CELL

THE BASIC UNIT OF LIFE

CYTOPLASM AND NUCLEUS

STRUCTURE & ORGANISATION

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INTRODUCTION

The Cell is the fundamental unit of life.

It is the basic structural and functional unit of all living matter.

All organisms are composed of cell.

The cell is derived from Latin word “cella” which means a small room.

History

- Robert Hooke (1665)

  looked at thin slice of cork through a compound microscope found small room like structures – "Cell"
  Published in the book named "MICROGRAPHIA" .

Anton van Leeuwenhoek
1632-1723

In 1673 Anton van Leeuwenhook perfects the simple microscope and observes cells and microorganisms.

He discovered bacteria in 1674 and four years later, he discovers protozoa.

- Jakob Matthias Schleiden (1838) & Theodor Schwann (1839)

  Discovered plant and animal parts are made up of cells.

  In 1839, proposed the “CELL THEORY”

- Rudolph Virchow (1855)

  States that all living cells come only from living cells.

CELL THEORY

1)Organisms are composed of cell and its products.

2) Each cell is composed of small mass of protoplasm containing cytoplasm in its inside and a plasma membrane with or without cell wall on outside.

3) New cell arise from the pre-existing cell.

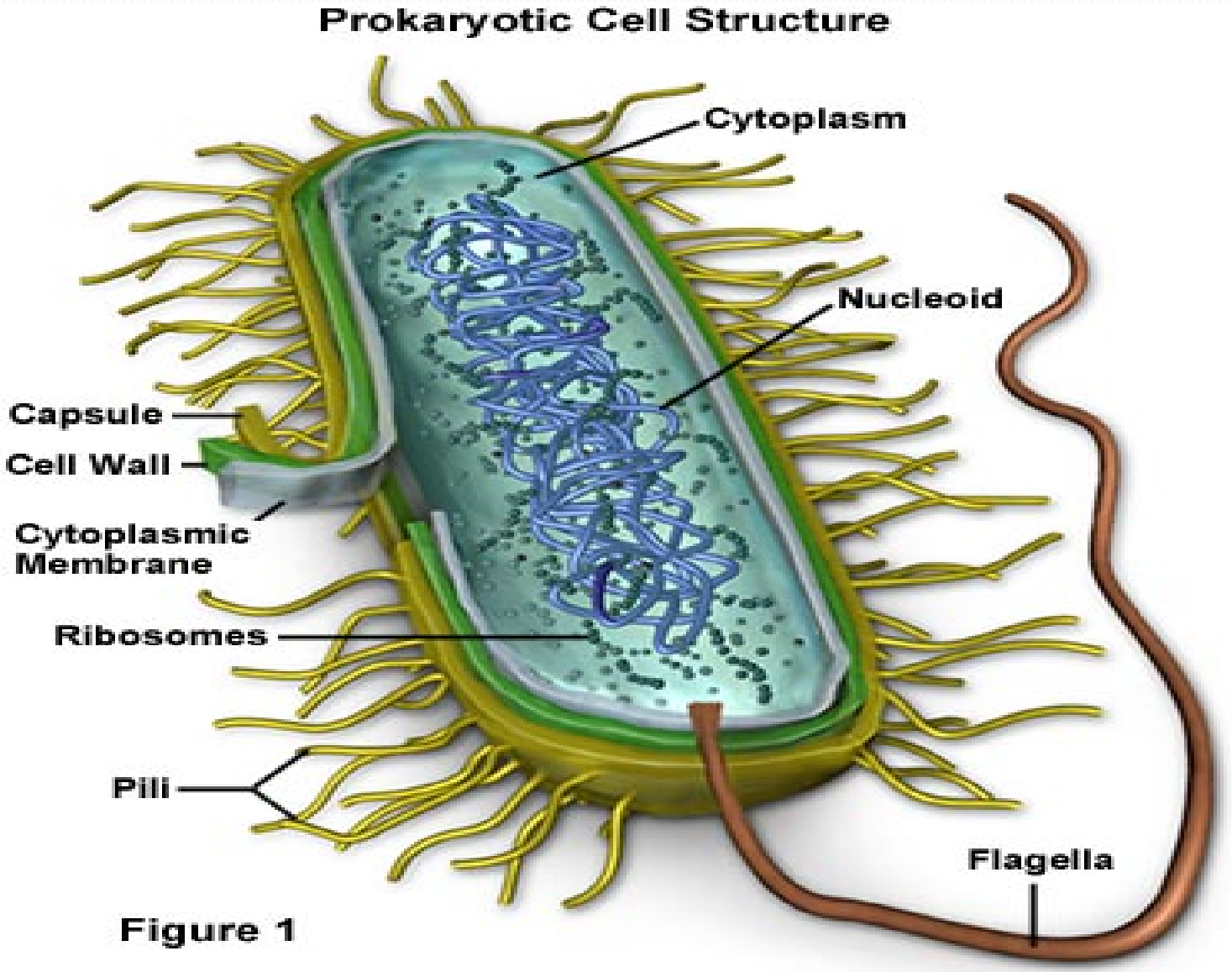
4) All cell are similar in physiology and chemistry.

5) The activities of all organisms are a result of interaction between the cells.

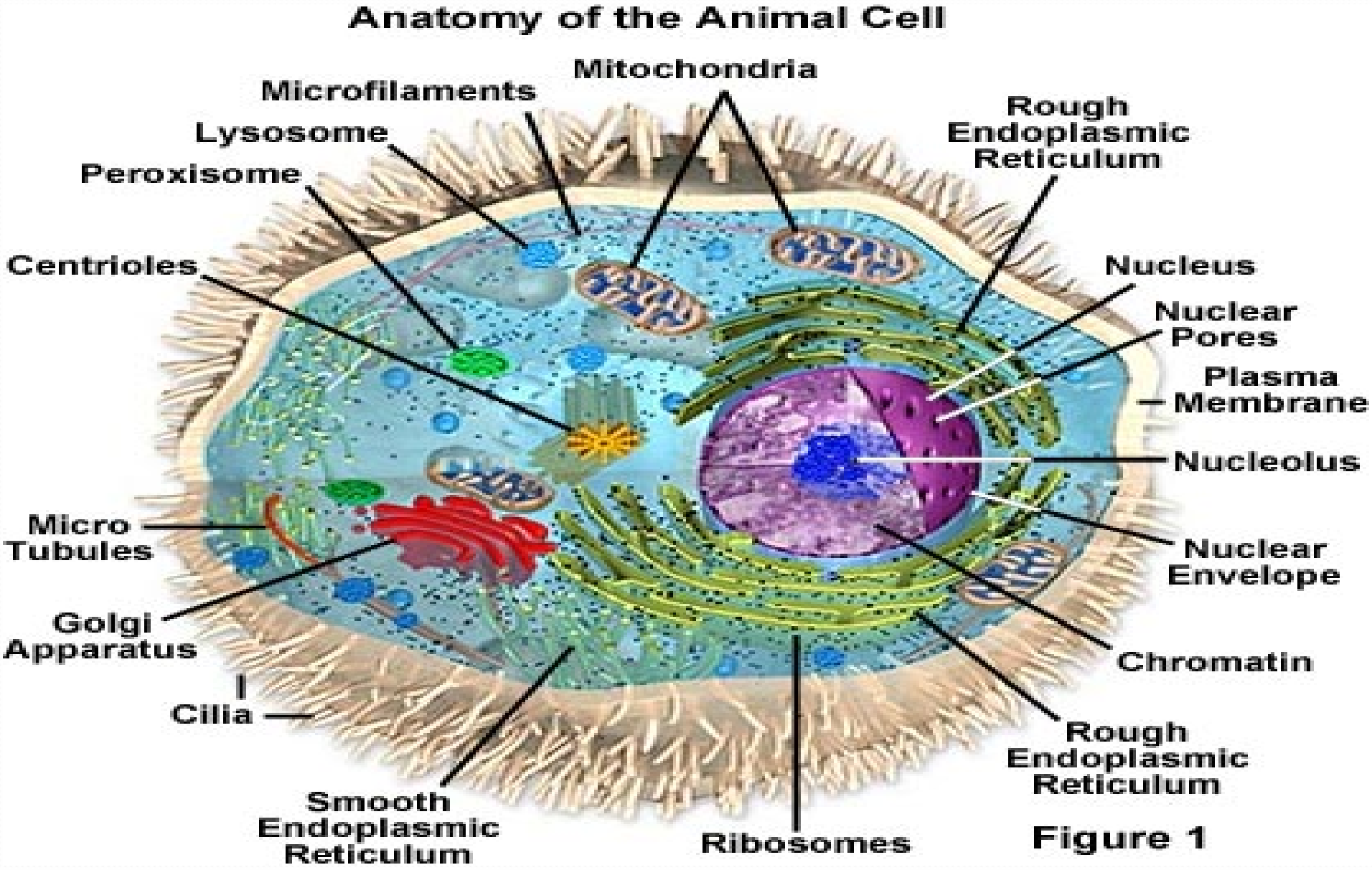
TYPES OF CELL

The living cell are divided into two types:

PROKARYOTIC



EUKARYOTIC


Anatomy of the Animal Cell
Mitochondria
Microfilaments
Lysosome
Peroxisome
Rough Endoplasmic Reticulum
Centrioles
Nucleus
Nuclear Pores
Plasma Membrane
Nucleolus
Micro Tubules
Nuclear Envelope
Golgi Apparatus
Chromatin
Cilia
Rough Endoplasmic Reticulum
Smooth Endoplasmic Reticulum
Ribosomes
Figure 1

Comparison of Prokaryotes and Eukaryotes

	Prokaryotes	Eukaryotes
Organisms	Bacteria	Protists, fungi, plants and animals
Cell size	Generally 1 to 10 μm measured lengthwise	Generally 10 to 100 μm, lengthwise
Metabolism	Anaerobic or aerobic	Anaerobic or aerobic
Organelles	None	Nucleus, mitochondria, chloroplasts, endoplasmic reticulum, Golgi apparatus, lysosomes, etc.
Cell support	External cell wall	Internal cytoskeleton
DNA	Circular DNA in single cellular compartment	Very long linear DNA contained within a membrane-bounded nucleus
RNA and protein	RNA and protein synthesized in the single compartment	RNA synthesized and processed in nucleus; proteins synthesized in cytoplasm
Transmembrane movement	No endocytosis or exocytosis	Endocytosis and exocytosis
Cell division	Chromosomes pulled apart by attachments to inner membrane	Chromosomes pulled apart by attachments to cytoskeletal components
Cellular organization	Mainly unicellular	Unicellular or multicellular, with many differentiated cell types

