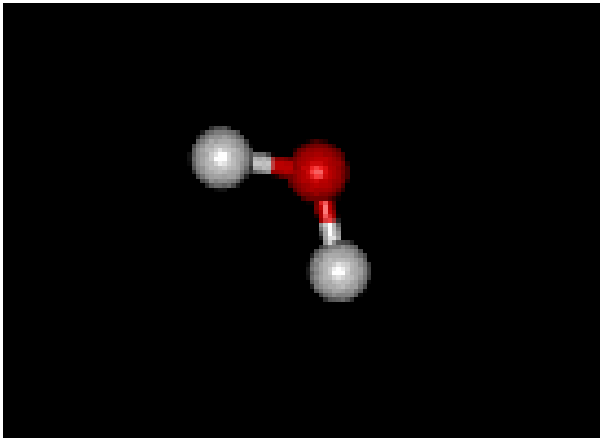


# Cell Biology

**(4 Lectures)**

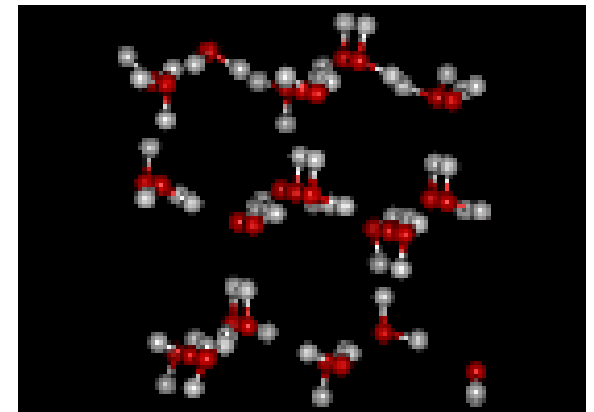
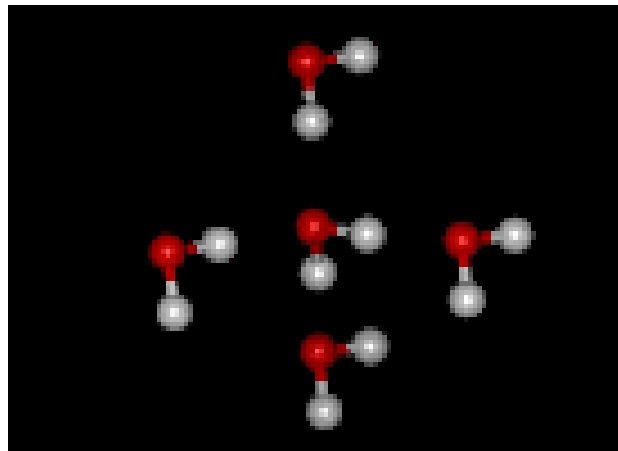
**Prof. A.A. Mahdi**

**Department of Biochemistry  
King George's Medical University  
Lucknow**



# Water

Atomic view



# Ice

# Water

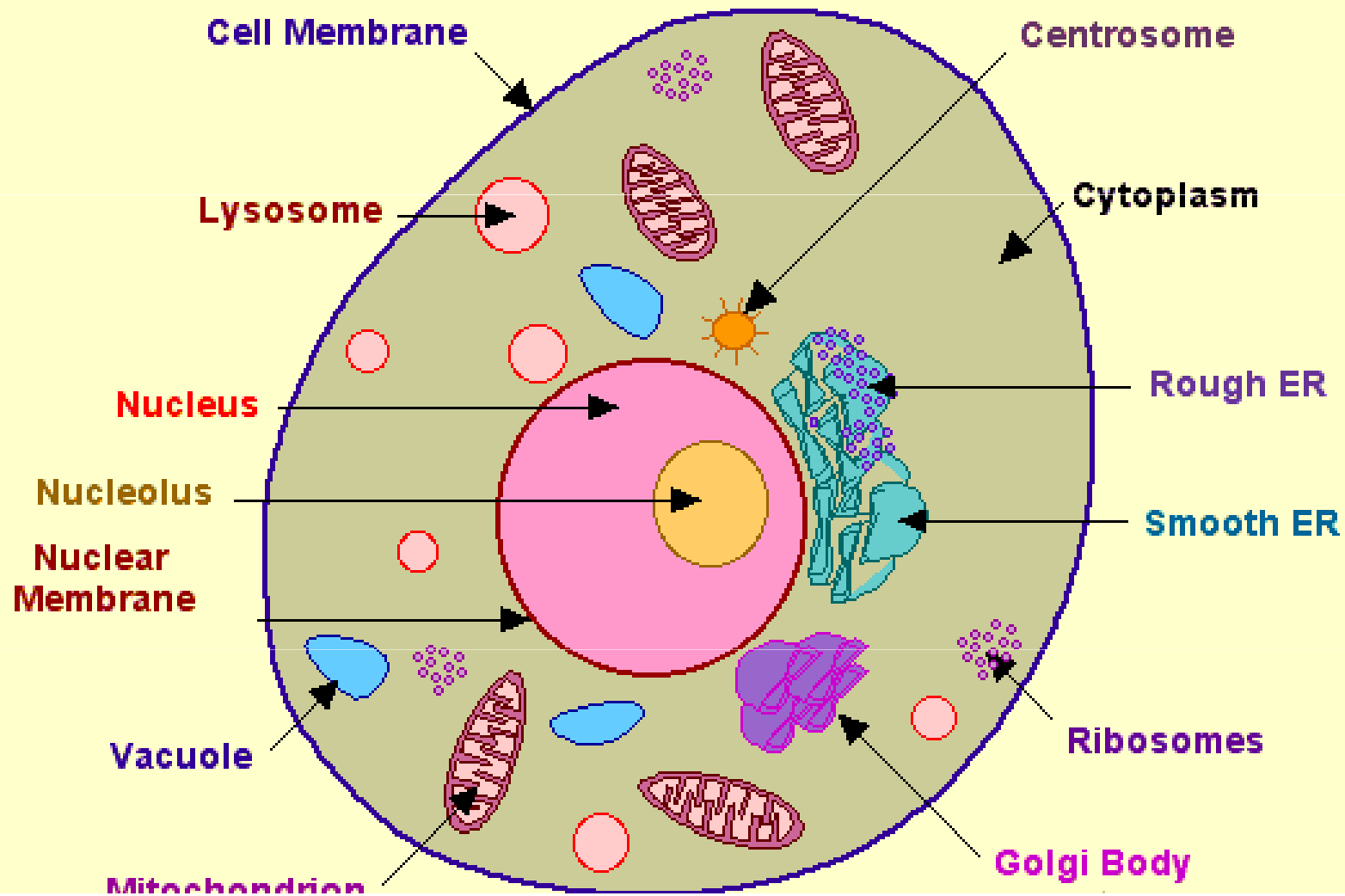
Vessels : Intercellular (ECF) : Intracellular (ICF)

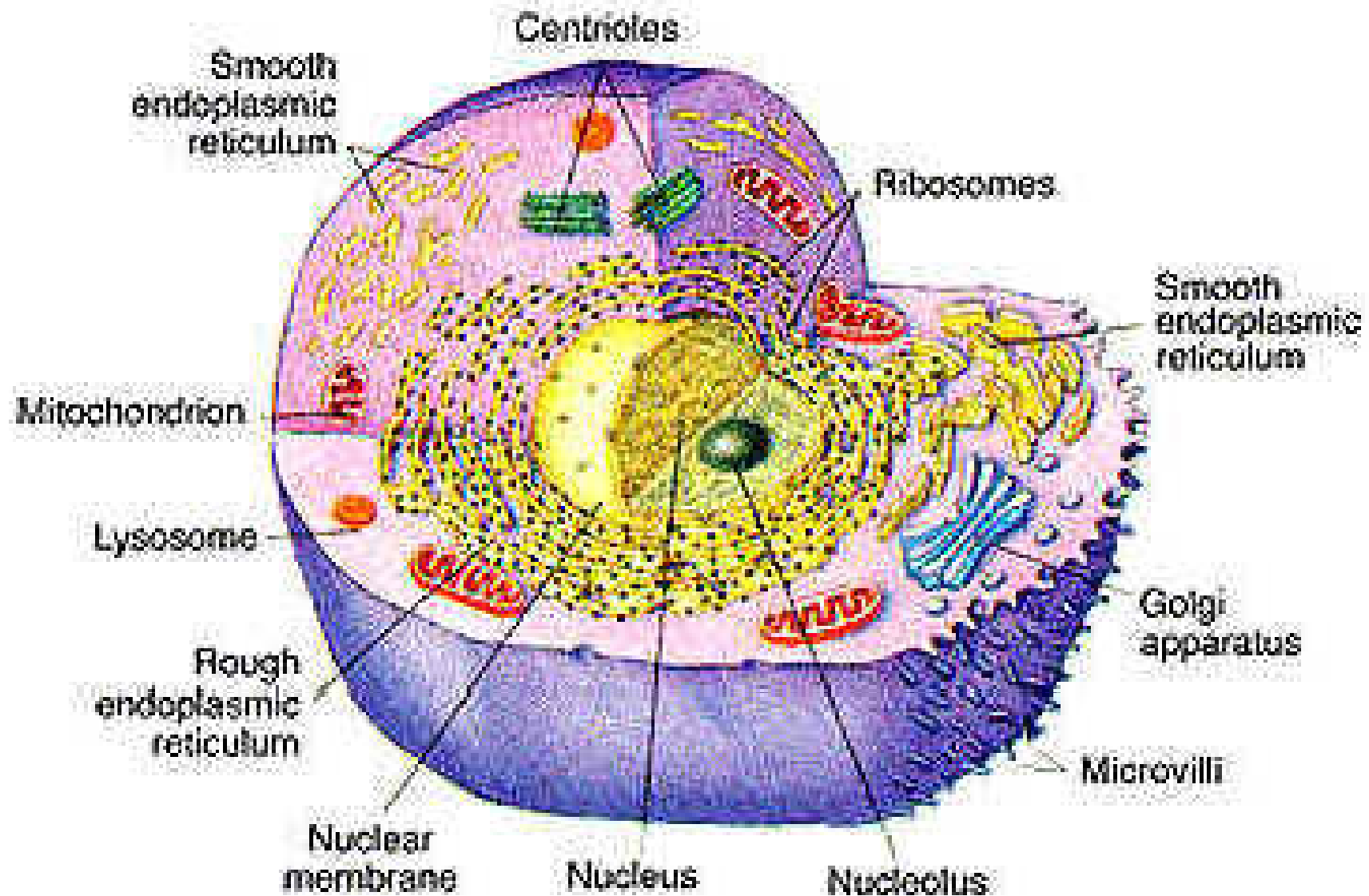
Liters : 3; 13; 30

% : 5; 15; 50

- 75% to 50%.
- 90% in brain tissue; 10% adipose tissue.
- Ions/neutral molecules – Soluble, Proteins – Colloids.  
Lipoproteins – Pseudomicelles.
- Substrate as well as a product.
- Both deficiency as well as excess impairs functioning.

