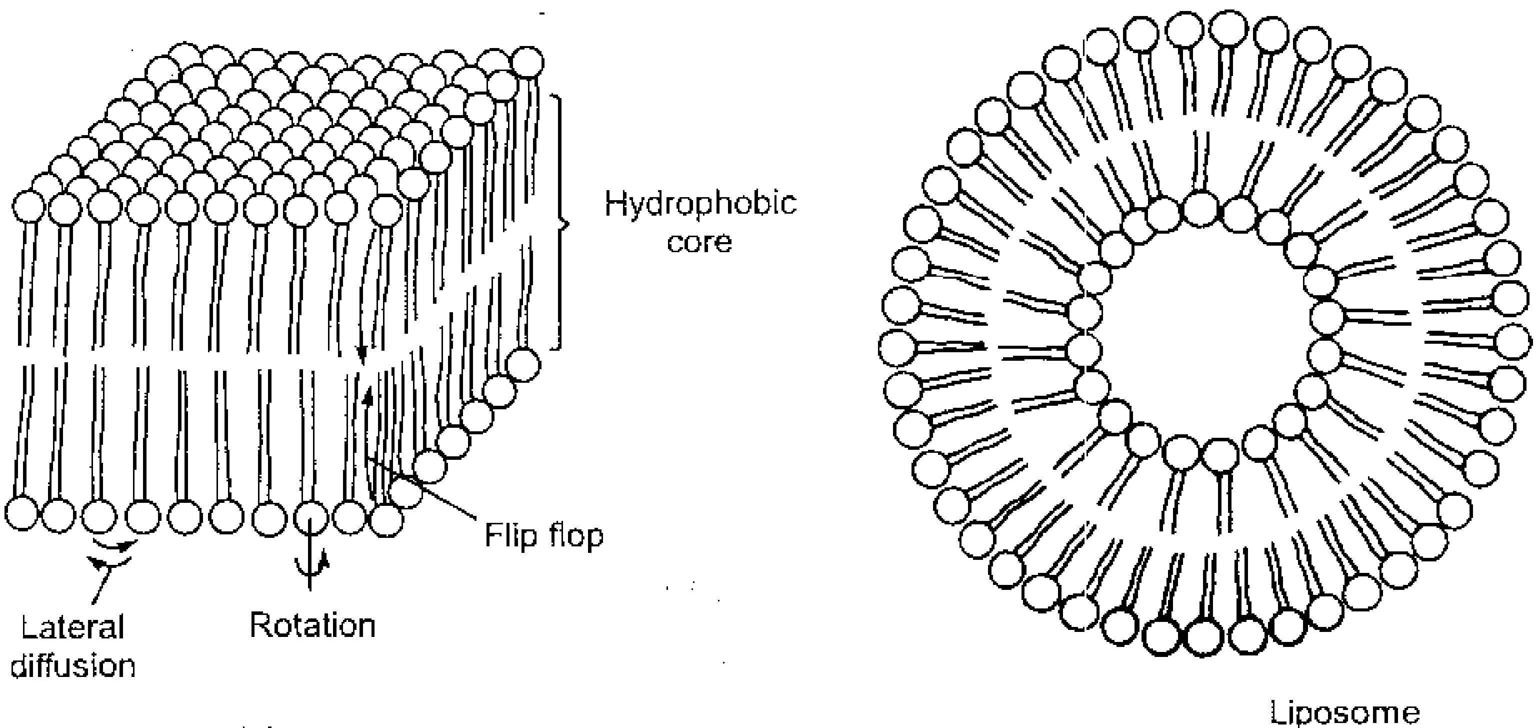
Membrane phase transitions

- Structure of lipid bilayer depends on T,
- Gel phase and fluid phase,
- Melting Tm is characteristic feature and depends on the type of lipid



Increase in bilayer fluidity, decrease in thickness

Artificial membrane - liposomes

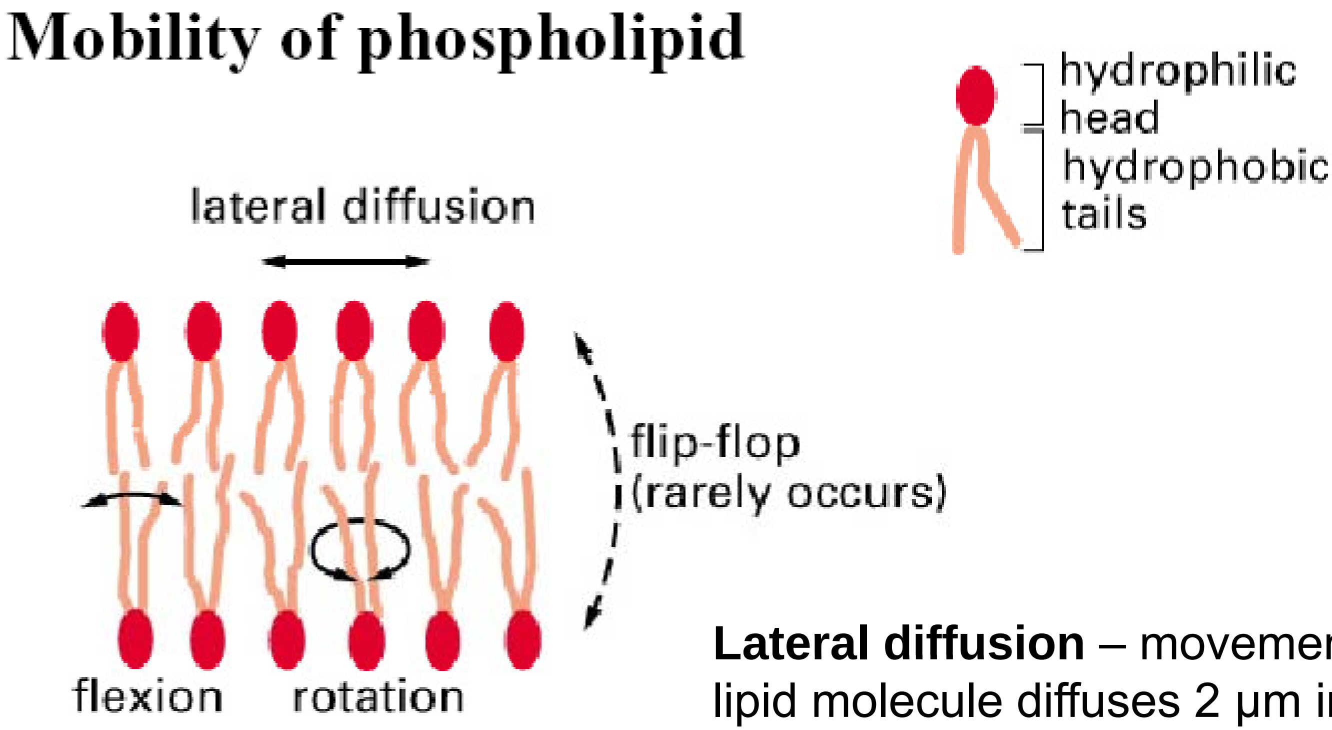


(a) (b)

Bilayer is formed in a small spherical structures – vesicles or liposomes when lipid solution is shaken by unltrasonic waves