CLASSIFICATION OF CELL

A) BASED ON TISSUE THEY FORM

1. Bone cell
2. Cartilage cell
3. Muscle cell
4. Blood cell
5. Adipose cell
6. Epithelial cell

B) BASED ON FUNCTION

1. Conductive cell
2. Connective cell
3. Glandular cell
4. Storage cell
5. Stem cell

ORGANISATION OF CELL

Cell is composed of two major parts:-

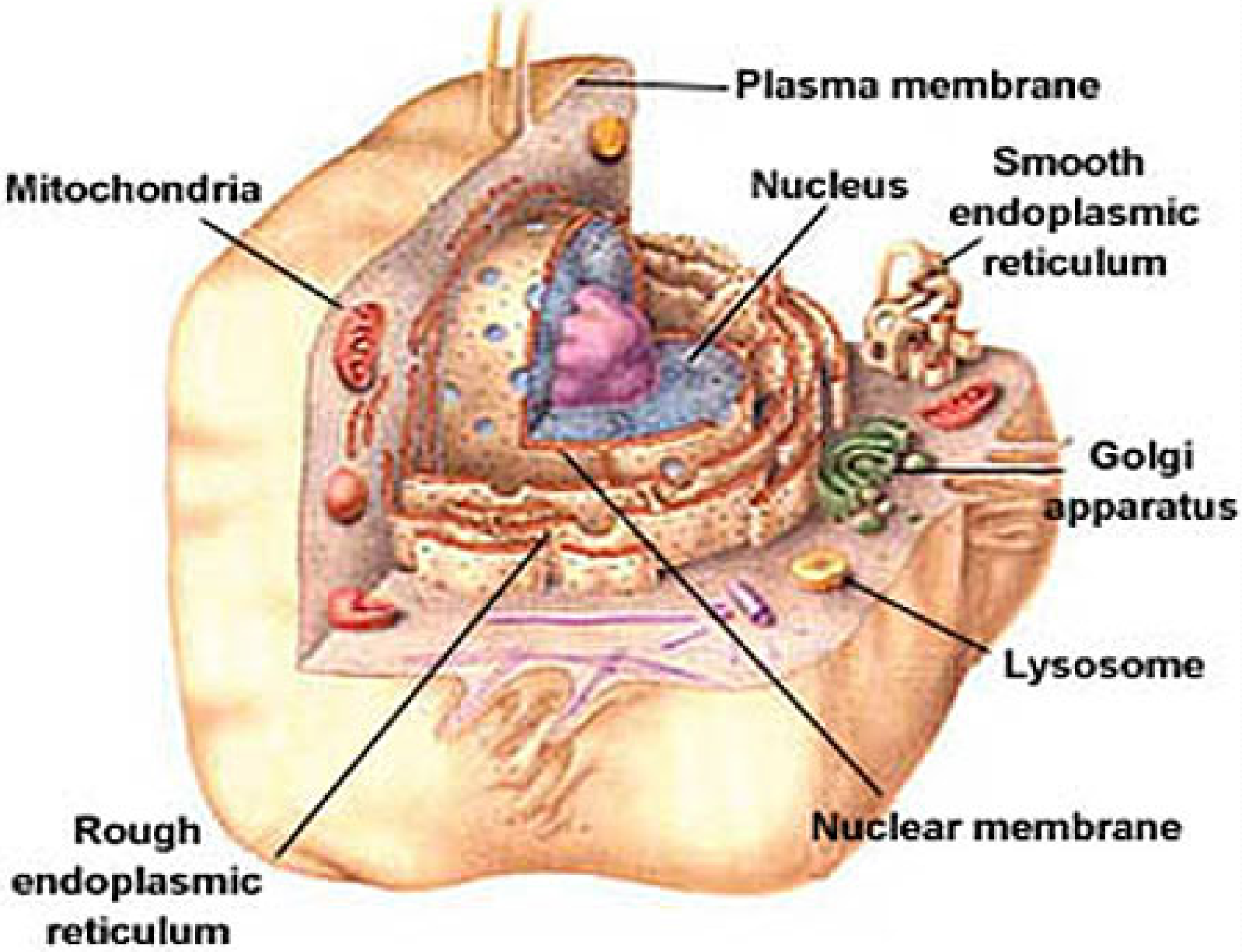
NUCLEUS

CYTOPLASM

CELL MEMBRANE- It separates the cell from surrounding fluids.

NUCLEAR MEMBRANE- It separates the nucleus from cytoplasm.

PROTOPLASM- Different substances which make up the cell.


Plasma membrane
Mitochondria
Nucleus
Smooth endoplasmic reticulum
Golgi apparatus
Lysosome
Rough endoplasmic reticulum
Nuclear membrane

Protoplasm

It is the complex, semi fluid, translucent substance that constitutes the living matter of plant and animal cells and manifests the essential life functions of a cell.

It includes the nucleus and cytoplasm and is composed mainly of five basic substances:

- Water
- Electrolytes
- Proteins
- Lipids
- Carbohydrates

Water

- 70 to80% - Principle fluid medium of the cell
- Many cellular chemicals are dissolved in water and some are suspended in it as solid particulates
- Chemical reactions take place among dissolved chemicals and water.

Proteins

- 10 to20% - Second largest component

Structural protein	Globular protein
• Present mainly in the form of long filaments. •Mitotic spindles of dividing cells •Provide contractile mechanisms of all muscles. •Holds the parts of cytoplasm and nucleoplasm together in their respective compartments	•Basically enzymes of the cell. • Mostly soluble in oral fluids. •Catalyse specific intracellular chemical reactions.

Electrolytes

- *Potassium, magnesium, phosphate, sulphate, bicarbonate* - important ions present in cell.

- Small quantities of *sodium, chloride* and *calcium* are also present.

- Provide inorganic chemicals for cellular reactions
- Necessary for operating some of the cellular control mechanisms.

Lipids

- Phospholipids and cholesterol
- Constitute about 2% of the cell mass
- Insoluble in water, form cell membranes as well as intracellular membranous barriers that separate different cell compartments.

Carbohydrates

- About 1% of their total mass but increases to as much as 3%in muscle cells and, occasionally, 6% in liver cells
- Structural function
- Play a major role in nutrition of the cell

CELL MEMBRANE/ PLASMA MEMBRANE/ PLASMALEMMA

- Covers the cell

It is bilayered structure of phospholipids and protein molecules.

Selectively permeable.

Thickness- 7.5 to 10 mm

COMPOSITION

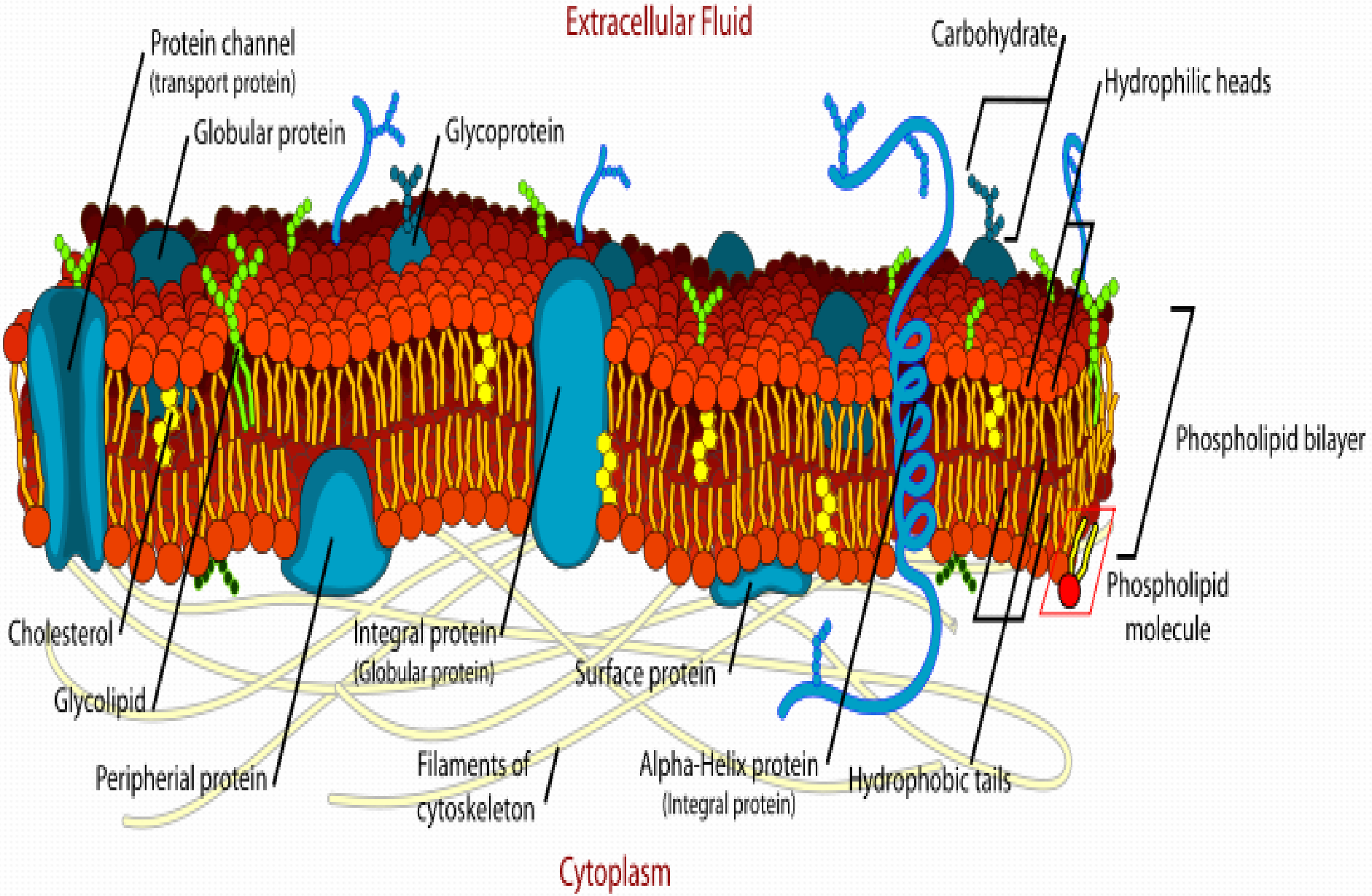
Phospholipids- 25%

Cholesterol-13%

Protein-55 %

Lipids-4%

Carbohydrates-3%


Extracellular Fluid
Protein channel
(transport protein)
Globular protein
Glycoprotein
Carbohydrate
Hydrophilic heads
Phospholipid bilayer
Phospholipid
molecule
Cholesterol
Glycolipid
Peripherial protein
Integral protein
(Globular protein)
Filaments of
cytoskeleton
Surface protein
Alpha-Helix protein
(Integral protein)
Hydrophobic tails
Cytoplasm

Concepts of cell membrane

- Classic concept : Physiological experiments showed cells immersed in solutions would swell or shrink; indicating that they must be surrounded by a membrane with special permeability properties.