# Cross-Section of an Animal Cell





# CYTOSOL

Fluid compartment, permeates whole internal environment, represent 50-60% of total cell volume.

Contains cytoskeleton having microtubules and microfilaments.

Composition: Viscous gel having proteins 20 gm/100 ml.

Have storage molecules like glycogen granules in liver or fat droplets in adipocytes.

Enzymes of glycolysis, HMP shunt, glycogen metabolism, AA metabolism, Fatty acid synthesis, heme biosynthesis, urea cycle.

Transport proteins and carrier of metals/steroid hormones.

Inorganic ions such as Sodium, potassium, calcium, magnesium, Chloride, phosphate, etc.

# Biological Membranes

- Composed of mainly lipids and proteins
- Give cell its individuality and also compartmentalize intracellular organelles.
- Biomembranes are thin films which are not rigid or impermeable, rather highly mobile and dynamic structures.
- They are gatekeepers of the cells.
- Control access to cell by inorganic ions, nutrients and biological compounds.

# IMPORTANCE

- ❖ Highly selective permeability barriers.
- ❖ Have specific receptors for external stimuli.
- ❖ Generate signals: chemical or electrical.
- ❖ Energy conservation processes occur in membranes.

# COMMON FEATURES

- ✓ Sheet like structures, form closed boundaries, thickness between 60-100 Å.
- ✓ Composed of lipids and proteins, ratio between 4:1 to 1:4.
- ✓ Non-covalent assemblies.
- ✓ Asymmetric.
- ✓ Fluid structure.



# LIPIDS

- ❑ Phospholipids : amphipathic molecules.
  - ❑ Phosphatidyl choline and Phosphatidyl ethanolamine.
- ❑ Neutral lipids : Cholesterol. Cholesterol esters, triglycerides, free fatty acids.

## ROLE OF LIPIDS

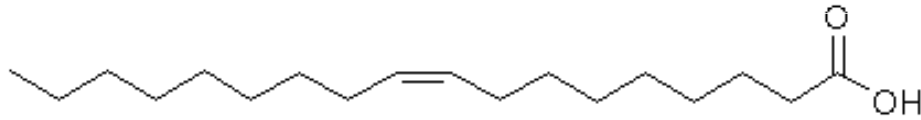
- Fluidity and flexibility of membrane dependent on degree of unsaturation of fatty acids. More unsaturation, more flexible and fluid.
- Conditions of nutritional deficiency of essential fatty acids are displayed.
- Damage to PUFA leads to loss of membrane structure and functioning.