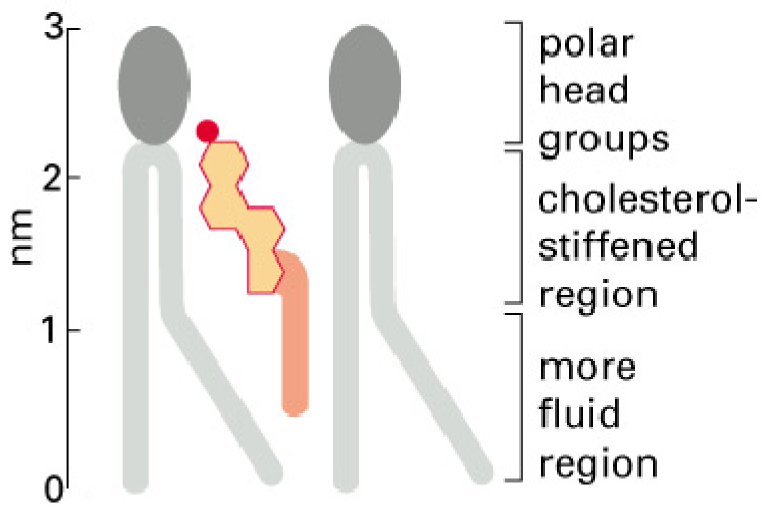
Dynamic model of cell membrane

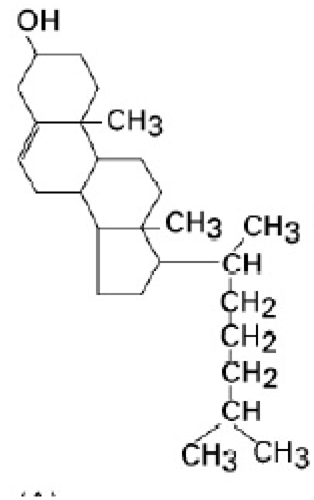
- Both lipids and proteins are mobile in the membrane at body T (37C), both lipids and proteins diffuse along and across membrane

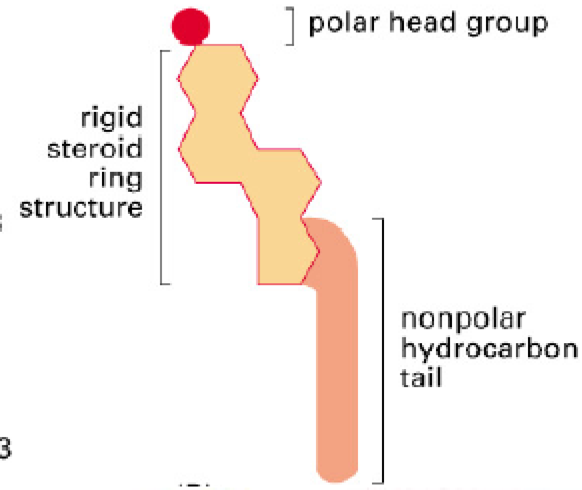


Lateral diffusion – movement along the plane, lipid molecule diffuses 2 µm in 1 sec,
Flip-Flop – movement of lipid across membrane, 109 times slower
Rotation is also possible

Cholesterol



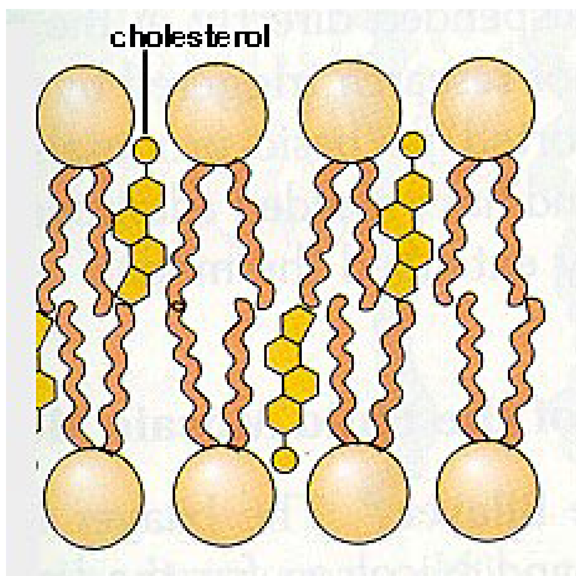


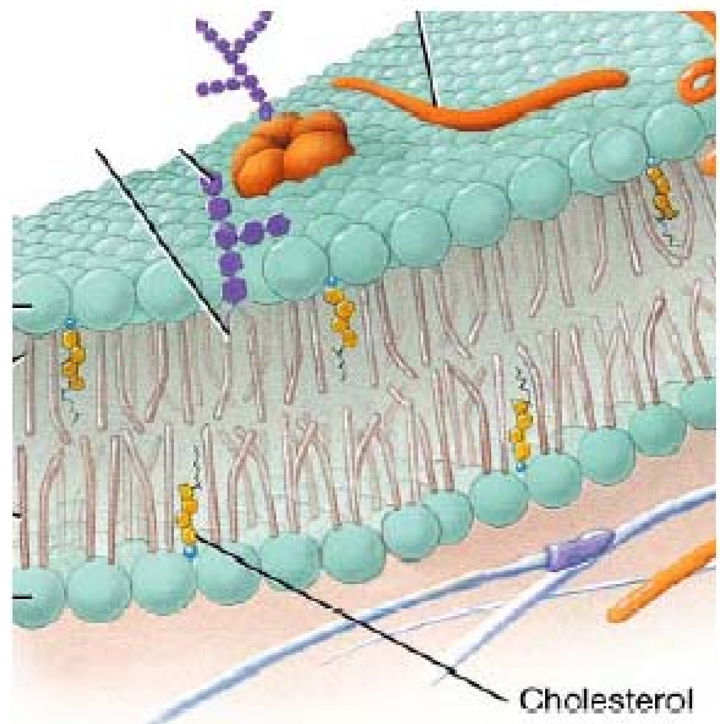


Dual effect on lipid structure:

Makes gel lipid more fluid

Makes fluid lipids more gel-like

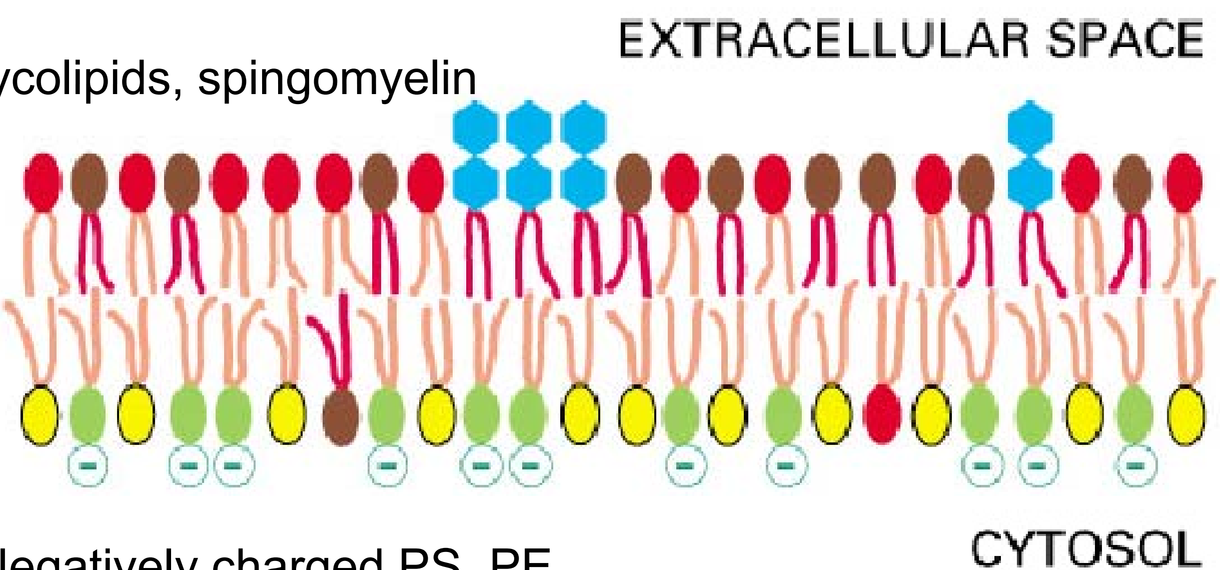




Membrane asymmetry

- Membrane is an asymmetrical system both structurally and functionally:
- Lipids and proteins on opposite sides of the membrane are not the same
- Asymmetry is required for regulation of a selective transport

Glycolipids, spingomyelin

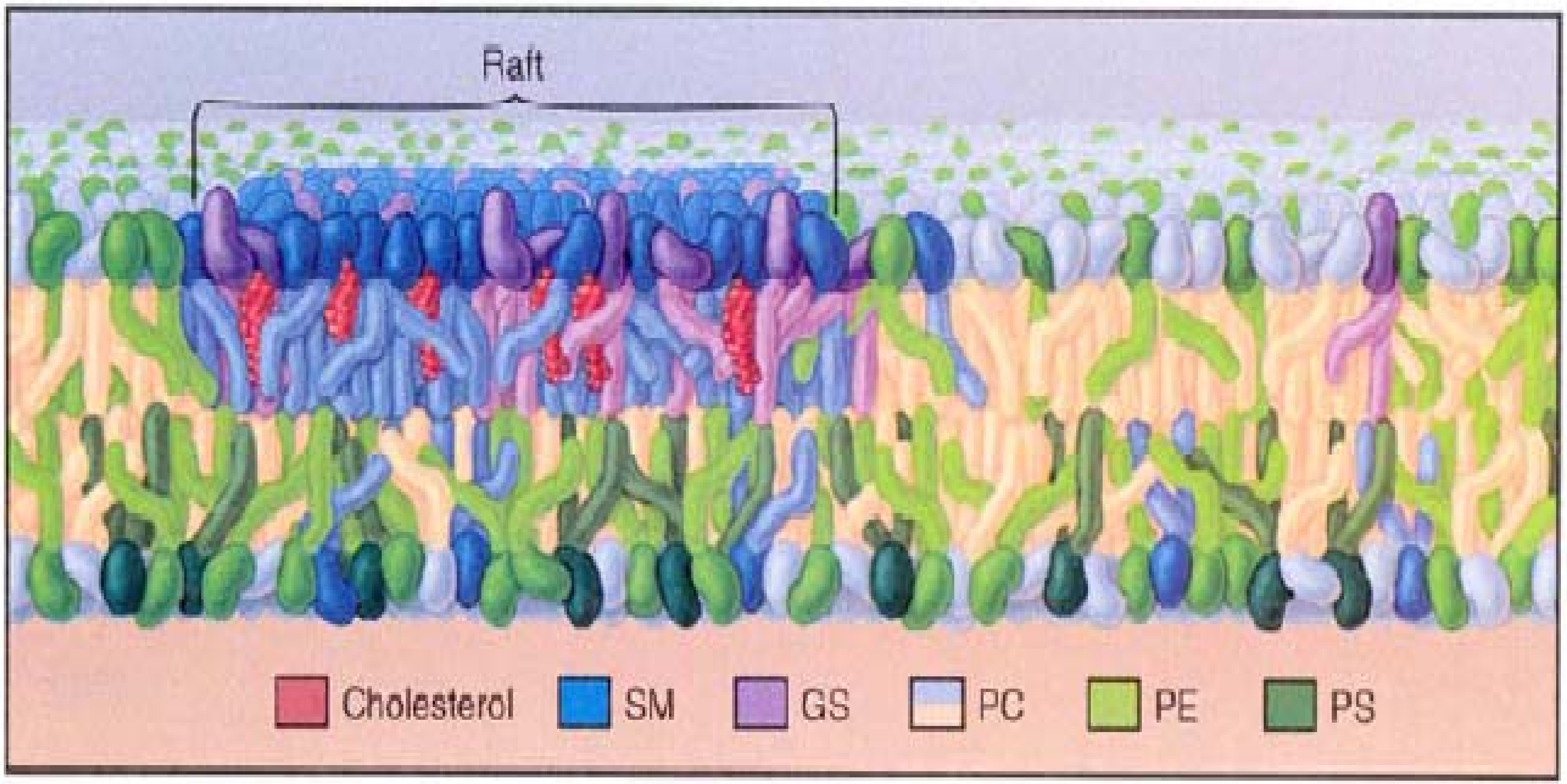


Asymmetry due to lipid composition gives potential difference

Negatively charged PS, PE

Lipid rafts

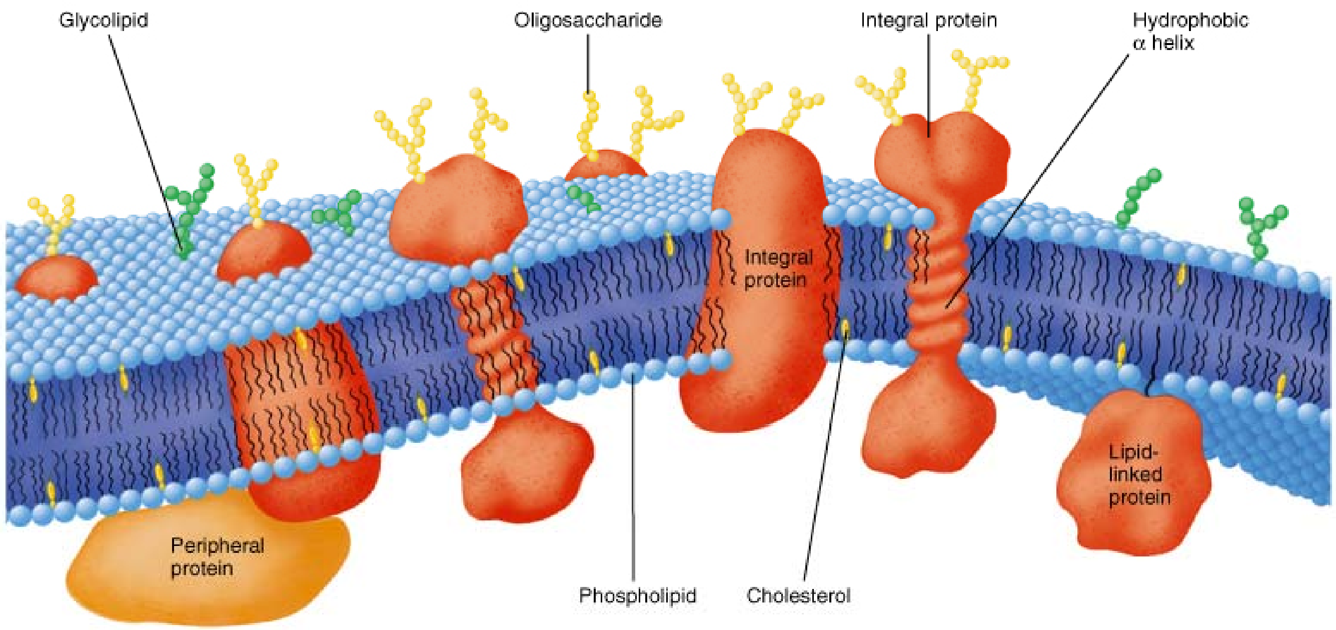
Areas of condensed lipids where cholesterol and spingomyelin are concentrated