- Trilaminar concept

  Robertson noted trilaminar or three layered structure of cell membrane.

  External and internal layers are more electron dense than the middle layer which appears electroluscent.

Plasma Membrane Structural Components

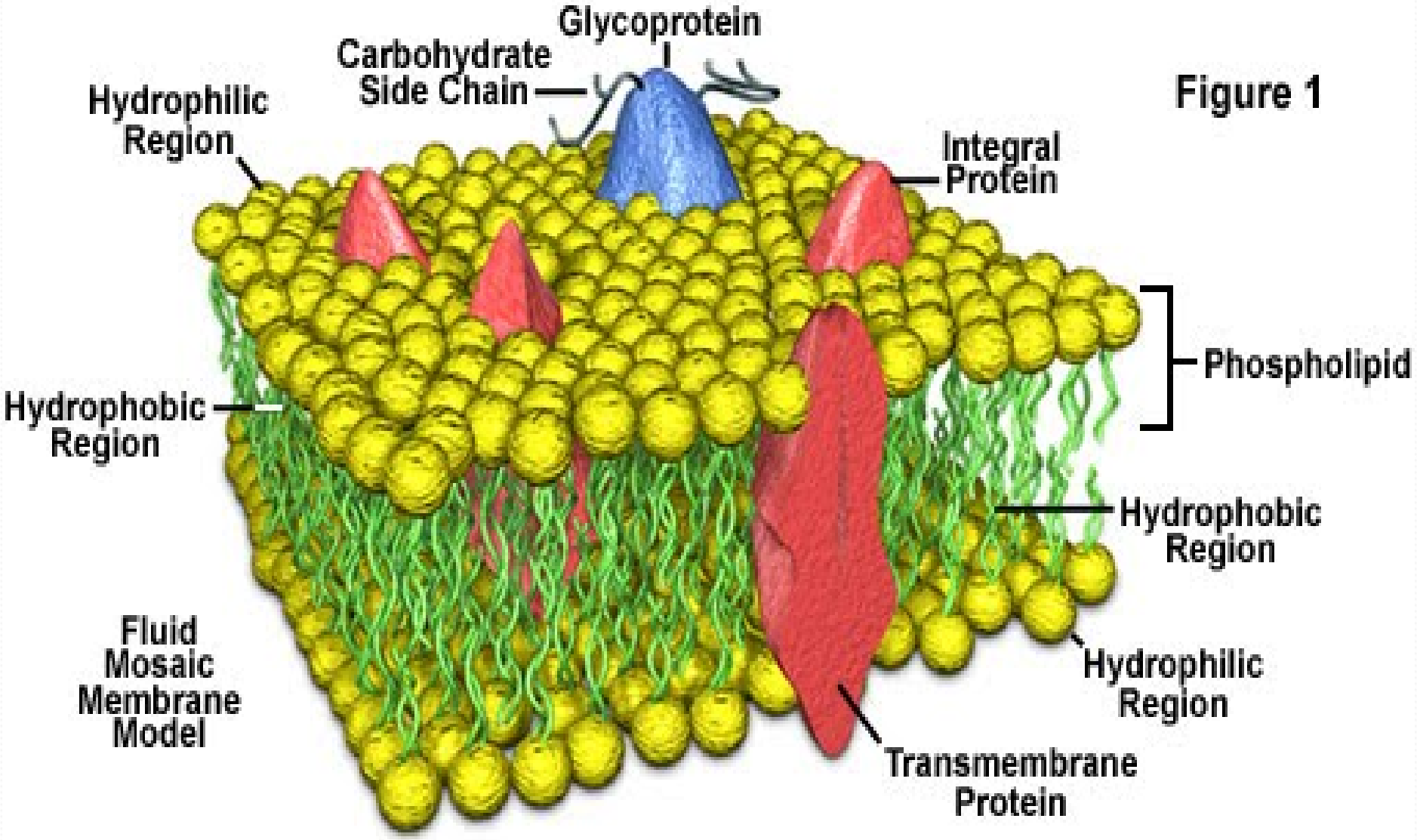


Figure 1

Fluid mosaic model

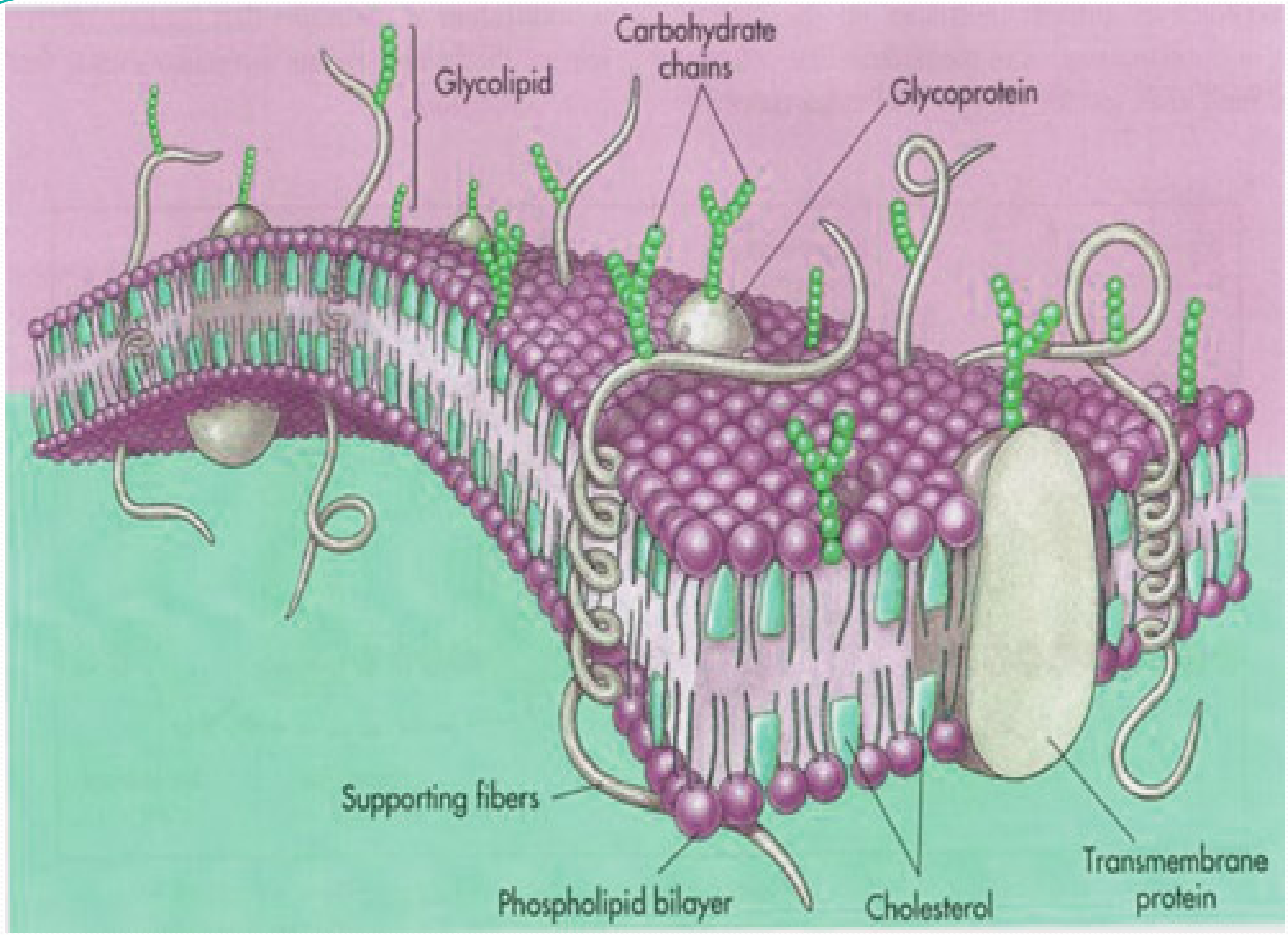
- First proposed by S.J. SINGER (1971) as a lipid-protein model
- Extended to include the fluid character in a publication by G.L.NICHOLSON (1972)
- Cell membrane consists of a bilayer of phospholipid molecules which are amphipathic in nature.
- Polar heads: glycerol conjugated to nitrogenous compounds.
- Non-polar tail of the phospholipid molecule: two long chain fatty acids, each covalently linked to glycerol component of the polar head.

- Amphipathic nature: phospholipids in aqueous solutions spontaneously form a bilayer; with polar heads directed outwards and non polar tails forced together inwards.

- Cholesterol: phospholipids = 1:1

- Cholesterol prevent overdense packing of fatty acids tails and regulate fluidity of the phospholipid bilayer.

- Composition of each half of lipid bilayer is different.


Carbohydrate chains
Glycolipid
Glycoprotein
Supporting fibers
Phospholipid bilayer
Cholesterol
Transmembrane protein