## Molecular structure

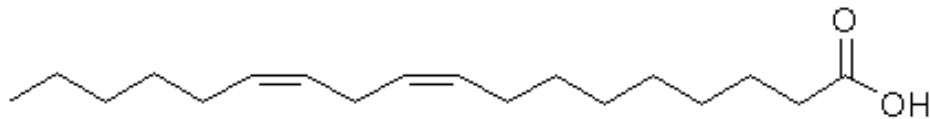


## Name

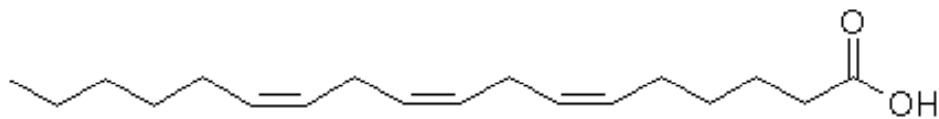
Stearic acid: saturated C18



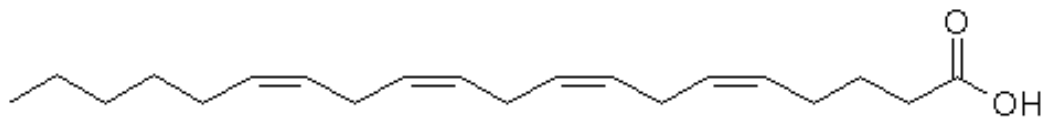
Oleic acid: monounsaturated C18



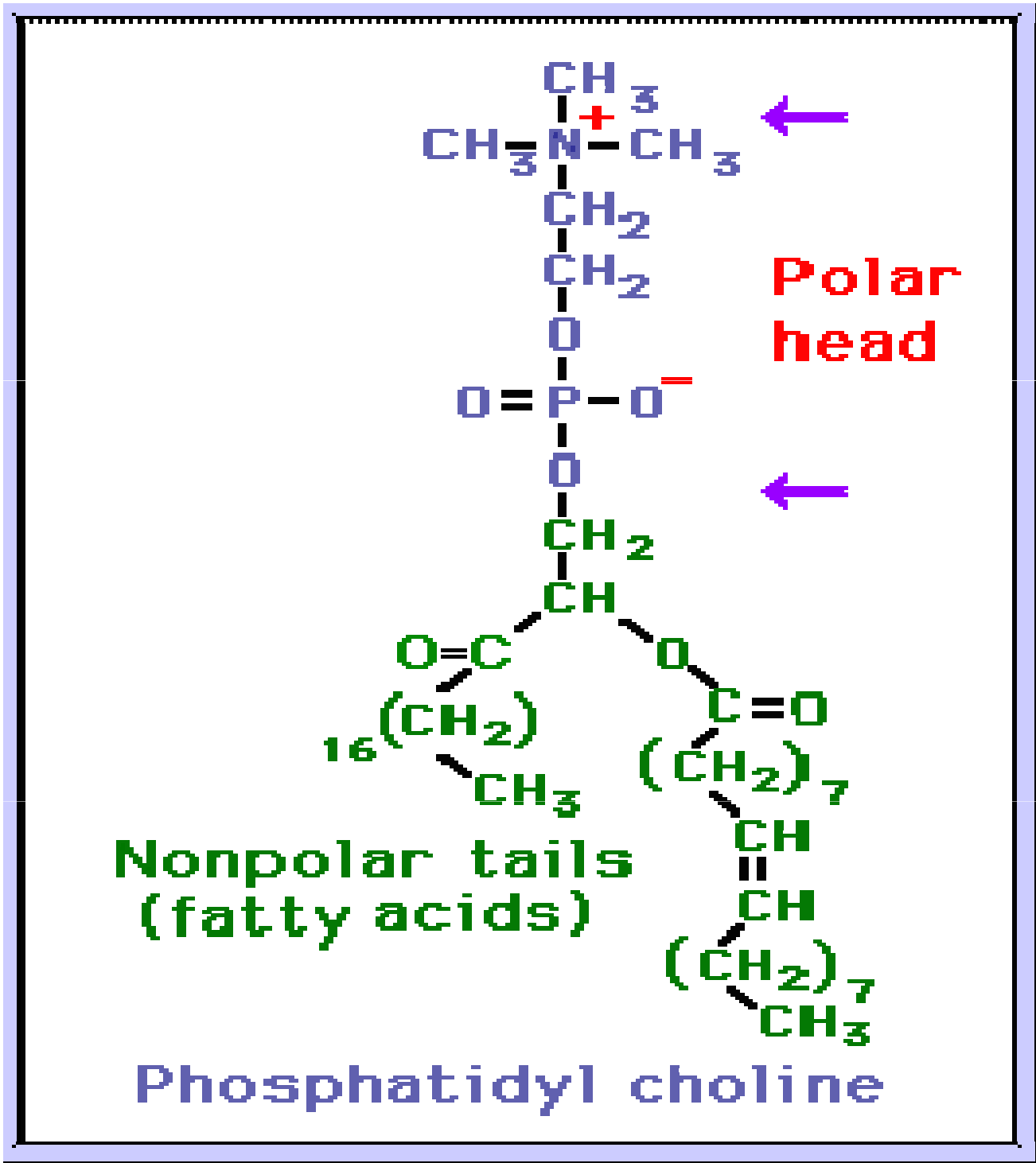
Linoleic acid: diunsaturated C18

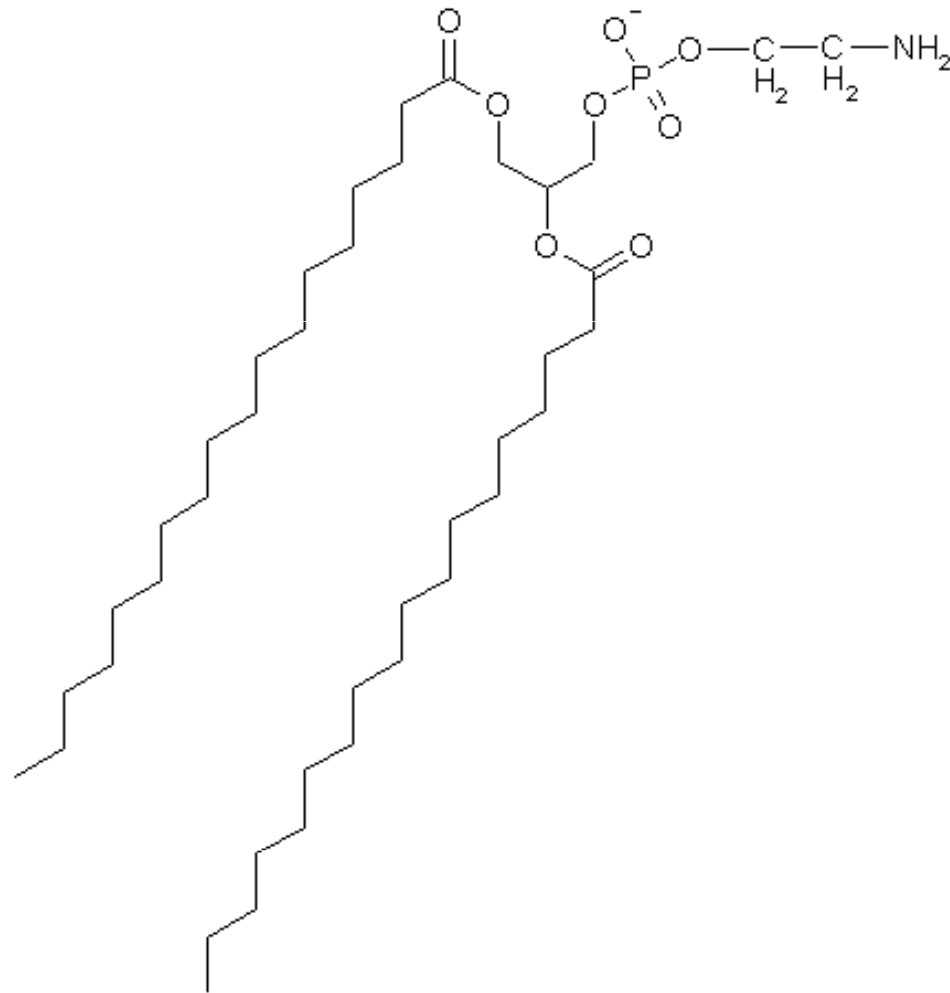


γ-Linolenic acid: triunsaturated C18



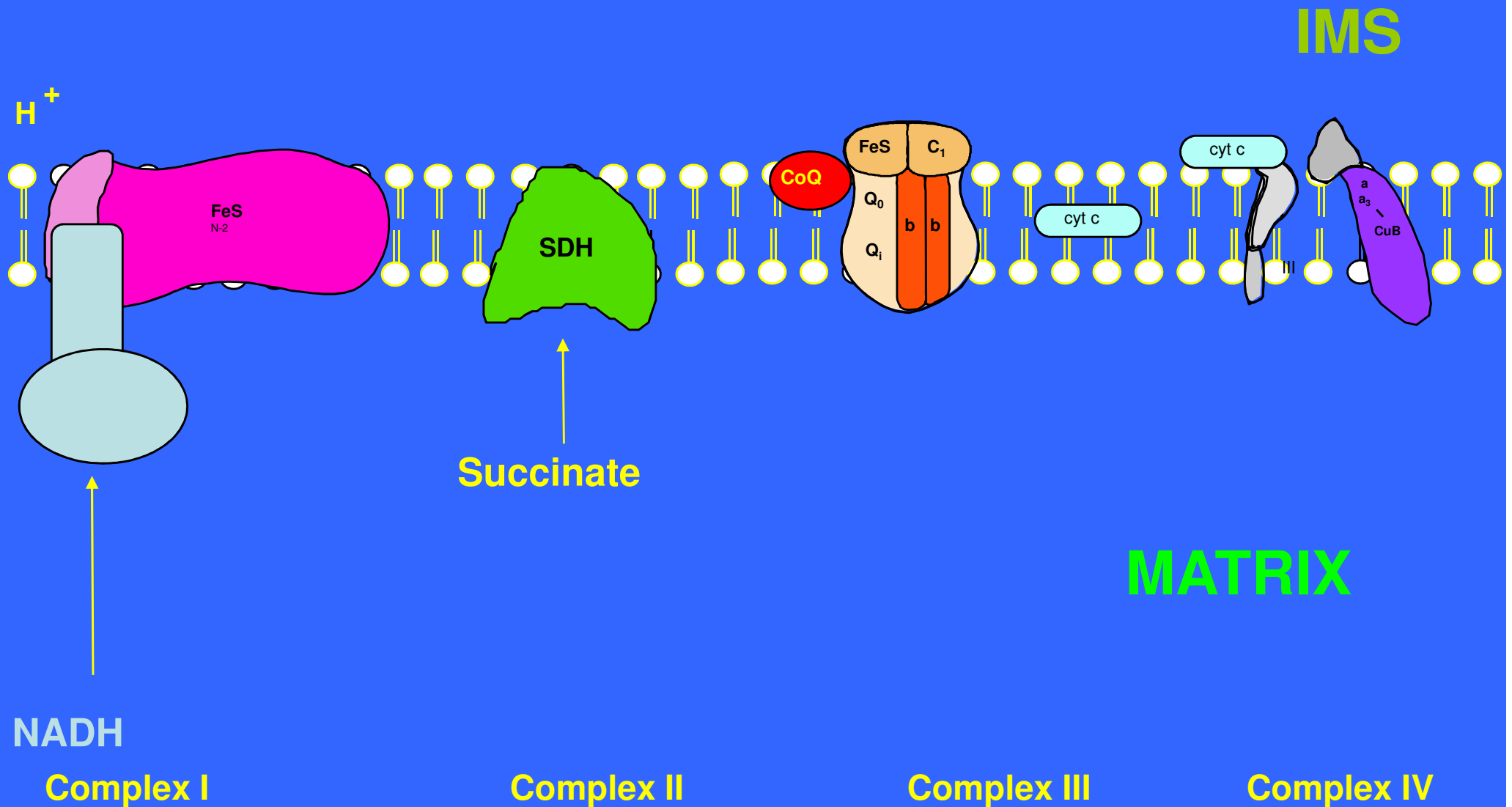
Arachidonic acid: tetraunsaturated C<sub>20</sub>



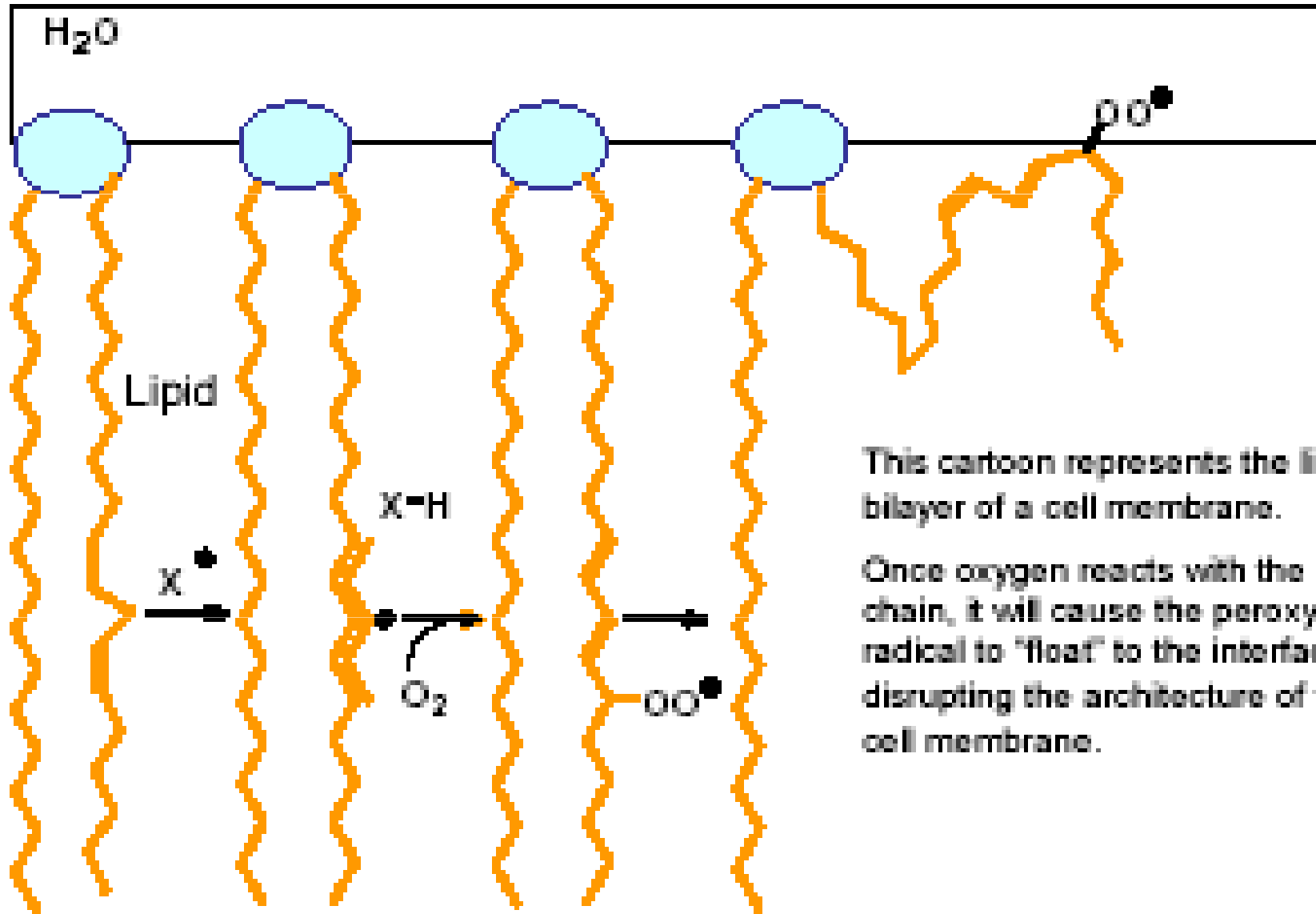


**Phosphatidyl ethanolamine**

# Respiratory Chain



# Lipid Peroxidation



This cartoon represents the lipid bilayer of a cell membrane.

Once oxygen reacts with the lipid chain, it will cause the peroxy radical to "float" to the interface, disrupting the architecture of the cell membrane.