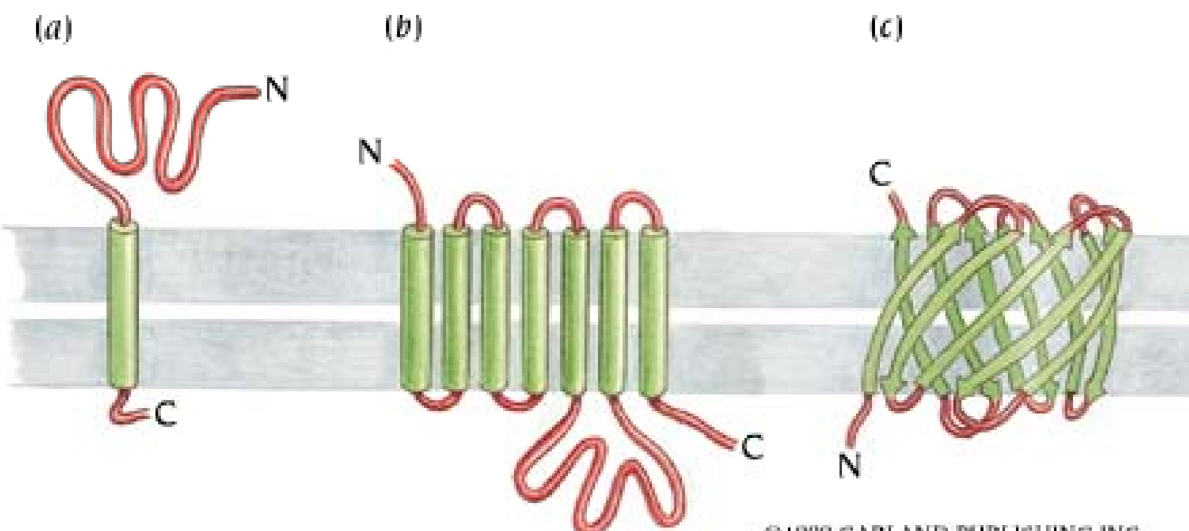


Proteins in membrane

- Lipids provide the structure and support for proteins
- Specific membranes contain specific proteins in different compositions, most common 25-75%
-
- Function of the membrane are defined by these proteins, their nature and arrangements
- Different regions of membrane have different proteins and have different tasks for ex:
- adsorbs molecules like sugars, aminoacids, lipids
- transfer them across membrane
- Cell Membrane also has small pores 0.5 – 0.8 nm, the exact structure is not known, serve transport of ions and fluids

Membrane Bilayer with Proteins





In order to be stable in this environment, a polypeptide chain needs to
(1) contain a lot of amino acids with hydrophobic side-chains, and
(2) fold up to satisfy backbone H-bond propensity

Protein diffusion

- Proteins diffuse more slowly than lipids
- Lipid membrane is a viscous fluid for protein diffusion

- **Lateral diffusion** :
- Surface proteins diffuse 20 μm in 10-60 min
- Diffusion coefficient is 10^{-9} – 10^{-12} compared to lipids $10^{-7\ -8}$

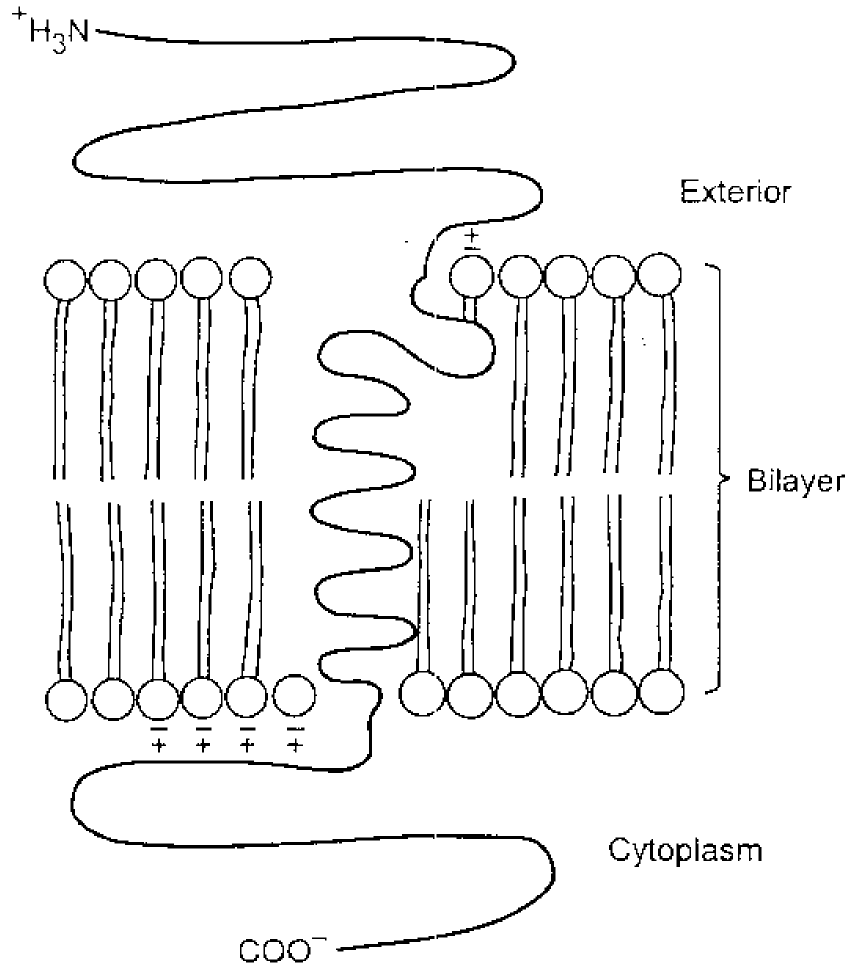
- **Rotation** - yes

- **Flip-Flop** - has not been observed for proteins – this is necessary for membrane asymmetry

Membrane proteins are:

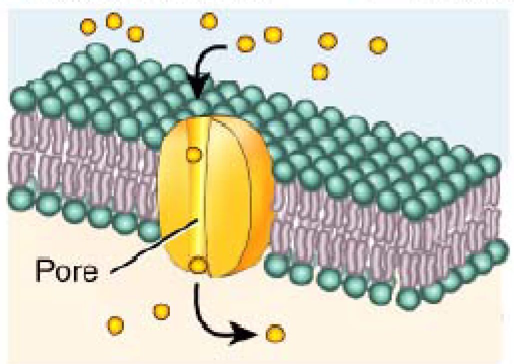
- **Surface proteins**
- Polar, charged, located at the inner or outer surface of membrane, do not penetrate into the membrane or penetrate into a small extent, bound by electrostatic interactions
- **Inner or trans-membrane proteins**
- Hydrophobic, inside the membrane, sometimes have hydrophilic tails and go outside membrane –example Glycophorin