Cell membrane- Protein molecules

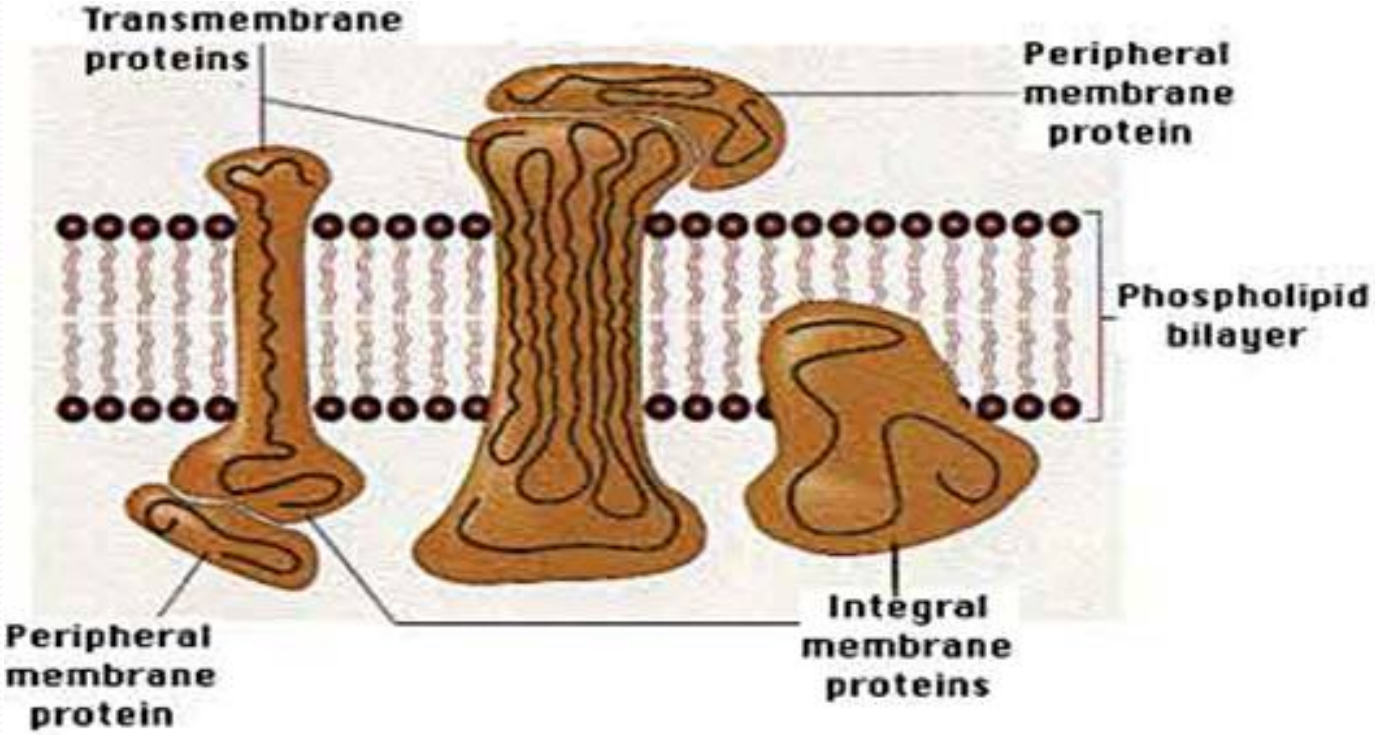
- Protein molecules occur at places both inside and on the outer side of lipid bilayer.

  Protein are icebergs in a sea of lipids .

  Mainly of two types:

- Extrinsic or peripheral: held loosely to outer surface by weaker electrostatic forces.
- Intrinsic or integral: incorporated within membrane.
- Some integral proteins span the membrane from one side to another: Transmembrane proteins

- Integral proteins: Structural channels (or pores) through which water molecules can diffuse between the extracellular and intracellular fluid.
- Integration of the proteins within lipid bilayer - result of hydrophobic interactions between the lipids and the non polar amino acids present on the outer shell of integral proteins.



Membrane carbohydrates The cell GLYCOCALYX

- Occur in combination with proteins or lipids in the form of glycoproteins or glycolipids.
- “Glyco” portions of these molecules almost invariably protrude to the outside of the cell.
- The entire outside surface of the cell often has a loose carbohydrate coat called the Glycocalyx.

Functions of glycocalyx

- Many of them have a negative electrical charge, that repels other negative objects.
- The glycocalyx of some cells attaches to the glycocalyx of other cells.
- Many carbohydrates act as receptor substances for binding hormones, such as insulin.
- Some carbohydrate moieties enter into immune reactions.

Functions of cell membrane

- Protective function
- Maintains homeostasis
- Forms barrier to water soluble materials
- Allows only fat soluble substances
- Absorptive function -Endocytosis is the process in which cells absorb molecules by engulfing them.
- Excretory function- Exocytosis
- Exchange of gases
- Maintains shape and size of the cell

Transport across cell membrane

- Passive diffusion:

  Diffusion depends on the presence of concentration gradient across the membrane.

- Facilitated diffusion:

  Also called as concentration dependent but requires presence of protein carrying molecules to which molecules bind specifically but reversibly.

- Active transport:

  Independent of concentration gradient.

  Example: Sodium pump : A transmembrane protein complex (Na-K ATPase) exchanges a Na+ for a K+ ion across the membrane. ATP is converted into ADP in the process as energy is required.

Bulk transport

Transport of large molecules or small particles into the cells occur by a range of mechanisms collectively known as Endocytosis.

It includes:-

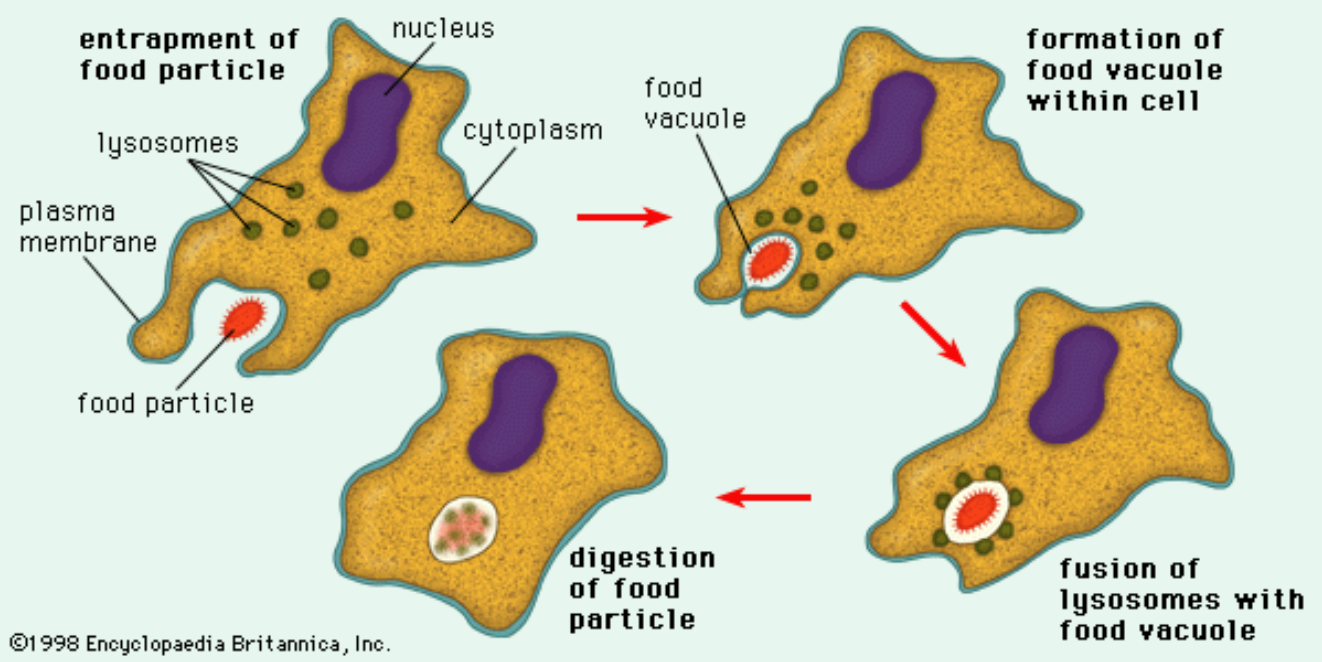
- PHAGOCYTOSIS (cell eating): ingestion of particulate matter, including bacteria and other cells. E.g., Neutrophils, Macrophages.

- PINOCYTOSIS (cell drinking): ingestion of substances initially in the molecular dispersion and the ingestion of bulk fluid stimulated by ionic changes.

Two forms seen of pinocytosis are-:

1. **Smooth** pinocytic vesicles (fluid phase pinocytosis)
2. **Coated** vesicles (receptor mediated endocytosis)

Phagocytosis

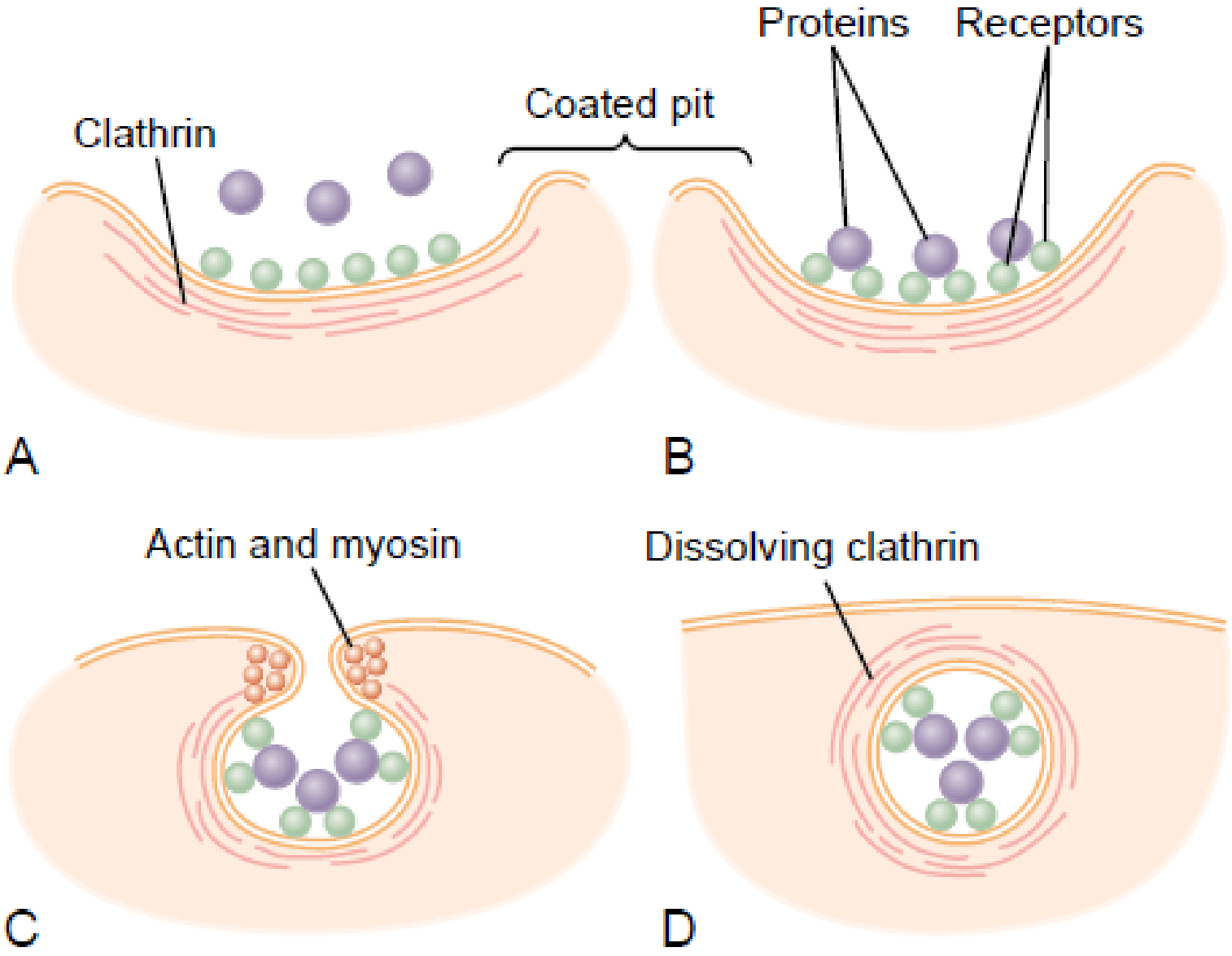


Fluid phase pinocytosis

- Plasma membrane invaginates to form small pits or *caveolae* that project into the cell
- Opening of the pit constricts into a narrow neck, and further constriction results in the separation of a vesicle from the membrane.
- Numerous in the endothelium of blood vessels and under the plasma membrane of smooth muscle cells.