# Lipid Composition of Membranes

	ER(%)	PM(%)
<b>Total Phospholipids</b>	84.9	61.9
Phosphatidyl choline	60.9	39.9
Phosphatidyl ethanolamine	18.6	17.8
Phosphatidyl inositol	8.9	7.5
Sphingomyelin	3.7	18.9
<b>Total Neutral lipids</b>	15.1	38.1
Cholesterol	24.6	34.5
Free fatty acids	40.6	35.5
Triacylglycerols	24.7	22.4
Cholesterol esters	10.1	8.0

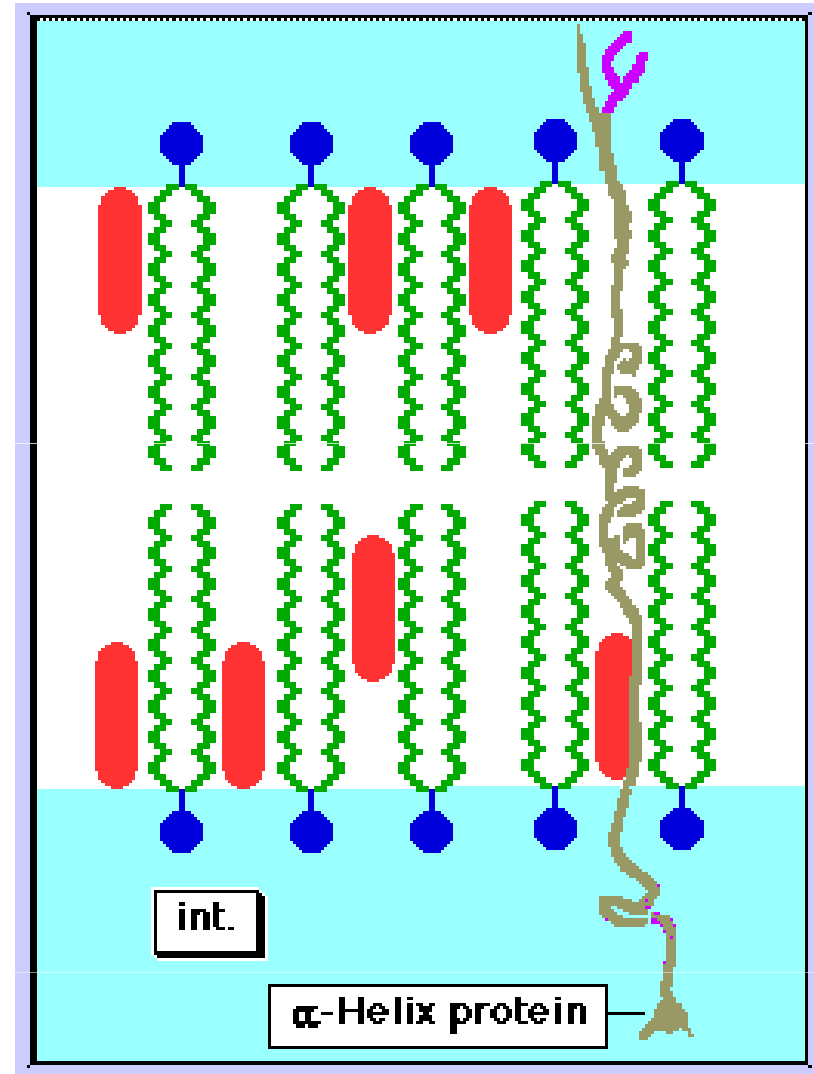
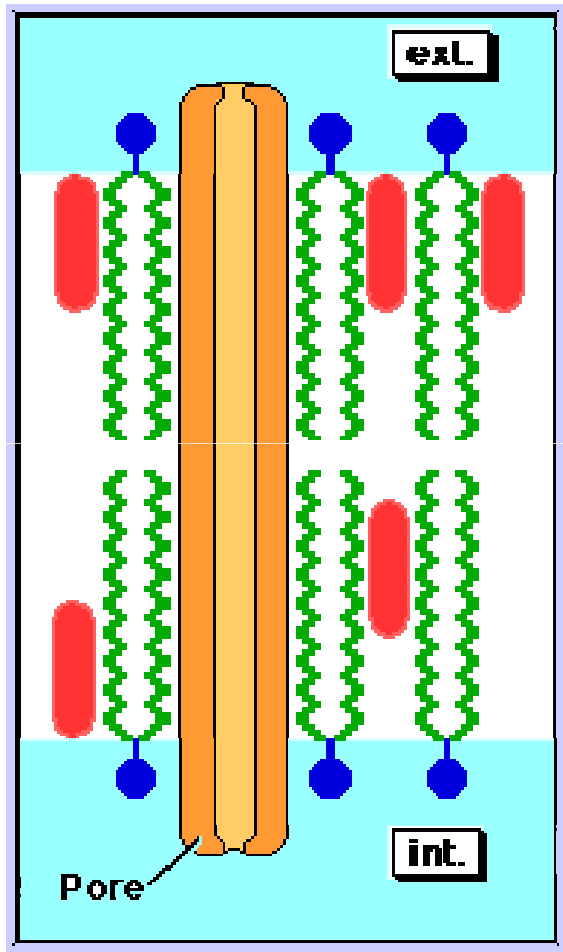
Animal	PC
Rat Liver	60%
Sheep liver	58%
Sheep kidneys	40%
Sheep heart	20%
Sheep brain	30%

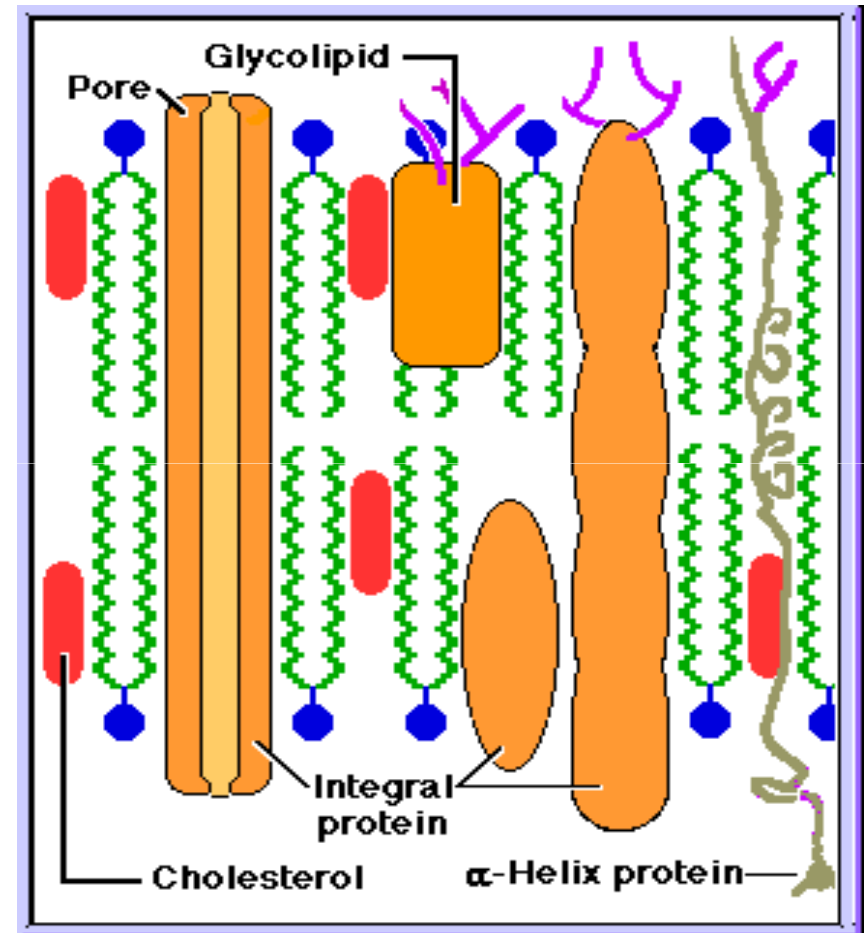
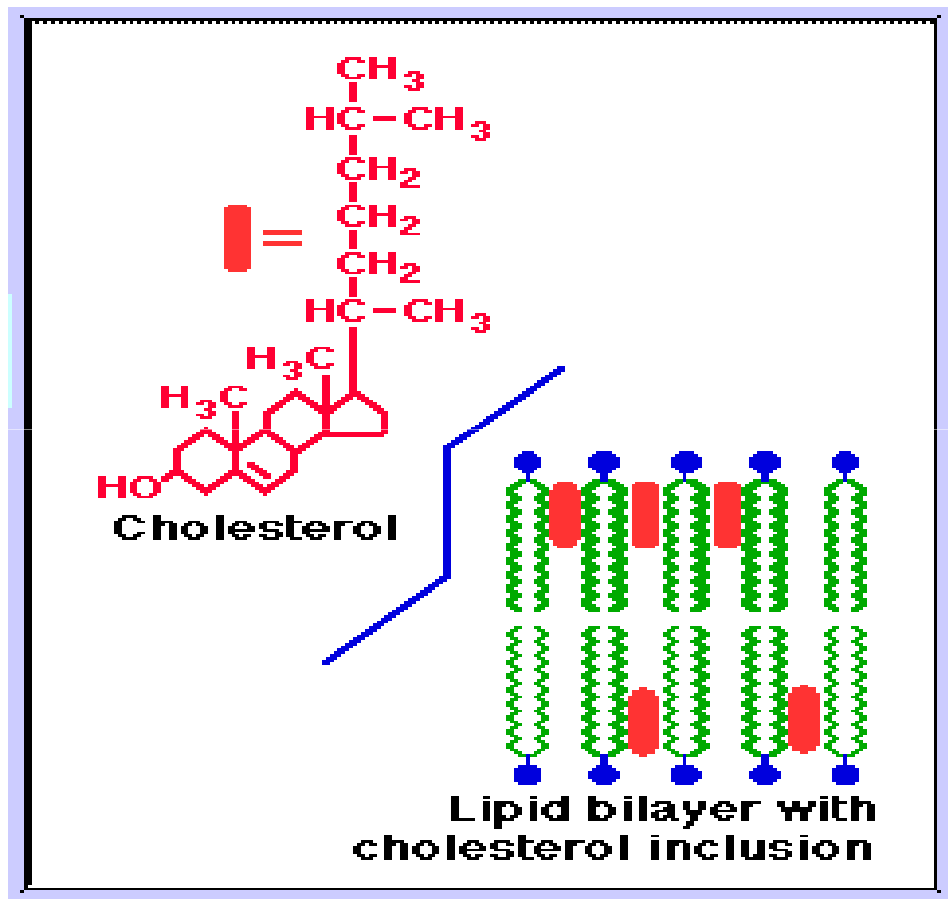
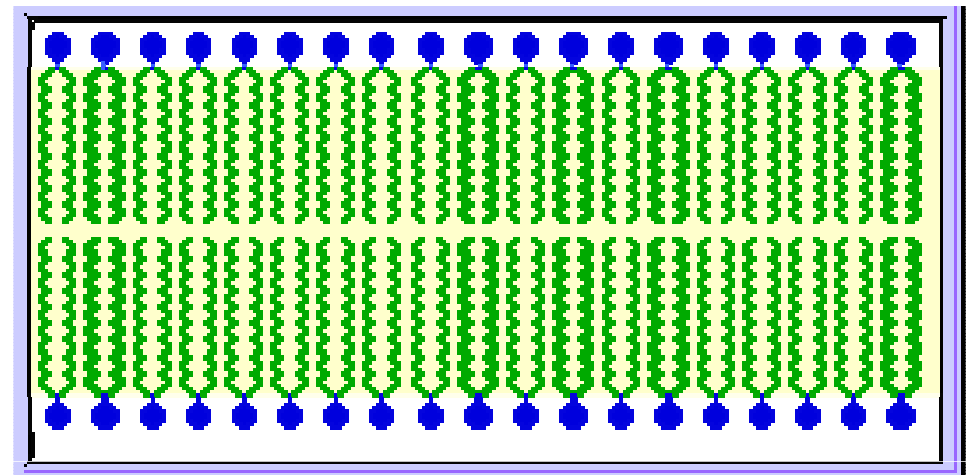
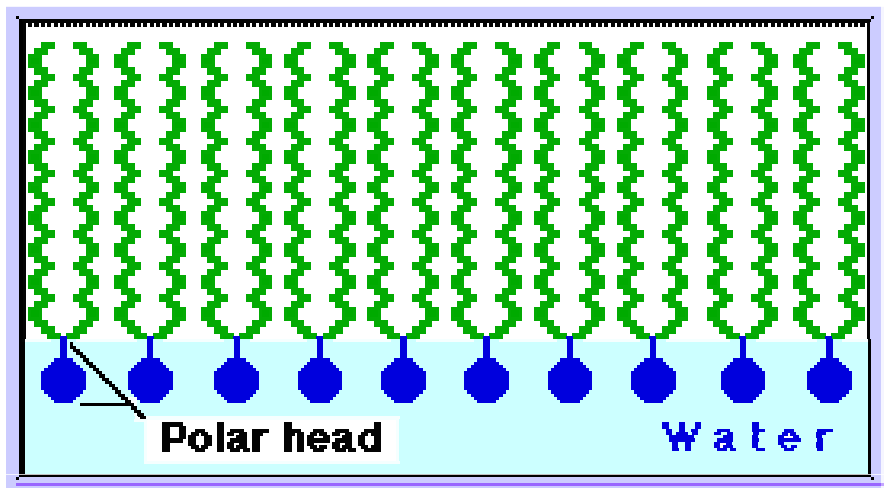
RBCs	C	PL
Rat	28%	60%
Human	25%	58%
Sheep	28%	60%
Ox	32%	55%