Glycophorin A in RBC

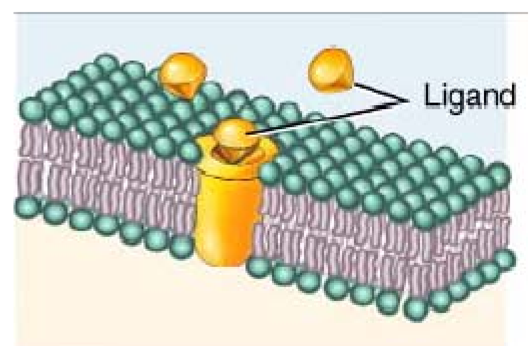


Types and functions of transmembrane proteins

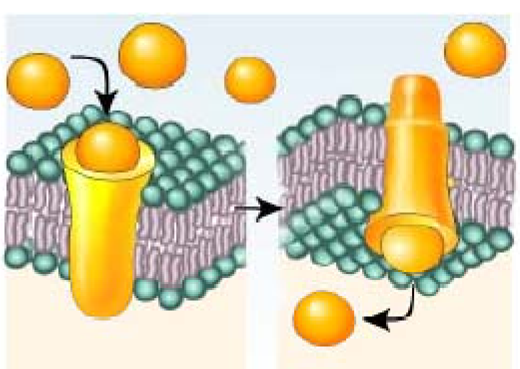
Extracellular fluid   Plasma membrane   Cytosol



Ion channel
Allows specific ion (●) to move through water-filled pore. Most plasma membranes include specific channels for several common ions.

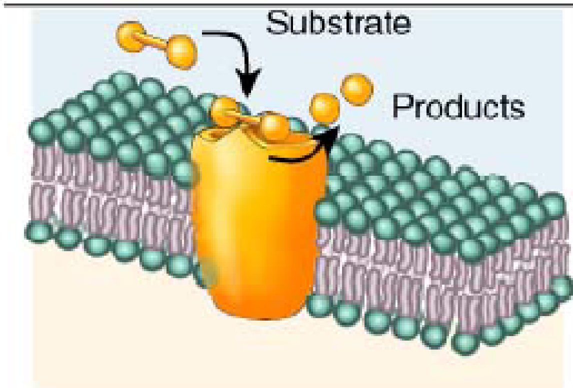


Receptor
Recognizes specific ligand (▼) and alters cell's function in some way. For example, antidiuretic hormone binds to receptors in the kidneys and changes the water permeability of certain plasma membranes.

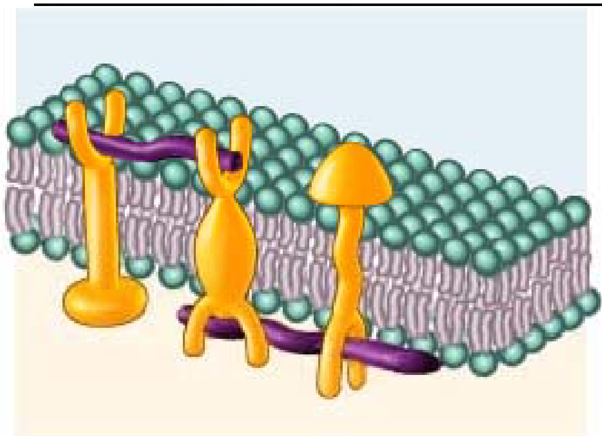


Transporter
Transports specific substances (●) across membrane by changing shape. For example, amino acids, needed to synthesize new proteins, enter body cells via transporters.

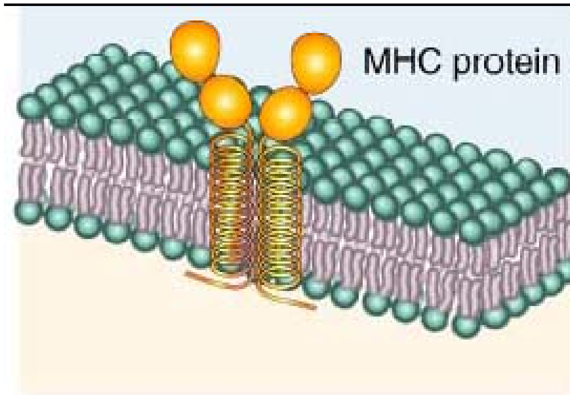
Types and functions of transmembrane proteins



Enzyme
Catalyzes reaction inside or outside cell (depending on which direction the active site faces). For example, lactase protruding from epithelial cells lining your small intestine splits the disaccharide lactose in the milk you drink.