Receptor mediated endocytosis

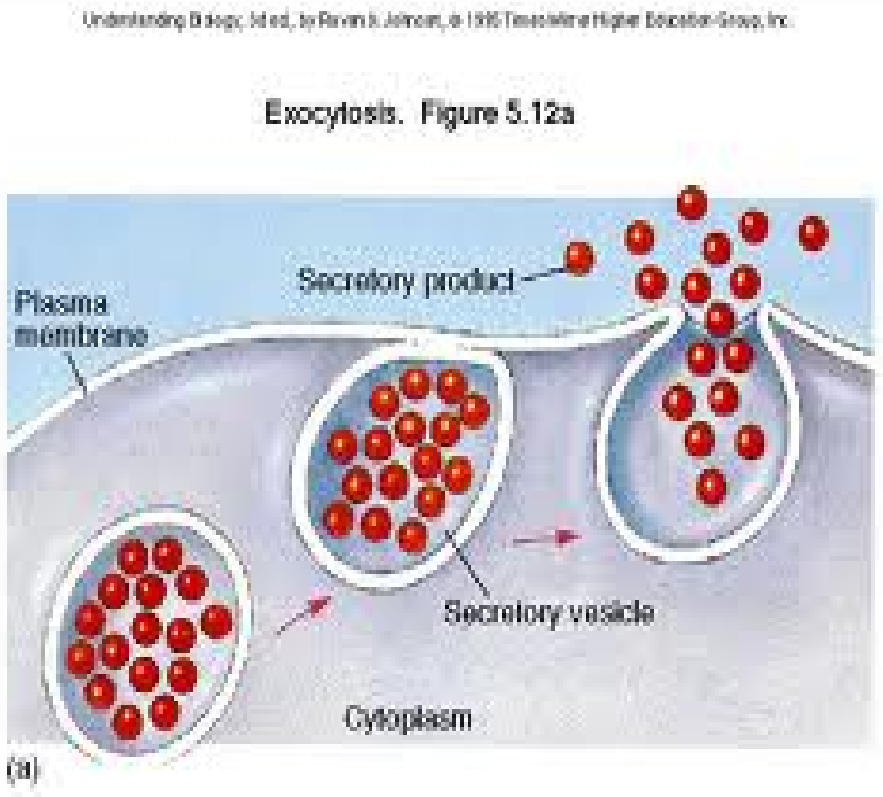
- Receptors are either widely dispersed or aggregated in special regions called Coated pits.
- Coating on the cytoplasmic surface of the membrane is composed of several peptides the major one being clathtrin.
- Coated pit invaginates and pinches off from the cell membrane, forming the coated vesicle.
- Carries the ligand and its receptor into the cell.


Proteins
Receptors
Coated pit
Clathrin
A
B
Actin and myosin
Dissolving clathrin
C
D

Exocytosis

- Process by which a vesicle moves from the Cytoplasm to the plasma membrane where it discharges its contents to the extracellular space.
- Two pathways:

1. Constitutive pathway
2. Regulated secretory pathway



- Constitutive pathway

  Process is continuous.

  Proteins that leave the cell by this process are secreted immediately after their synthesis and exit from the Golgi apparatus.

- Regulated secretory pathway

  Proteins that are concentrated and transiently stored in secretory granules pass along the regulated secretory pathway

  A regulatory event must be activated for secretion to occur

  E.g.. release of zymogens granules by chief cells of the gastric mucosa and by acinar cells of the pancreas

Cytoplasm

- Made up of two zones:
  - Endoplasm: Between ectoplasm and nucleus
  - Ectoplasm: Just beneath the cell membrane

Cytoplasmic components

1. **Cytosol/Cytoplasmic matrix/Hyaloplasm**

Makes up about 70% of the cell volume and is composed of water, salts and organic molecules, soluble proteins, electrolytes, and glucose.

2. **Cytoplasmic structures**

- Non living structures are called inclusions.
- Living structures are membrane bound & called organoids or organelles.

Inclusions:

- Constituted by stored food, Glycogen granules
- Secretory substance in the form of granules
- Includes oil drops, tri-glycerols, glycogen & starch granules.

Cytoplasmic orgenelles

They are of two types:

1. Membranous
2. Non membranous

MEMBRANOUS ORGENELLES

- Mitochondria
- Golgi Apparatus
- Rough Surface Endoplasmic Reticulum (RER)
- Smooth Surface Endoplasmic Reticulum (SER)
- Secretory Granules(VESICLES)
- Lysosomes
- Spherosomes
- Microbodies (PEROXISOMES AND GLYOXYSOMES)

Non membranous orgenelles

- Ribosomes
- Cytoskeletal structure
- Centrioles
- Cilia & Flagella Filaments

Mitochondria

- Greek word : **mitos** means thread and **kondrion** means granules
- First seen by KOLLIKER in 1880 and named by BENDA in 1898.
- Recognized as ***sites of respiration*** by KINSBURY and co workers in 1948 and HAGEBOOM demonstrated it as powerhouse of cell.
- Spherical or filamentous organelles
- 5-10um wide
- Numbers differ in relation to the energy requirement of different kind of cells.
- Example: . Lymphocytes have only few mitochondria whereas liver cells possess several hundred

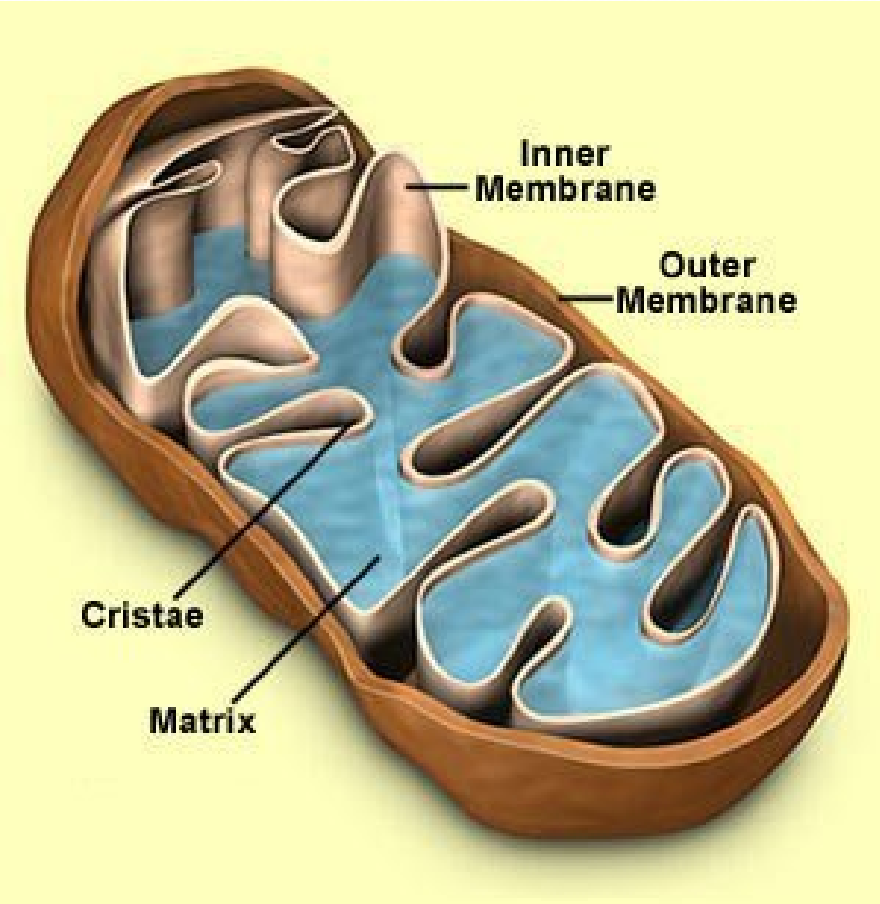
- Typical eukaryotic cell contains about 2,000 mitochondria.
- Mitochondrion are ‘cellular power plants’ because their primary function is to generate energy in the form of ATP. So they are called **Power house of cell.**
- Accumulate in parts of cytoplasm at which utilization of energy is more intense, such as apical ends of ciliated cells

STRUCTURE

- Composed of lipid bilayer-protein membranes: an outer membrane and inner membrane.
- Many infoldings of inner membrane form shelves onto which oxidative enzymes are attached.
- Inner cavity filled with a matrix which contains large quantities of dissolved enzymes - necessary for extracting energy from nutrients.