## Phospholipid composition of subcellular organelles prepared from rat:

	PC	PE	C	CE
Whole mitochondria	45%	40%	-	-
RER	62%	20%	5%	1%
Golgi	42%	15%	10%	2%
Plasma membrane	35%	20%	20%	1%
Inner Mito. Memb.	50%	38%	-	-
Outer Mito. Memb.	55%	32%	-	-





# Proteins

- Specific proteins mediate distinctive functions.
- Serve as pumps, gates, receptors, energy transducers and enzymes.
- Play most of the functions of the biological membranes.
- Not only structural components but also carry out membrane transport.
- Also act as recognizing sites for hormones.
- Distinguish between like and unlike cells.

## Carbohydrates

- Some oligosaccharidic units present in the membrane play role in cell-cell recognition

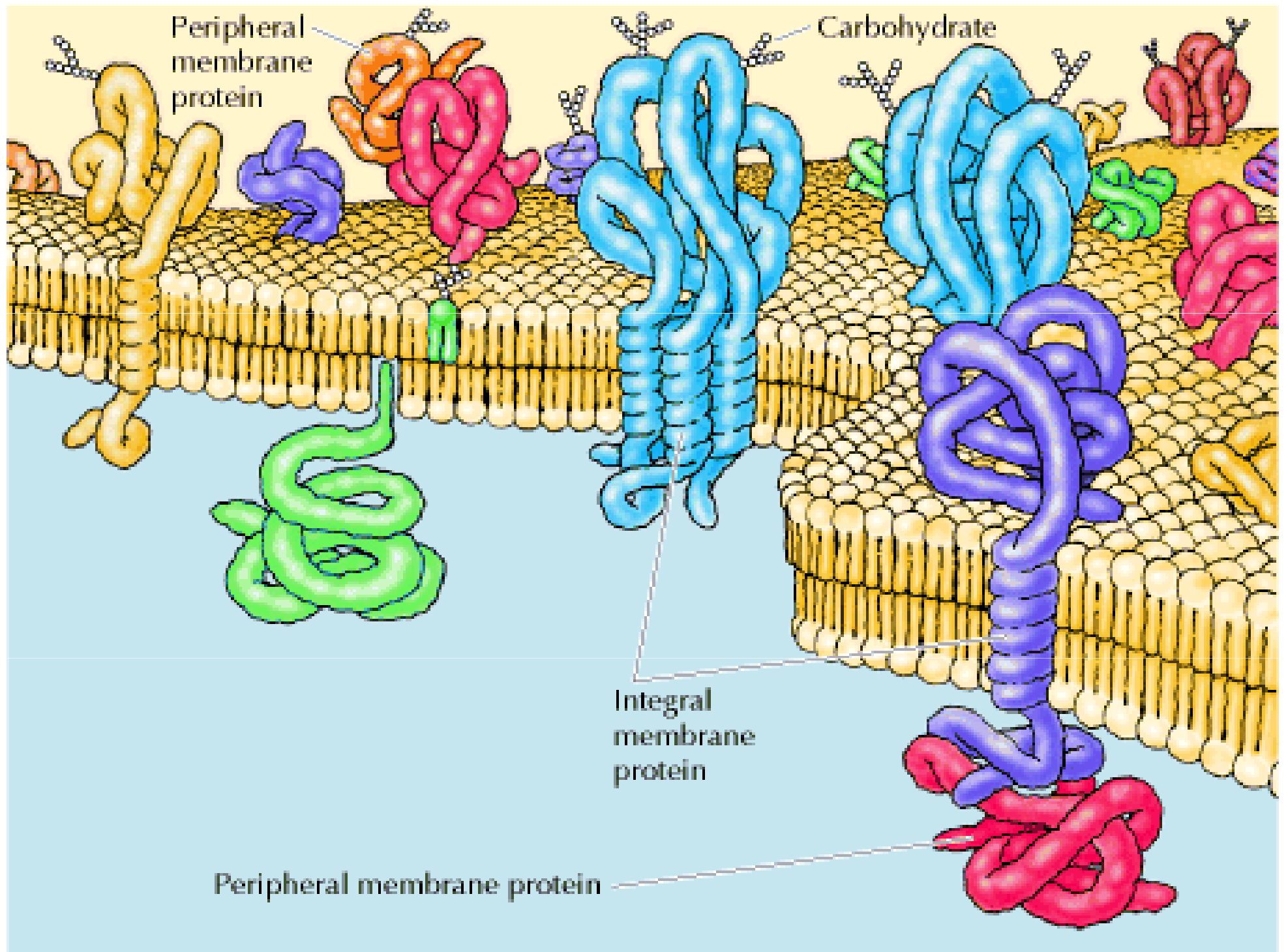
# Fluid Mosaic Model

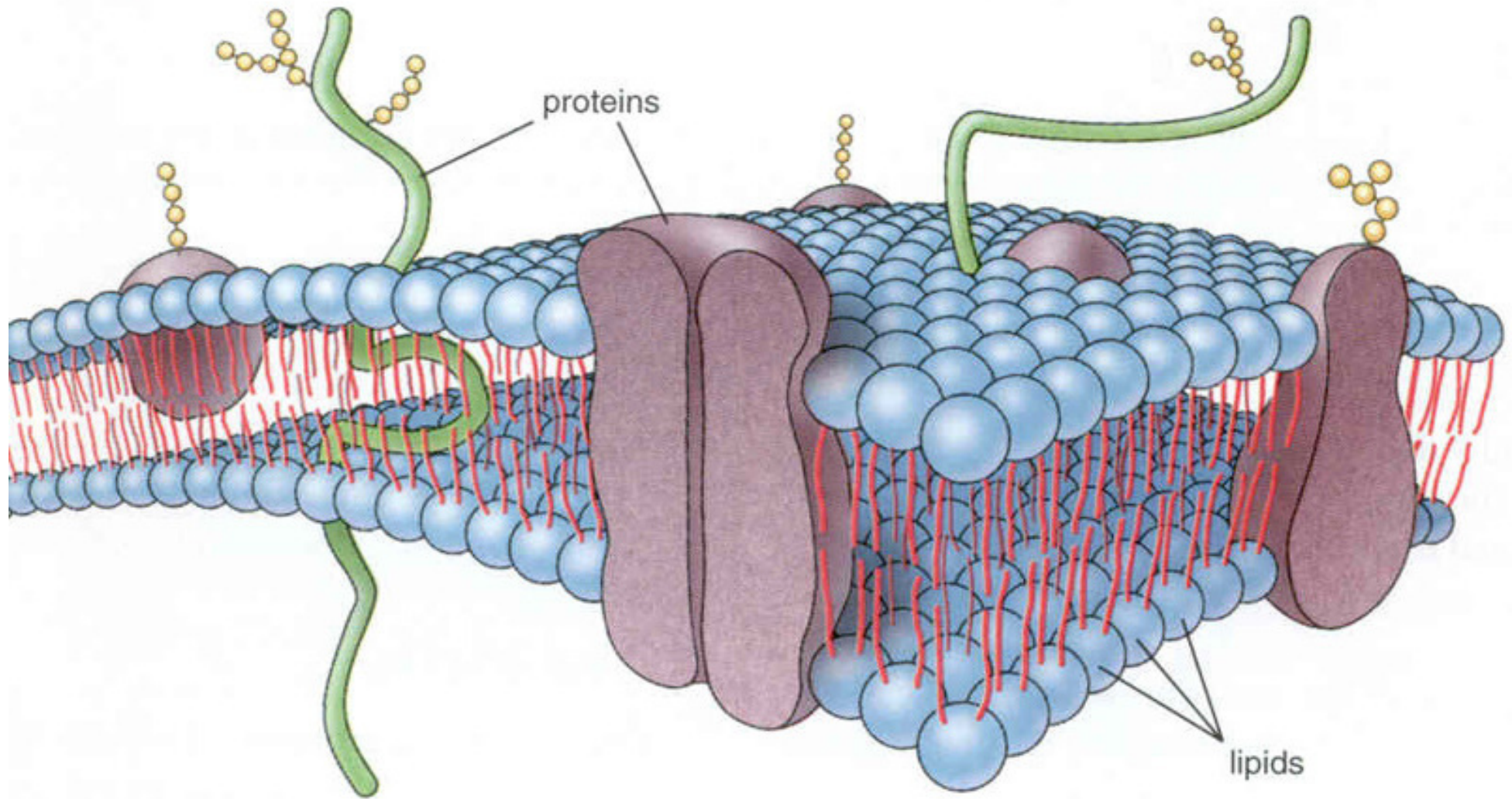
Proposed by **S. J. Singer** and **G. Nicholson** in 1972 for biological membranes