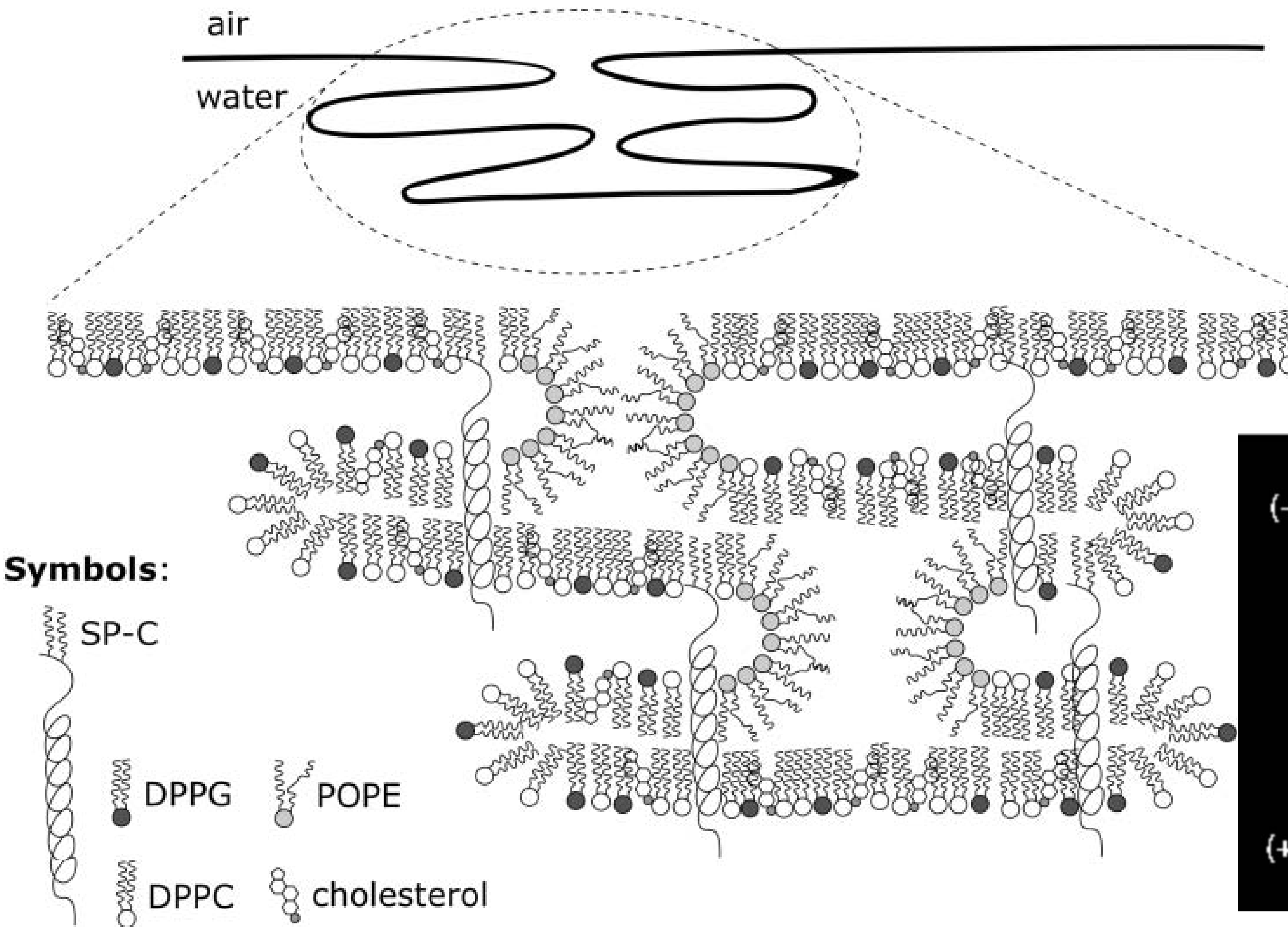


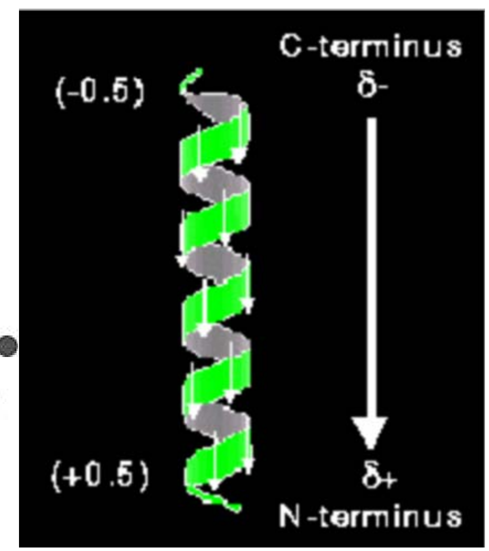
Linker
Anchors filaments inside and outside to the plasma membrane, providing structural stability and shape for the cell. May also participate in movement of the cell or link two cells together.



Cell Identity Marker
Distinguishes your cells from anyone else's (unless you are an identical twin). An important class of such markers are the major histocompatability (MHC) proteins.

surfactant protein C





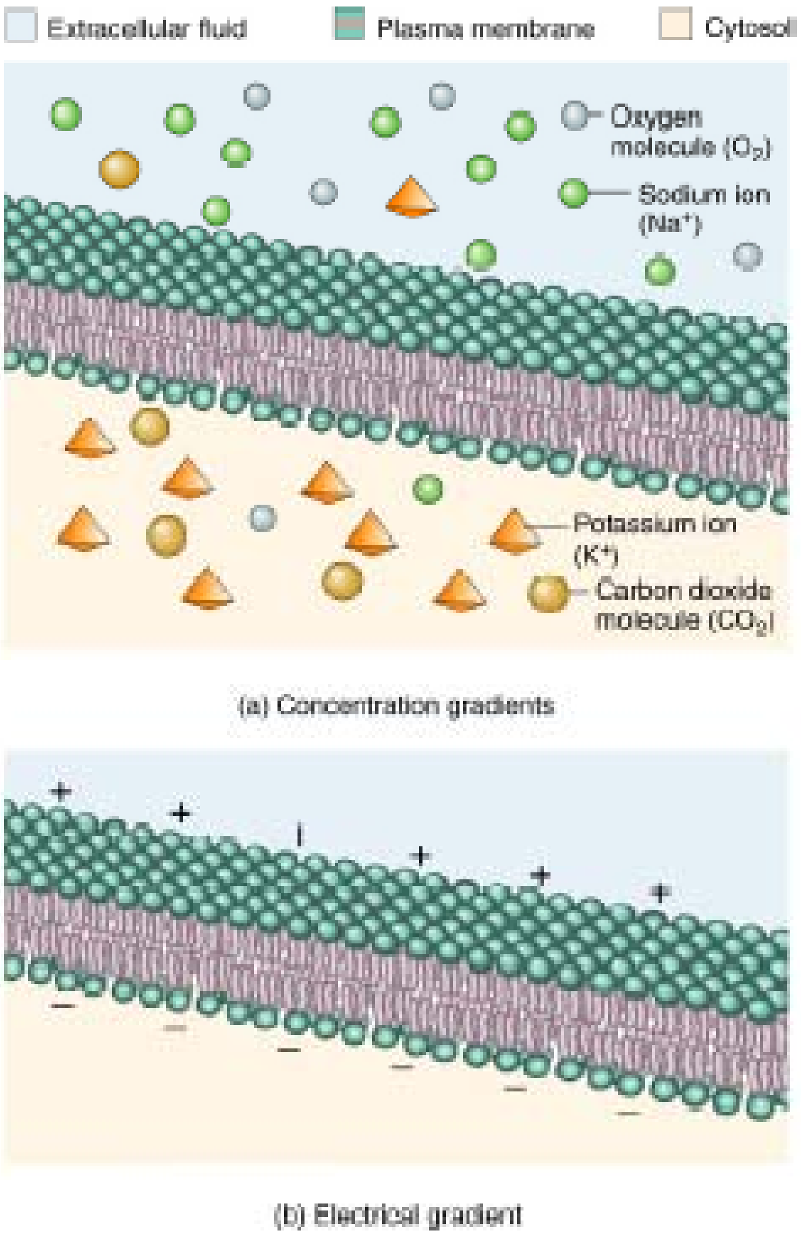
Transport through membrane

- Selective transport – main biomembrane function
- Membrane is a complex structure of two layers of lipids with proteins
- Transport of simple ions is difficult to describe

- Simplified model:
- Slab-like model of membrane – membrane is considered as homogeneous bilayer