Functions of mitochondria

- Formation of ATP via the process of oxidative phosphorylation.
- Energy producing reactions take place on cristae.
- Products of glycolysis enter the mitochondria to go through TCA cycle.
- Electron carriers ultimately transported across an electron-transport chain, which is situated across the inner mitochondria membrane



Endoplasmic reticulum

- Albert Claude discovered ER organelle with interconnected network of tubules, vesicles, cisternae within cells.
- Endoplasmic reticulum is of 2 types-

1. Rough endoplasmic reticulum.
2. Smooth endoplasmic reticulum.

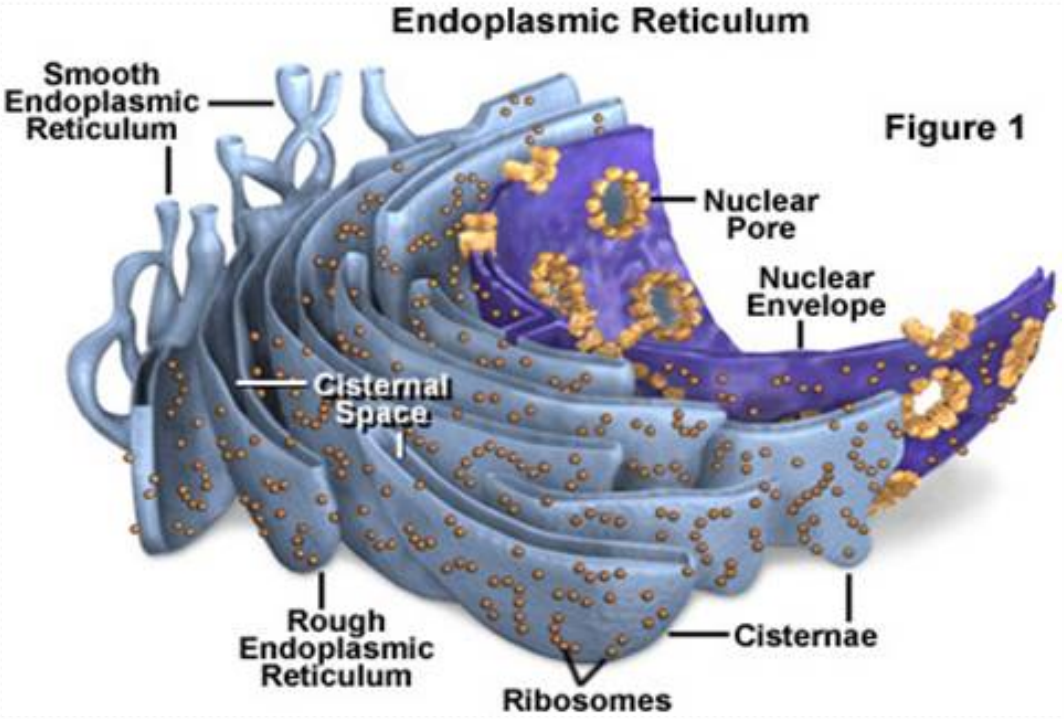
- Extensive network of membrane limited channels and the inner limb is continuous with segment of nuclear membrane, this part of nuclear membrane act as cistern of endoplasmic reticulum
- RER has ribosomes attached to the outer surface
- SER ribosomes are absent

Rough endoplasmic reticulum

- Seggregation of proteins.
- Glycosylation of glycoproteins.
- Synthesis of phospholipids.
- Post translational modification of newly formed polypeptides.
- Provides enzymes for detoxifying substances.

Smooth endoplasmic reticulum

- Synthesis of steroid hormones.
- Synthesis of phospholipids.
- Drug detoxification
- Glycogen formation
- Calcium storage:- SER in muscle cells surrounds the contractile elements and releases Ca ions to bring about contraction


Endoplasmic Reticulum
Smooth Endoplasmic Reticulum
Figure 1
Nuclear Pore
Nuclear Envelope
Cisternal Space
Rough Endoplasmic Reticulum
Cisternae
Ribosomes

Golgi apparatus

- Also called the Golgi body, Golgi complex, or dictyosome.
- First seen by George in 1867.
- Named in 1898 by the Italian physician Camillo Golgi.
- Present in all eukaryotic cells except sieve tubes of plants and RBC of mammals.
- Golgi is made up of 4 parts:

1. Cisternae
2. Tubules
3. Vesicles
4. Vacoules

- Pathway of synthesized proteins:-

  RER ➔ CIS Golgi ➔ Median Golgi ➔ Trans Golgi ➔ Secretory vesicles / lysosomes / peroxisomes

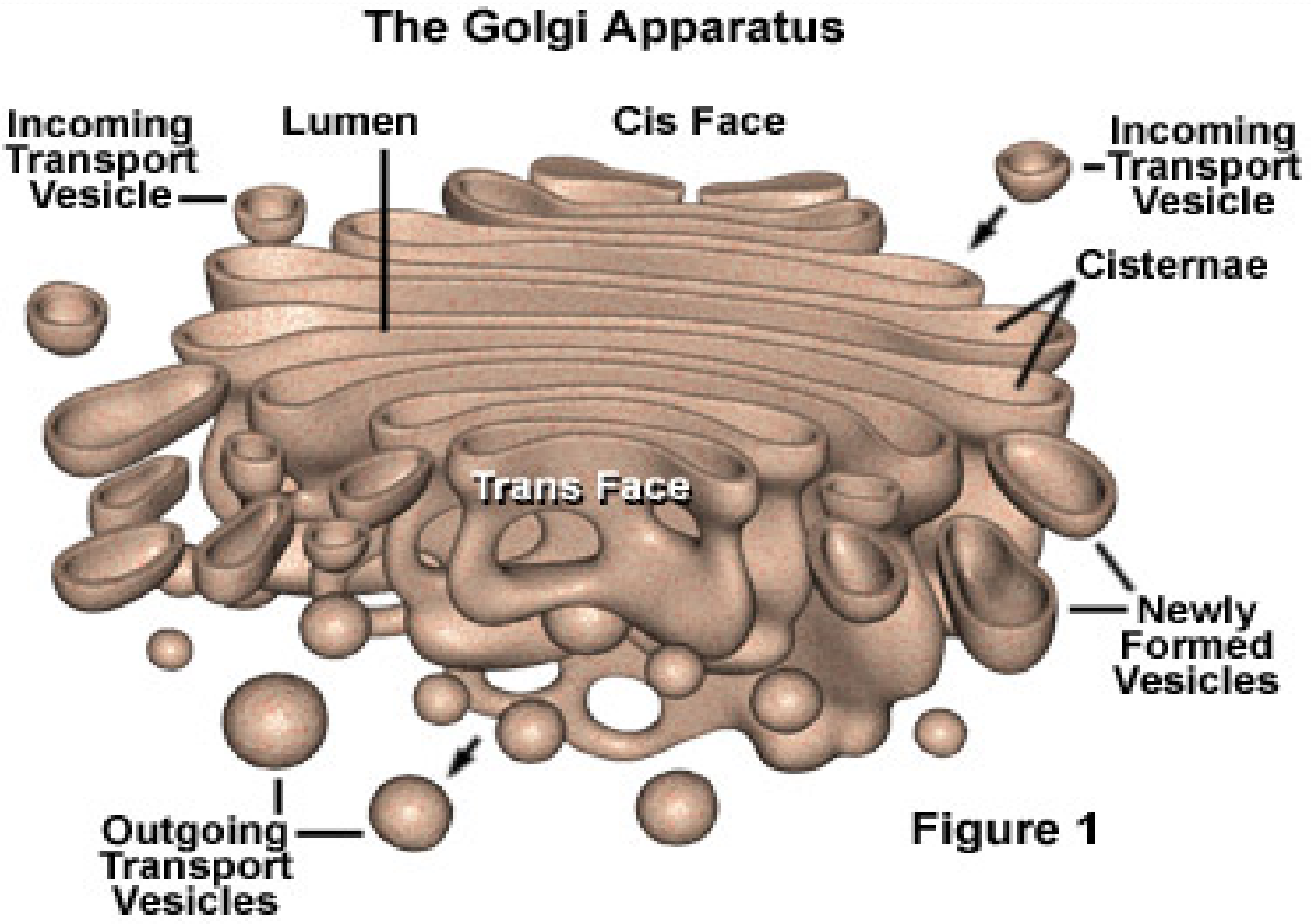


Figure 1

Functions of Golgi apparatus

- Glycosylation, phosphorylation.
- Packing, concentration and storage of secretory products.
- Transformation of membranes.
- Hormone production by endocrine gland.
- Matrix of connective tissue is formed by it.

Lysosomes

- Greek word -- Lysis –digestive or loose, soma-body
- Discovered by Belgium scientist Christian de Duve (1955)
- Novikoff (1956) coined the term lysosomes
- Contain hydrolytic enzymes in the form of minute crystalline or semi crystalline granules .
- Hydrolytic enzymes present :

1. Acid phosphatase
2. Deoxyribonuclease
3. Protease
4. Sulphatase
5. Lipases
6. Glycosidases.

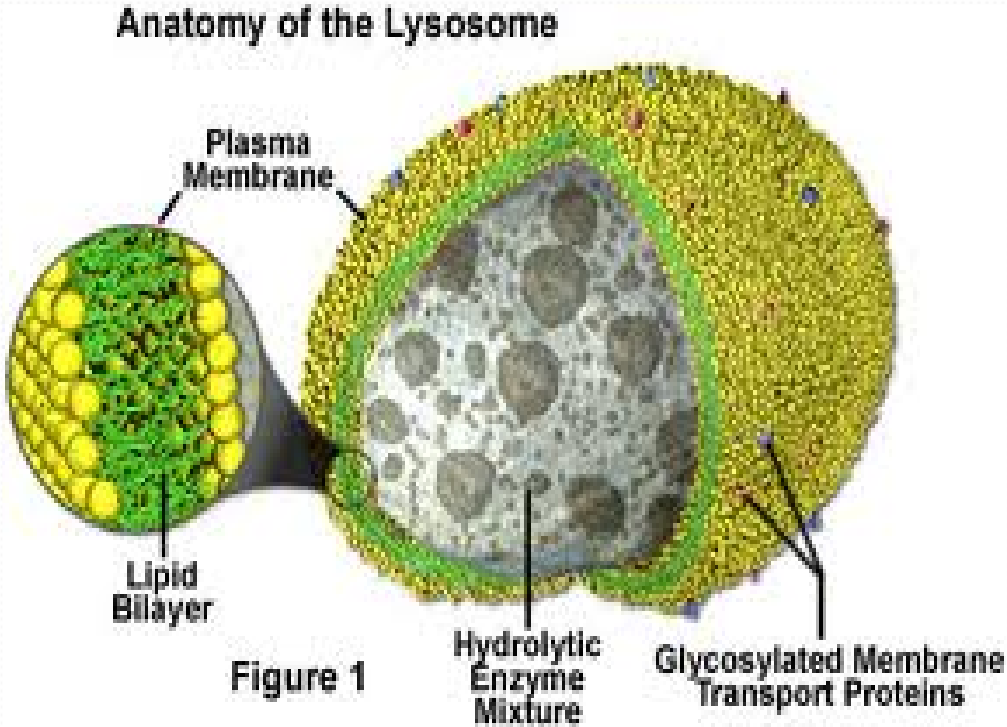


Figure 1

- Also called acid hydrolases because all these digestive enzymes usually function in acidic medium .
- "SUICIDE BAGS" because of the presence of large number of digestive enzymes or acid hydrolases in them.
- Occur in all animal cells except in the red blood corpuscles.
- Lysosome passes through various stages in the same cell called **Polymorphism**
- Four types, depending on their morphology, and function:

1. Primary lysosomes

- Newly pinched off vesicles, generally fuse with some endosomes to become fully functional.
- Small in size.

2. Secondary lysosomes

- Heterophagosomes or digestive vacoules.

2. Secondary lysosomes (Heterophagosomes or digestive vacoules)

- Formed by the fusion of food containing phagosomes with lysosomes.
- Digestion occurs and digested food passes out into cytoplasm and some undigested food left in the secondary lysosome.