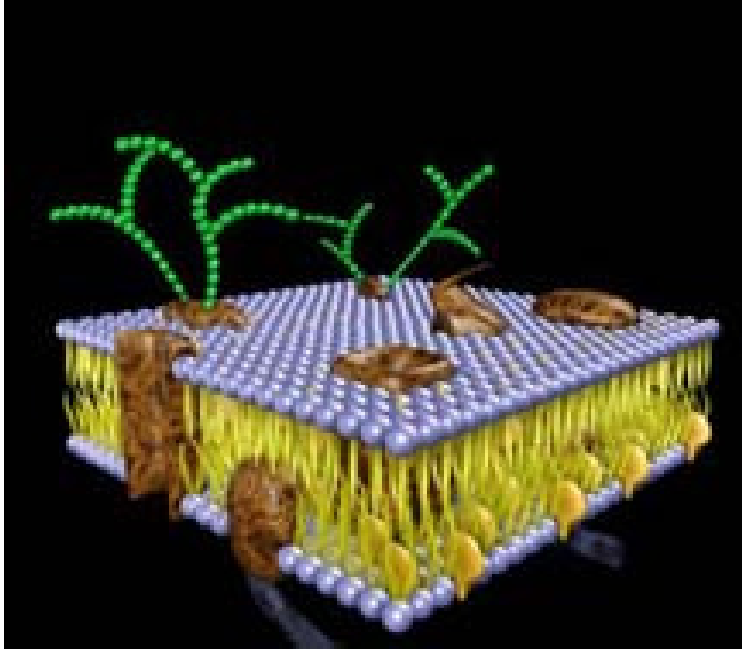
Membranes are two dimensional solutions of oreintal globular proteins and lipids.

Salient features are:

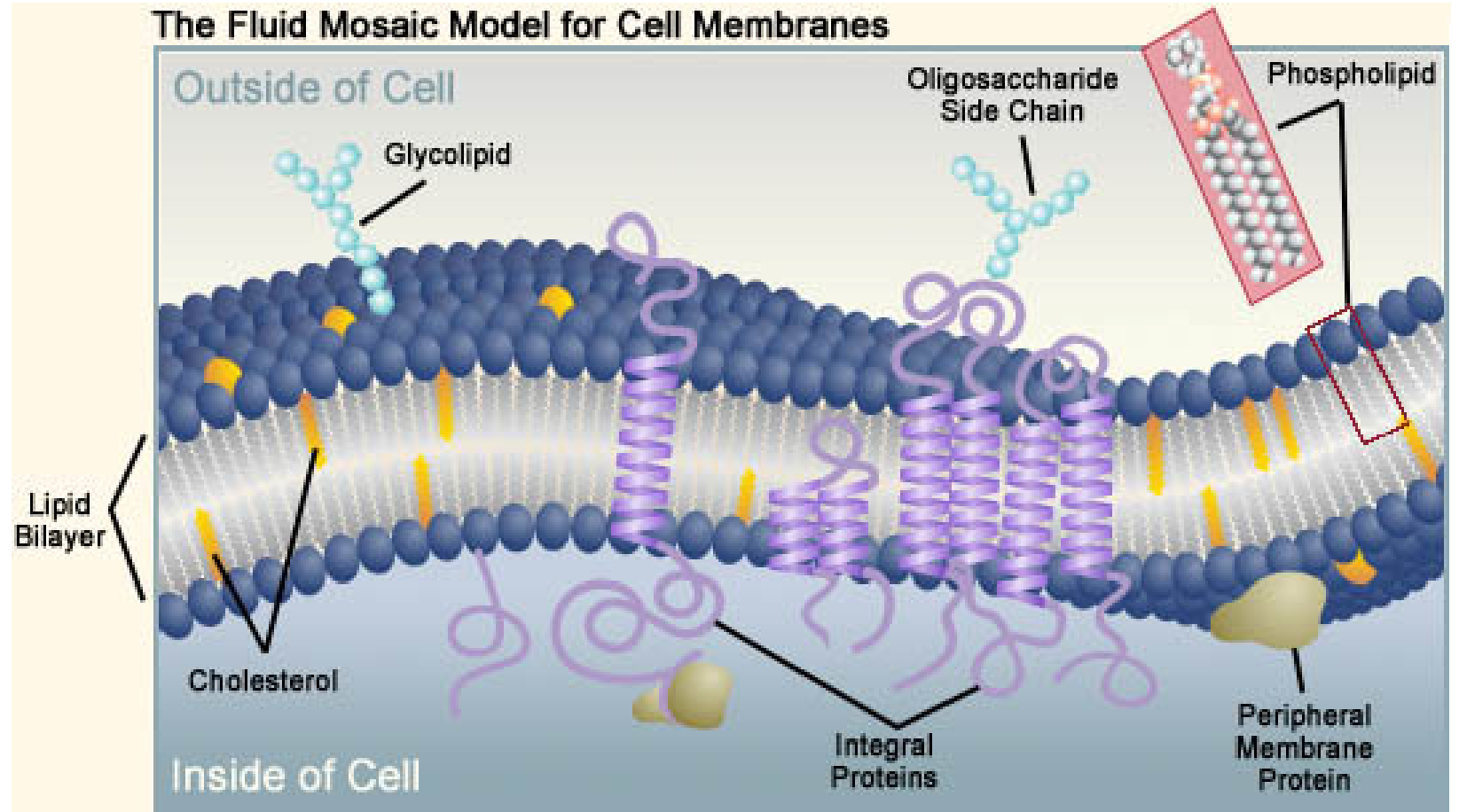
1. Most of the membrane phospholipids and glycolipid molecules are arranged in a bilayer. This bilayer has dual role; it is both a solvent and permeability barrier.
2. Small proportion of membrane lipids interacts specifically with particular membrane proteins and this may be essential for their functioning.
3. Membrane proteins are free to diffuse laterally in the lipid matrix, unless restricted by specific interactions, whereas they are not free to rotate from one side of the membrane to the other.





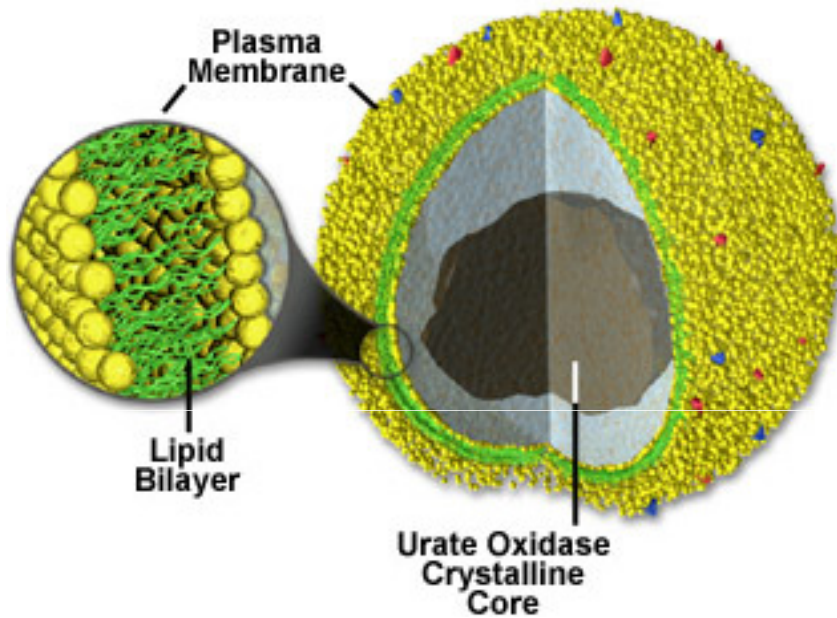


### The Fluid Mosaic Model for Cell Membranes



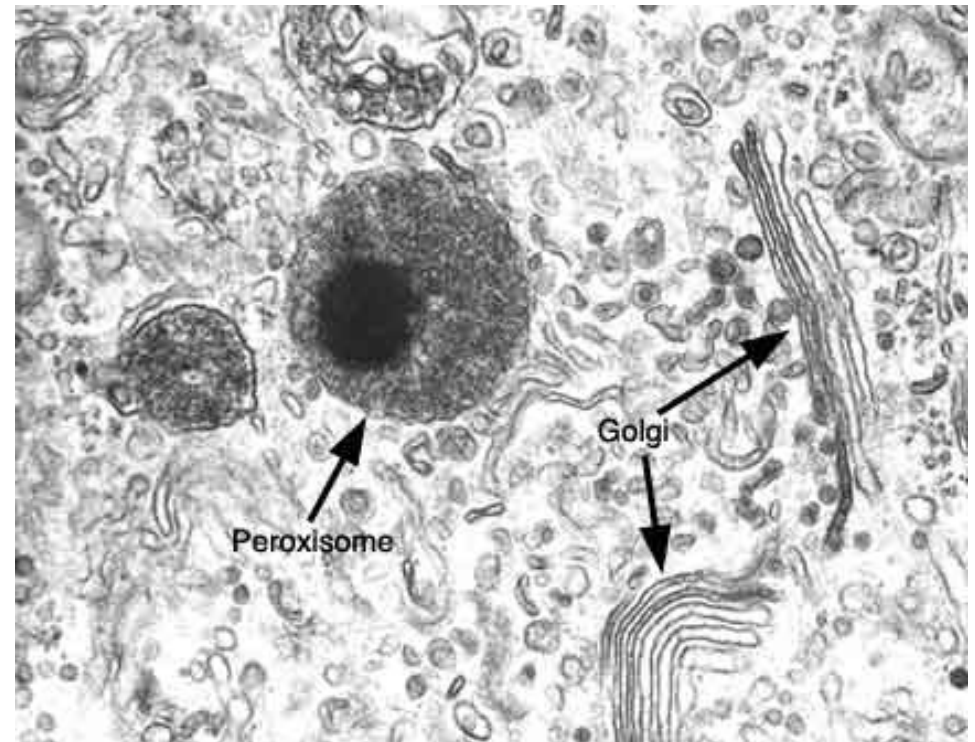


## Anatomy of the Peroxisome



## Diagrammatic view

# Peroxisome



## Electron microscopic view

# PEROXISOMES

Enzymes: Catalase, urate oxidase, D-AA/L-AA oxidase, glycolate oxidase, glyco-oxylate oxidase, isocitrate oxidase.