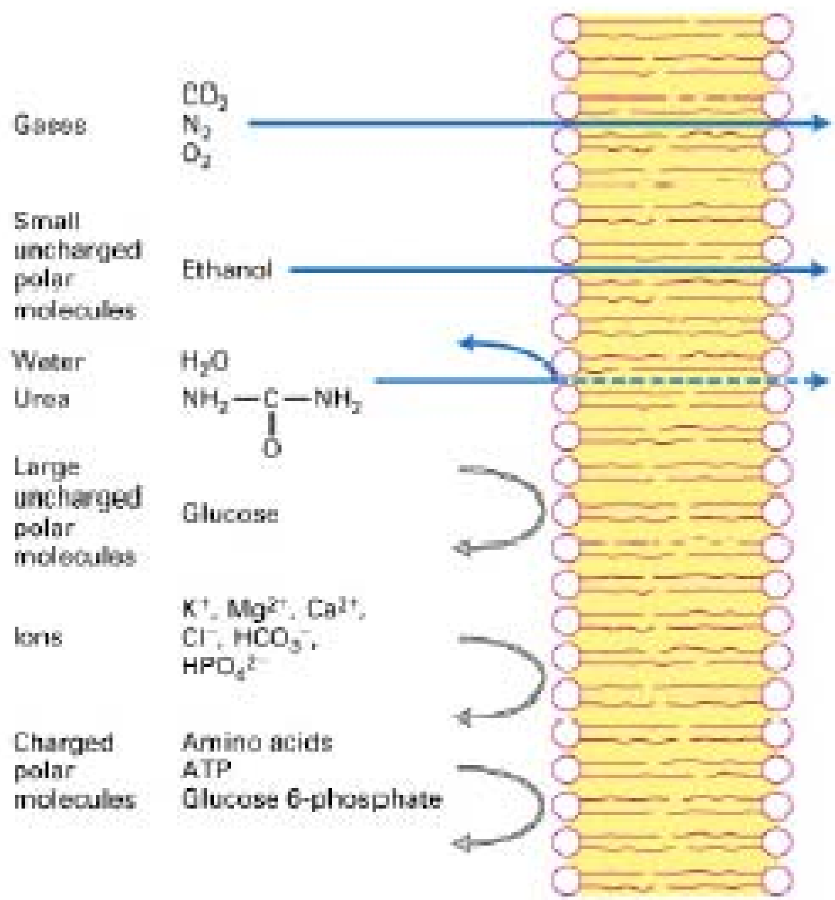
- Thermodynamically transport is classified :
- Passive Transport – originates from cell environment – cell does not spend energy
- Active transport – cell spends energy to facilitate this transport

Plasma Membrane: environmental boundary (barrier)



Electrochemical gradient
- **Membrane potential**

Unique intracellular environment
- **Stabilize pH**
- **Holds molecules inside**



Passive transport

- Passive transport - the molecule diffuses through the membrane due to concentration or potential gradient, cell does not spend energy

- Passive Transport – for non-electrolytes – driving force concentration gradient:

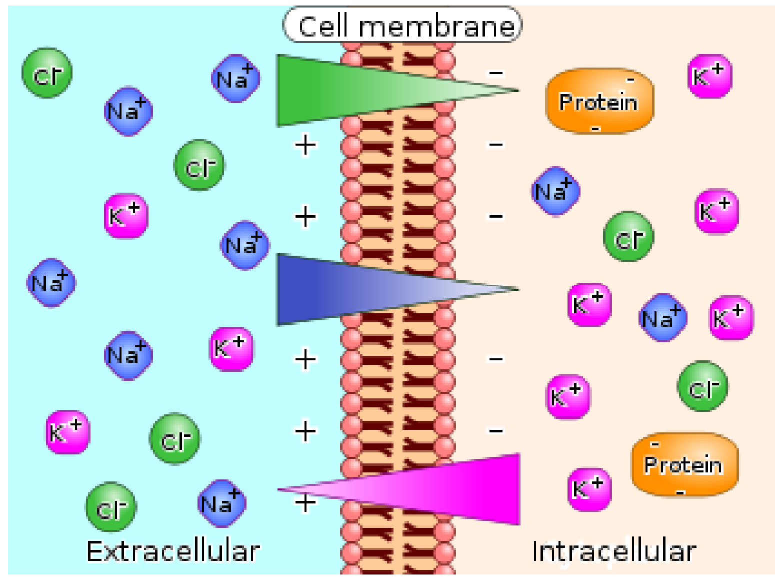
- **Diffusion** of solute across semi-permeable membrane (permeable to solute) from the region of high concentration to a region of lower concentration, characteristic for non-electrolytes
- Diffuse molecules - oxygen, carbon dioxide, water,

- **Osmosis** – if membrane is permeable to solvent only, the solvent will move to the areas of high concentration of solute
- Concentration gradient is a non-equilibrium state and system will slowly approach equilibrium

- **Solvent Drag** – if solvent is moving through the membrane – solute can be dragged by solvent

Passive transport

- Passive Transport – electrolytes:
- Electrolytes dissociate into
- ions in solution



- Driving forces for electrolytes:
- Concentration gradient
- Electric potential gradient

- Membrane transport is complex, and selective – concentration of ions inside and outside are different as well as lipid charges are different on each side – this creates potential
- Membrane permeability is different for different ions – it is an empirical parameter and characteristic of a membrane

Simple diffusion

- When a molecule or ion diffuses under the influence of its own concentration gradient (and /or electric potential gradient) – the process is called **simple diffusion**

- The molecules and ions are inside and outside the cell are in aqueous solution phase. They diffuse through membrane in two ways:
- If they are soluble in membrane – they dissolve and diffuse through
- If they are insoluble in membrane – they move through the protein channels or membranes pores, or they are moved by carriers molecules
- Oxygen, carbon dioxide, alcohols, are soluble in both water and lipids, Oxygen is more soluble in lipid membrane and diffuses faster
- Water cannot diffuse through the lipid membrane – through the pores and channels

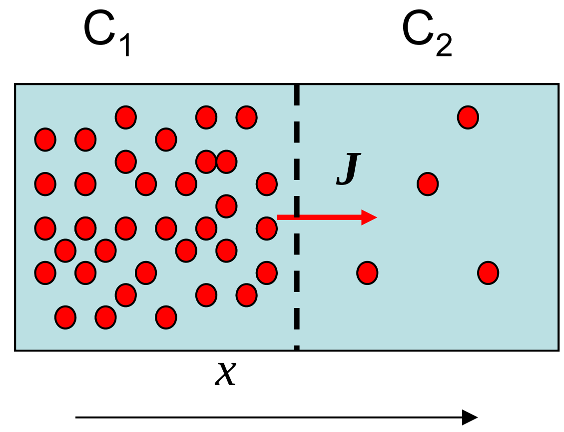
Facilitated diffusion

- Glucose, sucrose are not soluble in lipid membrane, are too large to go through pores – the diffuse with the help of carrier molecules – facilitated diffusion

Diffusion of non-electrolytes

Fick's Law of diffusion:

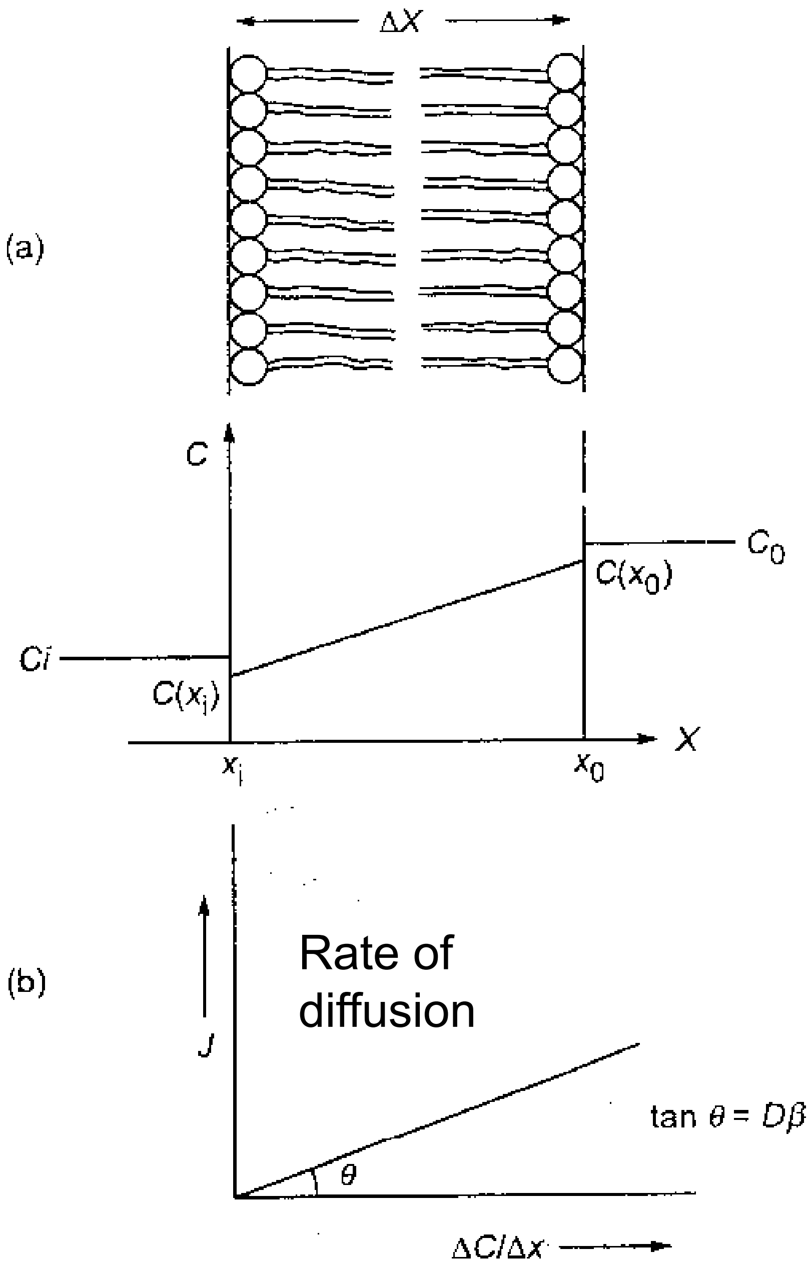
$$\boxed{J = -D\frac{\Delta C}{\Delta X}}$$



D – diffusion coefficient

In near equilibrium conditions, molar flux J of given molecules (number of moles) crossing normally through the unit area of membrane per second varies linearly with concentration gradient,

C – molar concentration (number of moles per unit volume)

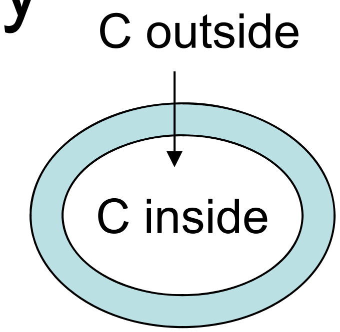


$$J = -D\frac{\Delta C}{\Delta X}$$

This model is used when:

1. The system only slightly away from equilibrium
2. Membrane is assumed to be a homogeneous slab of thickness Δx, made of uncharged molecules
3. Concentration changes uniformly by ΔC over membrane thickness
4. D – diffusion constant is independent of concentration C(x), pressure and T outside and inside the membrane medium

Partition coefficient and permeability



$$J_c = -D\frac{\Delta C}{\Delta x} = -D\frac{C_o - C_i}{x_o - x_i} = -D\frac{\Delta C}{\delta}$$

$$\boxed{C(x) = Ax + B \qquad C(x_i) = C_i \qquad C(x_o) = C_o}$$

Boundary conditions

Assuming that within the membrane, C changes linearly with distance within the boundary conditions, but this is not true

Need to use these boundary conditions:

$$C(x_i) = \beta C_i$$

$$C(x_o) = \beta C_o$$

β - Partition coefficient - fraction of solute concentration outside dissolves in membrane, independent on concentration

Membrane permeability

$$P = \frac{D\beta}{\delta}$$

$$J = -D\frac{C(x_o) - C(x_i)}{x_o - x_i} = -\frac{D\beta}{\delta}\Delta C = -P\Delta C$$

It is observed that diffusion coefficient varies inversely with square root of molecular weight M
On the other hand, mobility of several membrane bound proteins, which are large and heavy molecules, is very high

How this contradiction can be explained? By employing two different models:

- **Free volume model** local density fluctuations due to thermal movement of lipids inside the membrane create holes in the membrane, in which diffusing molecules can fall. Diffusion is transfer from hole to hole. In this case:

$$D \propto \frac{1}{\sqrt{M}} \quad \text{and} \quad \log D \propto \frac{1}{T}$$

This model works better for small molecules

- **Hydrodynamic model:** assumes that diffusion occurs through hydrodynamic flow of molecules through water or lipid phase. Diffusion depends weakly (logarithmically) on viscosities of water or lipid phase and radius of the diffusing molecule

Diffusion of electrolytes

If diffusing particles are charged – two driving forces:

concentration gradient

$$J_c = -D\frac{\Delta C}{\Delta x}$$

and

electric potential gradient

$$J_\phi = -DC\frac{zF}{RT}\frac{\Delta \phi}{\Delta x}$$

F-Faraday constant, electric potential gradient

The flux for charged particles is a sum:

Total potential gradient called electrochemical potential gradient

$$J = -D\frac{\Delta C}{\Delta x} - DC\frac{zF}{RT}\frac{\Delta \phi}{\Delta x} = -\frac{DC}{RT}\left[\frac{RT}{C}\frac{\Delta C}{\Delta x} + zF\frac{\Delta \phi}{\Delta x}\right]$$

Nernst-Planck equation, holds for one diffusing ion

If there are m simultaneously diffusing ions:

$$J_i = -\frac{D_i C_i}{RT}\frac{\Delta \mu_i}{\Delta x} \qquad i = 1, \ldots 1, m$$

$$\boxed{\Delta \mu_i = \frac{RT}{C_i}\Delta C_i + z_i F \Delta \phi_i}$$

Assuming that there is no coupling between ions

D_i – diffusion constant for i-th type of ions

Electrochemical potential for ith type of ions

concentration

Membrane potential

- In an equilibrium, when ionic flux across the membrane disappears, we get:

$$RT\frac{dC}{C}+zFd\phi=0$$

- Integrating between outside and inside membrane, we get membrane potential:

$$\int_o^i d\phi=-\frac{RT}{zF}\int_o^i\frac{dC}{C}$$

or

$$\boxed{\phi_i-\phi_o=\frac{RT}{zF}\ln\frac{C_o}{C_i}}$$

$$\boxed{C_o=C_i\exp\left(\frac{zF\Delta\phi}{RT}\right)}$$

equilibrium concentration distribution

Faraday constant

F = 96 485.339 9(24) C/mol

Additional material : Faraday constant

- In physics and chemistry, the **Faraday constant** (named after Michael Faraday) is the magnitude of electric charge per mole of electrons. While most uses of the Faraday constant, denoted *F*, have been replaced by the standard SI unit, the coulomb, the Faraday is still widely used in calculations in electrochemistry. It has the currently accepted value:
- *F* = 96 485.339 9(24) C/mol

- The constant *F* has a simple relation to two other physical constants:
  - *F* = *N*A*e*
- where
  - *N*A = 6.022 ×1023 mol-1
  - *e* = 1.602 ×10-19 C