3. Residual bodies or tertiary lysosmes

- In it, indigestible food materials have been left.
- Passes outwardly and fuses with plasma membrane to throw out the debris into the external environment by exocytosis or ephagy.

4. Autophagic Vacuoles (Autophagosomes or autolysosomes)

- Produced by the fusion of a number of primary lysosomes around worn out or degenerated intercellular organelles.
- Cell debris is digested and the phenomenon is called autophagy or autodigestion.

Functions of lysosomes

Lysosomes allows the cell to digest:

- Damaged cellular structures.
- Food particles that have been ingested by the cell.
- Unwanted matter such as bacteria.
- Removal of excessive excretory products in cell and unwanted cells in embryo.

Secretory granules or vesicles

- Found in the cells that store a product until its release is signaled by metabolic, hormonal or neural message.
- Formed from endoplasmic reticulum golgi apparatus complex .
- Contain a concentrated form of secretory product .
- Secretory vesicles containing digestive enzymes are referred to as zymogen granules.

Spherosomes

- Are small cell organelles bounded by single membrane
- Take part in storage & synthesis of lipids.
- Discovered by Perner(1953)
- Composition: 98% lipid + 2% proteins

Microbodies

- Are the small cell organelles.
- Bounded by single membrane which absorb molecular oxygen and take part in oxidations other than those involved in respiration.
- Two types –

1. Peroxisomes
2. Glyoxisomes

Peroxisomes

- Discovered and coined by De Duve (1965)
- Abundant in liver and kidney cells
- FUNCTIONS:

1. Associated with oxidation reactions
2. Prevents the accumulation of H_2O_2 in the cell
3. Reactions leading to formation of bile acids and cholesterol have also been localized to peroxisomes.

- Deficiency in peroxisomal enzymes causes the fatal Zellweger syndrome

Glyoxisomes

- Discovered by Briedenbech(1967).
- Contains enzymes for β-oxidation of fatty acids and glyoxylate pathway.
- Help in conversion of fatty acids into carbohydrates.
- Found only in **Plants.**

Ribosomes

- Are naked ribonucleoproteins.
- Site for protein or polypeptide synthesis.
- Known as protein factories.
- Discovered by PALADE(1955) .
- Term was coined by Richard B. Roberts(1958).
- Composed of 65 % ribosomal RNA and 35 % ribosomal proteins.

Consist of two separate subunits:

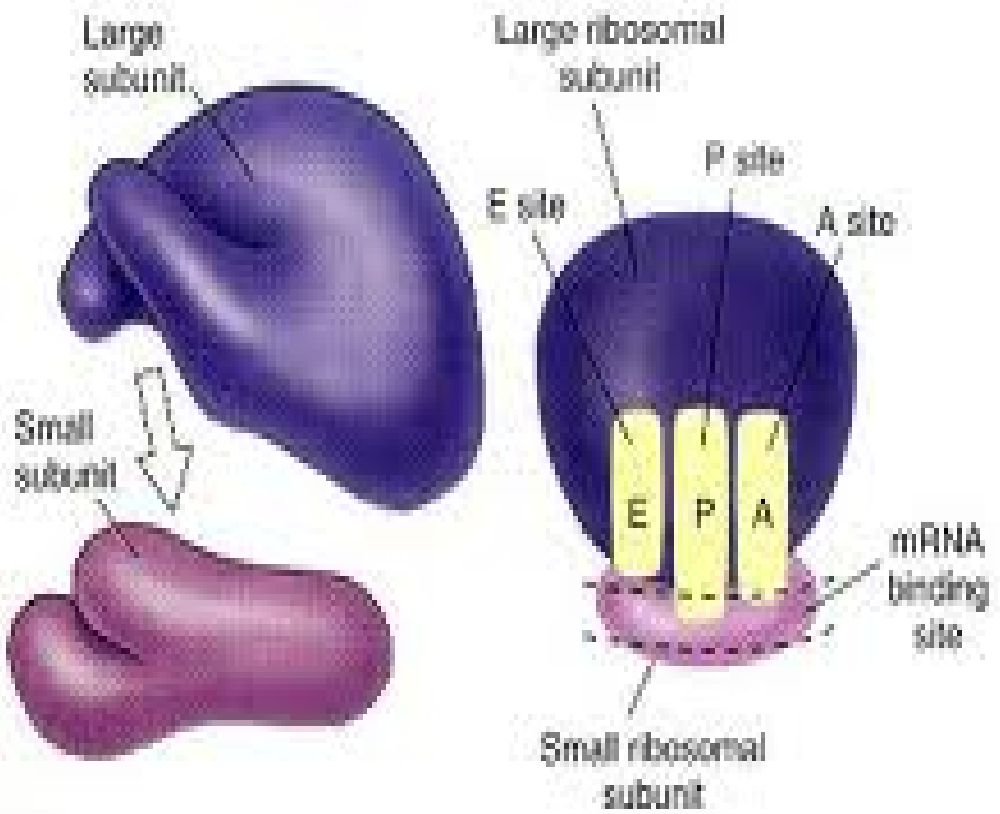
- Large, lower subunit
- Small, upper subunit
- Larger subunit is dome shaped and smaller subunit is ellipsoid

Ribosome has four sites for specific attachments:

- mRNA binding site
- A or aminoacyl site
- P or peptidyl site
- E or exit site

Functions

Protein synthesis (mRNA comprises a series of codons that dictate to the ribosome the sequence of a. a needed.)



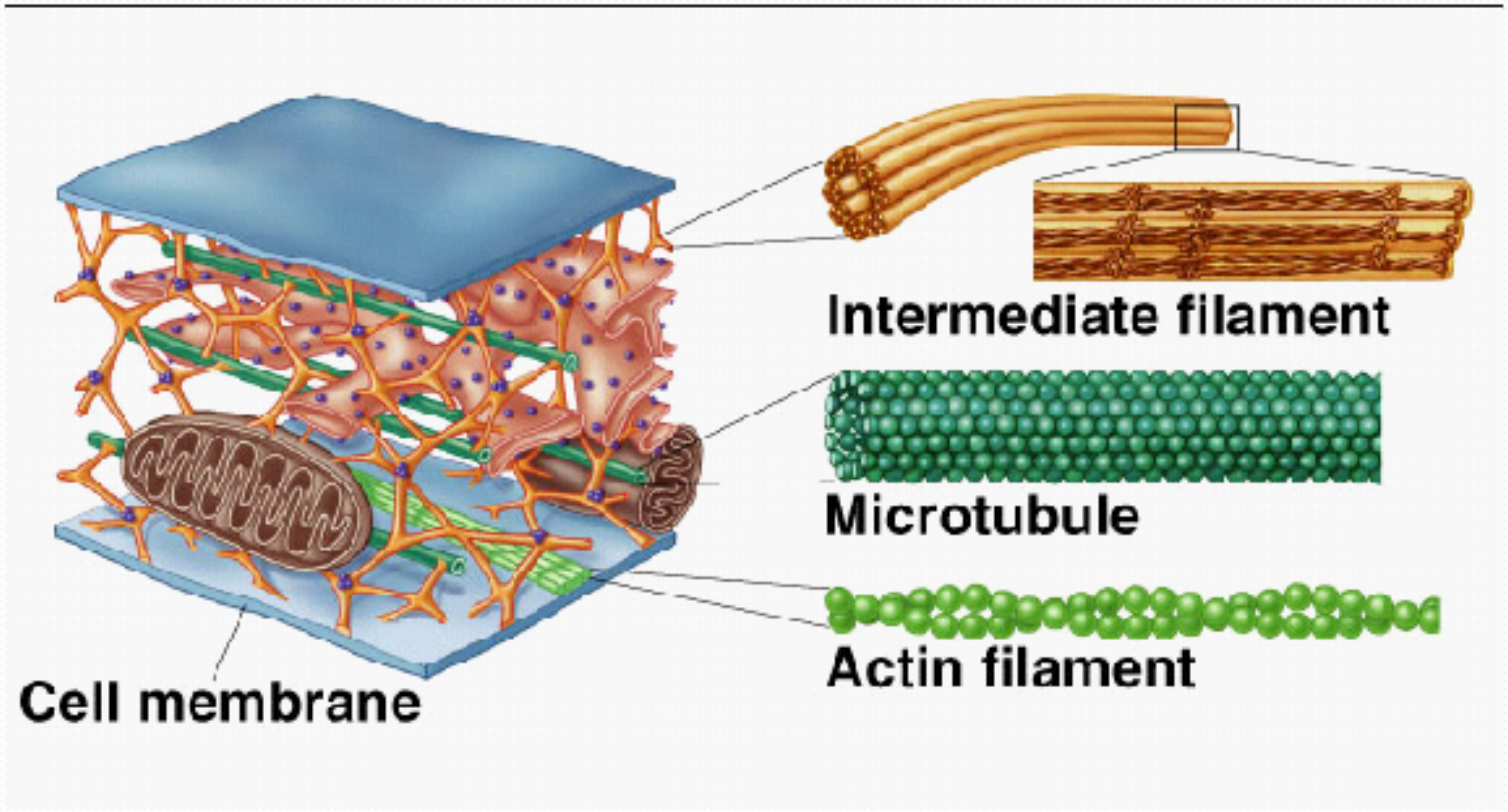
Ribosome Subunits

The smaller subunit fits into a depression on the surface of the larger one. The A, P, and E sites on the ribosome play key roles in protein synthesis.

Cytoskeletal structure

- Fibres that maintain structure of cell
- Regulate orientation and distribution of cell orgenelles.
- Three types:

1. Microtubules
2. Microfilaments
3. Intermediate filaments


Intermediate filament
Microtubule
Actin filament
Cell membrane

Microtubules

- Straight, hollow cylinders whose wall is made up of a ring of 13 protofilaments.
- Made up of alternate spirals of proteins called α- and β- tubulins.
- Diameter is 25nm.
- Formation initiated at special sites called microtubule organizing centers (MTOC).