Oxidation of fatty acids: **FA transport independent of carnitine**; instead of FAD-linked acyl-S-CoA dehydrogenase it has **FAD-linked acyl-S-CoA oxidase** which transfer electrons from oxygen to form hydrogen peroxide.



Peroxisomes also play an important role in detoxification. Almost half of alcohol consumed is oxidized to acetaldehyde in them.

# Golgi complex

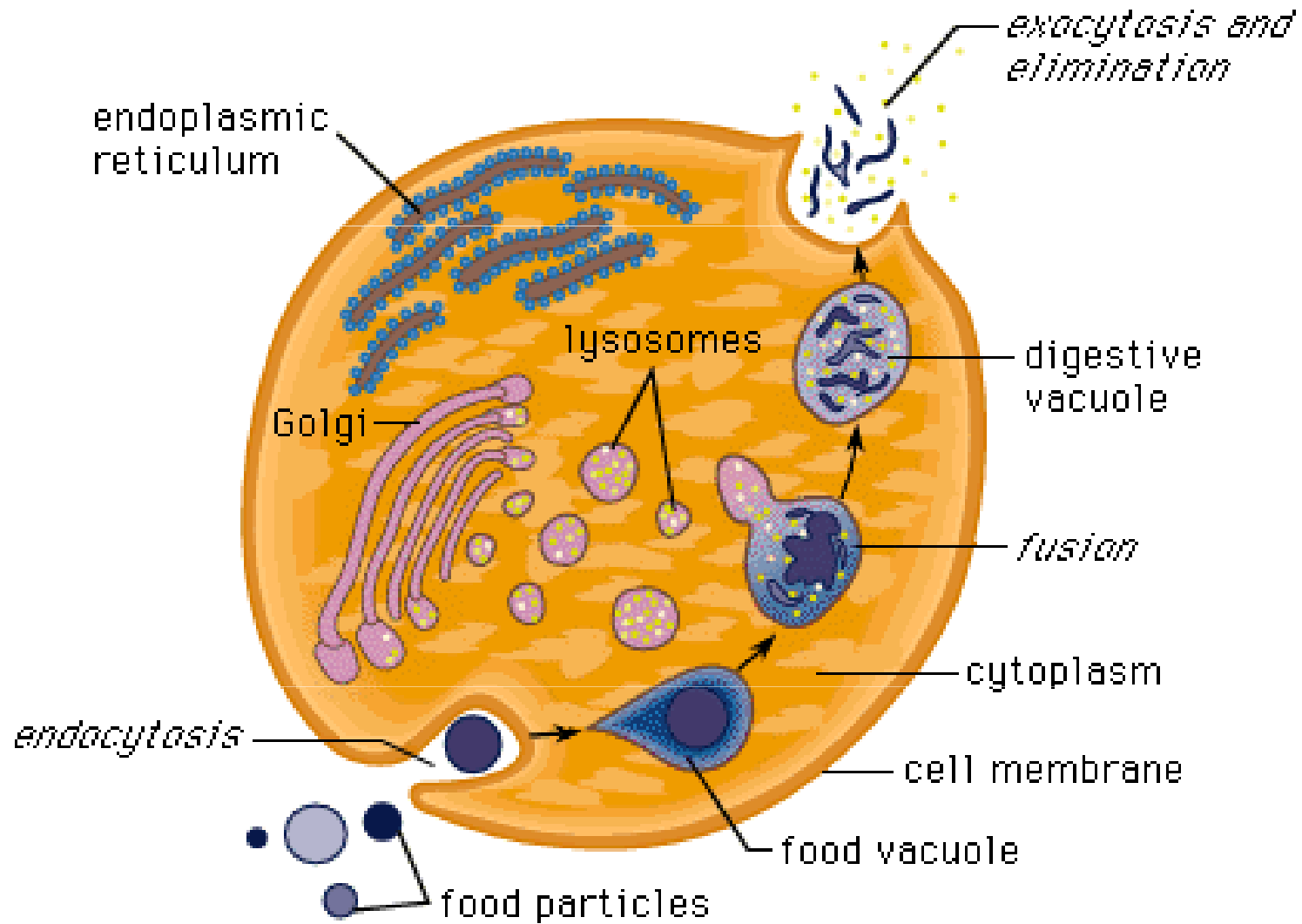


**Electron microscopic view**

# Golgi Body (Dictyosome)

- Director or editor of macromolecular traffic.
- Accurate sorting of proteins for selective export.

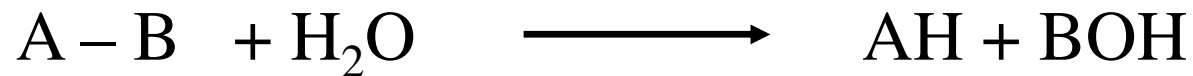
# Lysosome



# LYSOSOMES

Number varies, numerous in Macrophages, less in lymphocytes.

Contains hydrolytic enzymes, hydrolyses C-C, C-N, C-O bonds and general rxn. is :



Esterases, lipases, phospholipases, acid phosphatase, nucleotidase, DNAses, RNAses, collagenases, cathepsin, peptidases, hyaluronidase,  $\alpha$ -glucosidase,  $\beta$ -glucosidase, sulphatase, phosphotases, etc.

pH : 4-5 (acidic)

Cathepsins are sulphahydryl enzymes having -SH gps which are generally free. Enzymatic activity lost in presence of iodoacetamide, metal ions like copper and mercury.

Proteins, NA, polysaccharides cannot pass lysosomal membrane. They gain entry either through autophagy or by heterophagy. Products like AAs, monosaccharides, nucleosides can pass through the membrane.

Kidneys: Autophagy in all parts, but in proximal tubules heterophagy, Albumin and hemoglobin removed. 10-15% of total serum albumin degraded in kidneys.

Nervous system: Present in neurons and Schwann cells, have autophagic role. In diseased states lysosomes accumulate lipids and polysaccharides.

Bone: Hyaluronidase, peptidase, collagenase present play a role in reabsorbing and remodeling of osteocytes.

Spermatozoa: lysosomal hyaluronidase participate in fertilization process.

Vitamin A toxicosis: release of lysosomal enzymes.

Hurler's syndrome (mental retardation, dwarfism): increased dermatan sulphate and heparan sulphate.

Arthritis: Cathepsins, hyaluronidase.

Immunity:

Mammary glands, Uterus



# Fingers affected with rheumatoid nodules



# Comparison of normal and rheumatoid joints

## Normal joint

Synovial membrane

Cartilage

Pannus

Neutrophil  
Immune complex

## Rheumatoid joint

Infiltration of numerous cell types

Lymphocyte

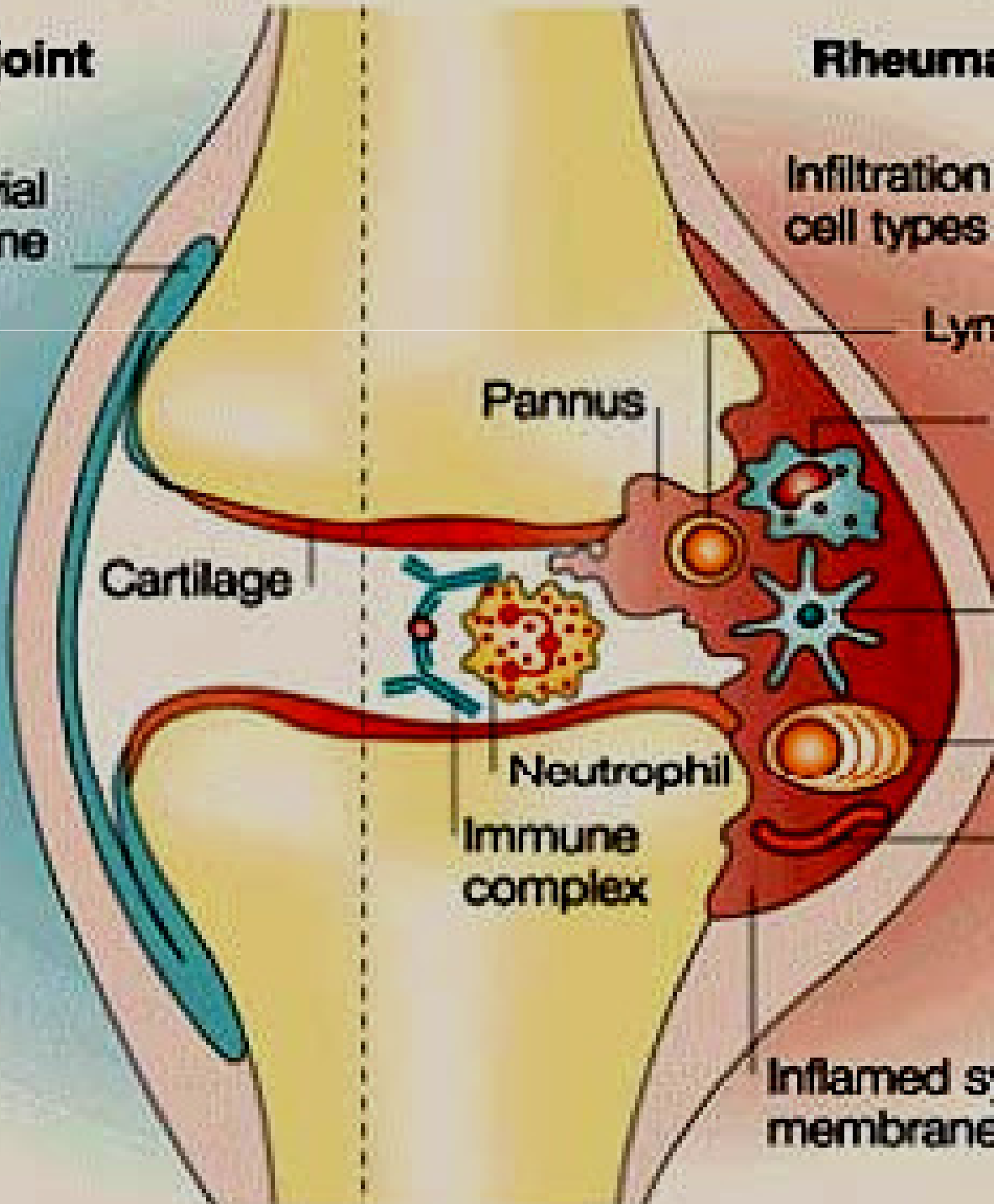
Macrophage

Interdigitating cell

Plasma cell

Angiogenesis

Inflamed synovial membrane



# ENDOPLASMIC RETICULUM

Detoxification of drugs and xenobiotics.

Steroid hormones are synthesized.

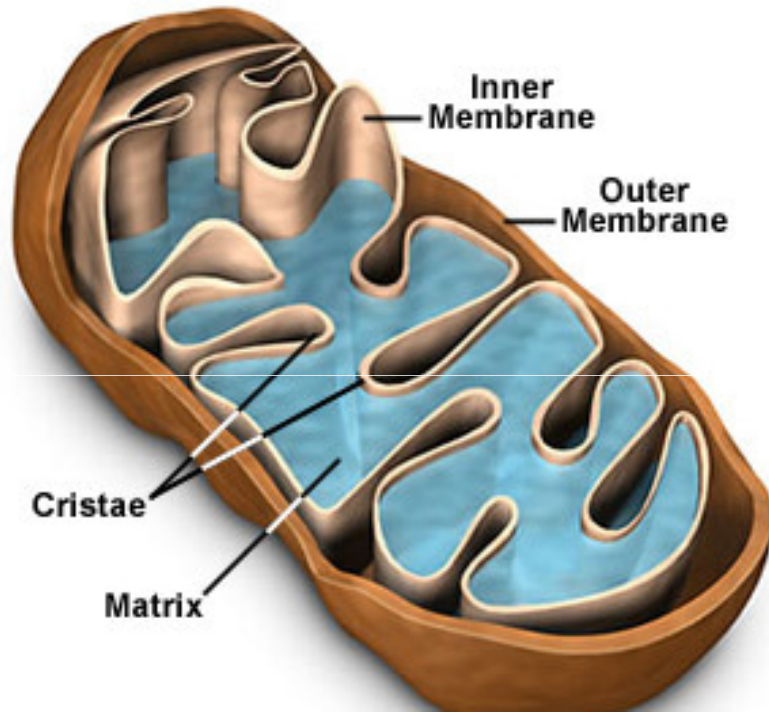
Glucose – 6 – phosphatase, plasma lipoprotein synthesis, synthesis of TGs, PL, cholesterol, bile acid, inactivation of steroid hormones, conjugation rxn., (phosphatidyl glycerol and cardiolipin not synthesized).

Muscle cells has sarcoplasmic reticulum.

Ribophorins.

Cisternae

## Mitochondria Structural Features



**Diagrammatic view**

# MITOCHONDRIA



**Electron microscopic view**

# MITOCHONDRIA

- Operation of citric acid cycle and production of reducing equivalents – NADH.
- $\beta$ -oxidation of fatty acids producing acetyl-SCoA, FADH and NADH.
- Oxidation of NADH/FADH by ETC and production of ATP.
- Accumulation of divalent ions such as calcium.

**Mitochondrion** (*mitos* thread + *khondrion* granule) or "cellular power plants". Convert organic materials into energy in the form of ATP.

There can be hundreds or thousands of mitochondria, which can occupy up to 25% of the cell's cytoplasm. Mitochondria have their own DNA and may, according to the endosymbiotic theory, be descended from free-living prokaryotes.

Mitochondrion has outer and inner membranes composed of phospholipid bilayers and proteins. The two membranes, however, have different properties. There are 5 distinct compartments within mitochondria: (1) outer membrane (2) intermembrane space (3) inner membrane (4) cristae space and (5) matrix.

# MITOCHONDRIA

***Outer Membrane:*** Fatty acid elongating enzymes, transferases, phosphatases, phospholipases.

***Inter-membrane space:*** Enzymes of nucleotide synthesis, adenylate kinase, creatinine kinase etc.

***Inner membrane:*** Transport systems (phosphate carrier, pyruvate carrier, glutamate carrier, ornithine carrier, tricarboxylate carrier), ETC and oxidative phosphorylation components and enzymes.

***Matrix:*** Enzymes of TCA cycle,  $\beta$ -oxidation of FAs, replication of DNA and protein synthesis including RNA polymerase, tRNA, ribosomes, AA activating enzymes.

## **Outer membrane:**

Encloses the entire organelle, has a protein-to-phospholipid ratio similar to the eukaryotic plasma membrane (about 1:1 by weight). Has integral protein called porins, which contain a relatively large internal channel (about 2-3 nm) that is permeable to all molecules of 5000 daltons or less. Larger molecules can only traverse the outer membrane by active transport. It also contains enzymes involved in such diverse activities as the elongation of fatty acids, oxidation of epinephrine (adrenaline), and the degradation of tryptophan.



## **Inner membrane:**

The inner membrane contain proteins with four types of functions:

Oxidation reactions of the respiratory chain.

ATP synthase, which makes ATP in the matrix.

Specific transport proteins that regulate the passage of metabolites into and out of the matrix.

Protein import machinery.

Contains more than 100 different polypeptides, with high protein-to-phospholipid ratio (more than 3:1 by weight, which is about 1 protein for 15 phospholipids). Has an unusual phospholipid, cardiolipin, a characteristic of bacterial plasma membranes. Does not contain porins, and impermeable;

Cristae, expand the surface area, enhancing ability to generate ATP. In typical liver mitochondria, for example, the surface area, including cristae, is about five times that of the outer membrane.

Mitochondria of cells which have greater demand for ATP.

## **Mitochondrial matrix:**

Contains concentrated mixture of hundreds of enzymes, in addition to the special mitochondrial ribosomes, tRNA, and several copies of the mitochondrial DNA genome. Of the enzymes, the major functions include oxidation of pyruvate and fatty acids, and the citric acid cycle.

Mitochondria has its own genetic material, and the machinery to manufacture their own RNAs and proteins. This DNA encodes a small number of mitochondrial peptides (13 in humans) that are integrated into the inner mitochondrial membrane, along with polypeptides encoded by genes that reside in the host cell's nucleus.

## **Mitochondrial functions:**

Although it is well known that the mitochondria convert organic materials into cellular energy in the form of ATP. mitochondria play an important role in many metabolic tasks,

- Apoptosis-programmed cell death
- Glutamate-mediated excitotoxic neuronal injury
- Cellular proliferation
- Regulation of the cellular redox state
- Heme synthesis
- Steroid synthesis

Mitochondria in liver cells contain enzymes that allow them to detoxify ammonia, a waste product of protein metabolism. A mutation in the genes regulating any of these functions can result in mitochondrial diseases.

## **Energy conversion**

A dominant role for the mitochondria is the production of ATP carried out by oxidising products of glycolysis: pyruvate and NADH, produced in cytosol. This process of cellular respiration, also known as aerobic respiration, is dependant on the presence of oxygen.

# Origin

Mitochondria contain ribosomes and DNA.

Formed by the division of other mitochondria, it is generally accepted that they were originally derived from endosymbiotic prokaryotes.

Mitochondrial DNA, is circular and employs a variant genetic code, show their ancestor, the so-called proto-mitochondrion, was a member of the Proteobacteria.

This relationship developed at least 2 billion years ago and mitochondria still show some signs of their ancient origin.

Mitochondrial ribosomes are the 70S (bacterial) type, in contrast to the 80S ribosomes found elsewhere in the cell. As in prokaryotes, there is a very high proportion of coding DNA, and an absence of repeats.

Unlike their nuclear cousins, mitochondrial genes are small, generally lacking introns, and many chromosomes are circular, conforming to the bacterial pattern.

## **Mitochondrial Genes:**

Mitochondrial genome is circular double-stranded. Each mitochondria has five copies of this genome. Human Mt chromosome contains 37 genes (16568 bp), including 13 that encode subunits of proteins of the respiratory chain, the remaining genes code for rRNA and tRNA molecules essential to the protein synthesizing machinery of Mt. About 900 different Mt. proteins are encoded by nuclear genes, synthesized on cytoplasmic ribosomes, then imported and assembled within the mt.

### **Mutations in Mt genes cause a number of diseases:**

Mitochondrial encephalopathies, affect brain and skeletal muscles  
Lever's hereditary optic neuropathy (LHON) : affects CNS including optic nerves, causing bilateral loss of vision

# Respiratory proteins encoded by Mt genes in Humans:

I NADH dehydrogenase	43	7
II Succinate dehydrogenase	4	0
III Ubiquinone cyt C oxidoreductase	11	1
IV Cytochrome oxidase	13	3
V ATP synthase	8	2

## Protein:Lipid Ratio in Membrane of

Myelin	0.23
Mouse liver	0.85
Human RBCs	1.1
Amoeba	1.3
Retinal rods	1.0
Mitochon. OM	1.1
SER	2.0
Mitochon. IM	3.2