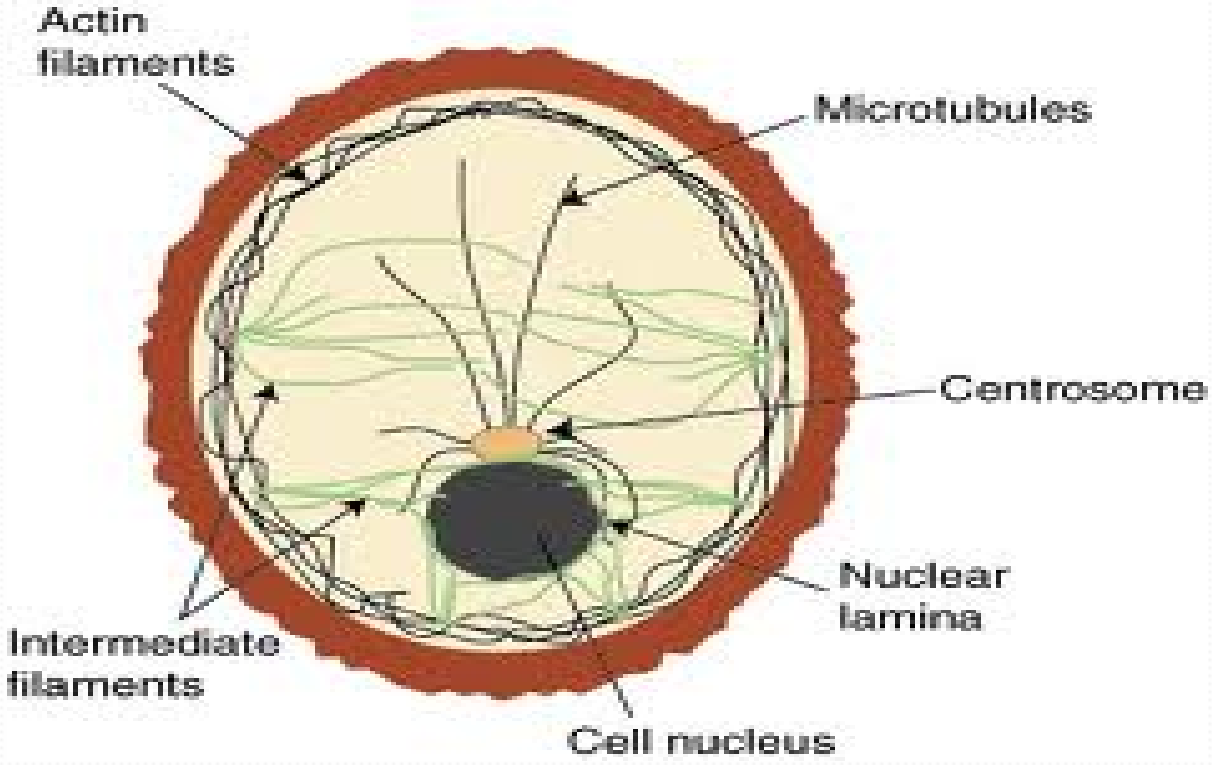
Functions

1. Structural constituents of spindle fibres, chromosomes, centrioles, basal bodies, flagella and cilia.
2. Provide rigidity and shape to the cells
3. Vital role in cell differentiation
4. Determine cell polarity

Intermediate filaments

- Types of intermediate filaments:

1. Keratin
2. Neurofilaments
3. Vimentins
4. Glial filaments
5. Desmins



- They provide supporting framework within the cells.

  ex: nucleus held within the cell by basket like network of intermediate filaments.

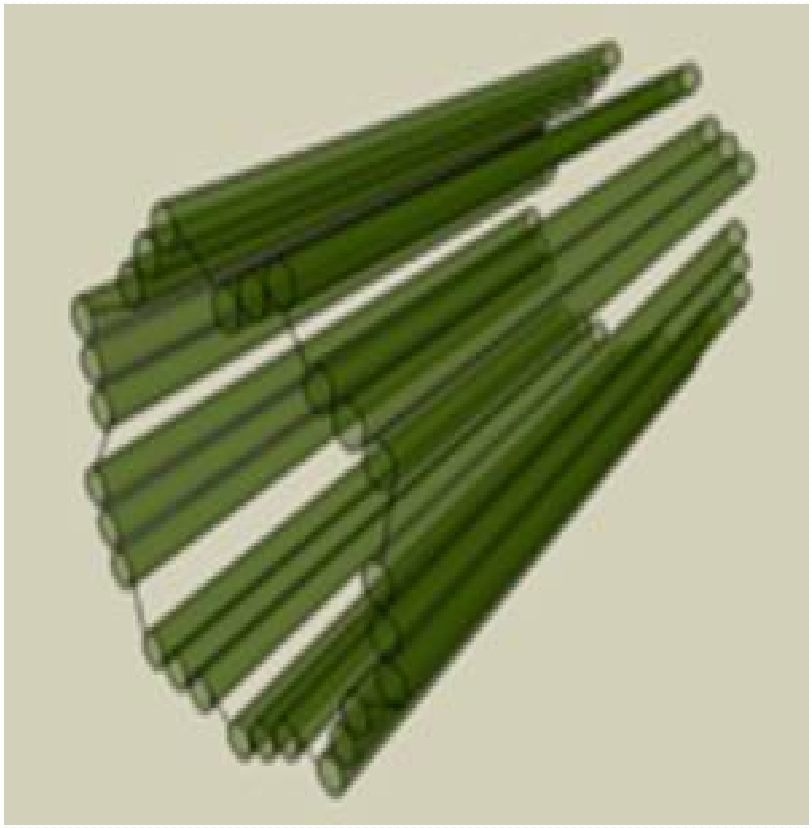
Centriole

- Are cylindrical structures.
- 15um in diameter.
- 0.3 to 0.5 um in length.
- Pair of centrioles -- diplosome
- Diplosome lies in a common specialized part of cytoplasm called centrosphere or kinoplasm.
- The complex formed of centrioles and centrosphere is called centrosome.
- A centriole possesses a whorl of nine peripheral fibrils.
- Fibrils are absent in the centre.
- Arrangement is called 9+0.
- Each fibril is made up of three subunits called triplet fibril.

- Adjacent triplet fibrils are connected by C-A proteinaceous linker.
- Center : rod shaped proteinaceous mass known as hub.
- From the hub 9 strands develop towards the peripheral triplet fibrils known as spokes.
- Cart wheel appearance.

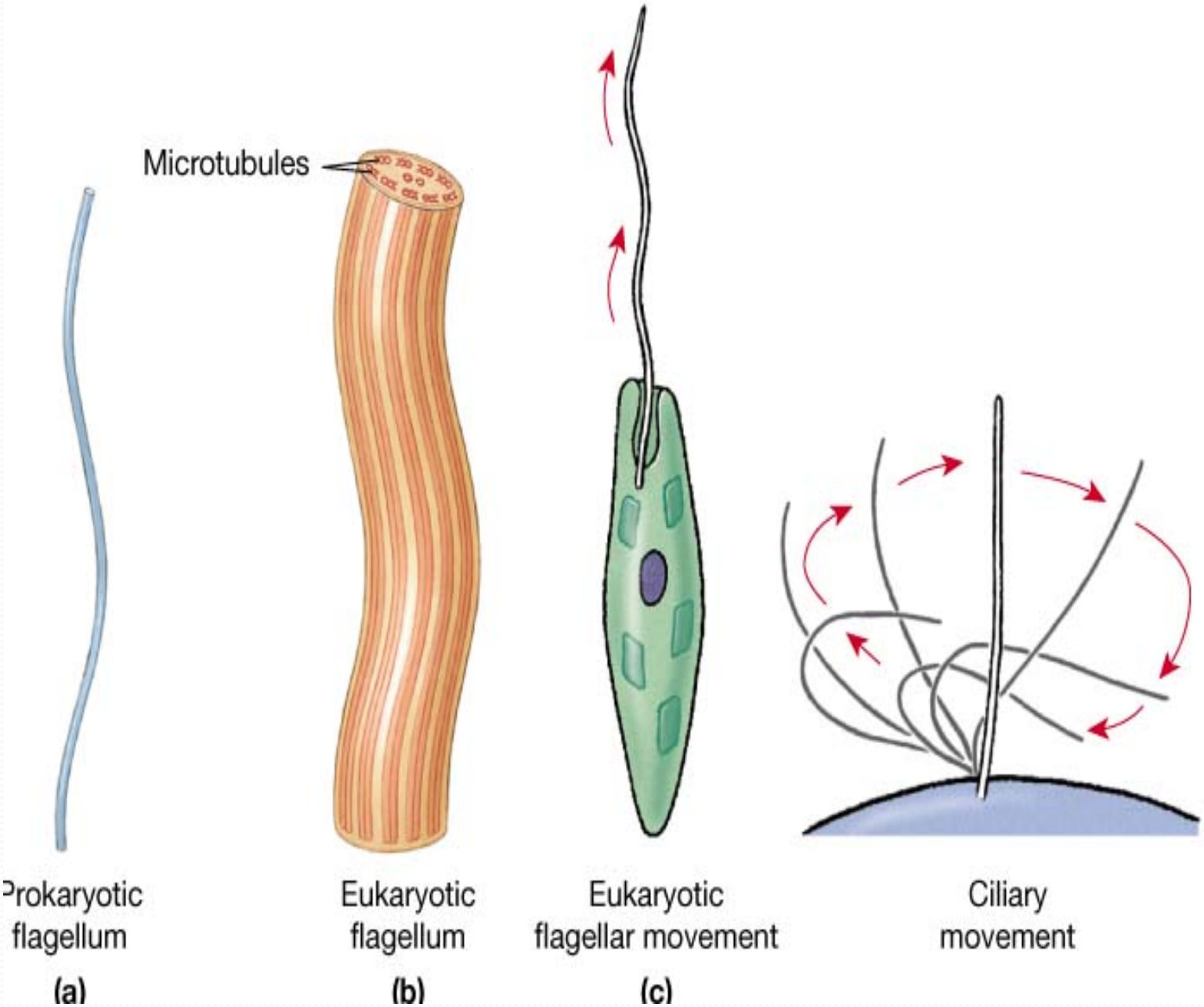
Functions

- Organize spindle fibres during cell division.
- Called microtubule organizing centers (MTOCs).
- Provide basal bodies which give rise to cilia and flagella.



Cilia and Flagella

- Cilia --- Latin word “cilium” means eyelid.
- Named so because these hair-like prosesses extending from cells; resembles eyelashes that extend from the free border of eyelids
- Flagellum --- Latin word means **whip like**
- Cilia and flagella arises from the Basal Bodies
- Basal bodies previously called Kinetosomes/ basal granules/ Blepharoplast.
- Made of a cylindrical array of 9 evenly-spaced microtubules
- 2 single microtubules run up through the center of the bundle, completing the so-called "9+2" pattern


Microtubules
Prokaryotic flagellum
(a)
Eukaryotic flagellum
(b)
Eukaryotic flagellar movement
(c)
Ciliary movement

CYTOPLASMIC INCLUSIONS

- Non moving materials.
- Result of metabolic activity within the cells.
- Present either in soluble or insoluble state.
- Can be organic or inorganic in nature.
- Called as

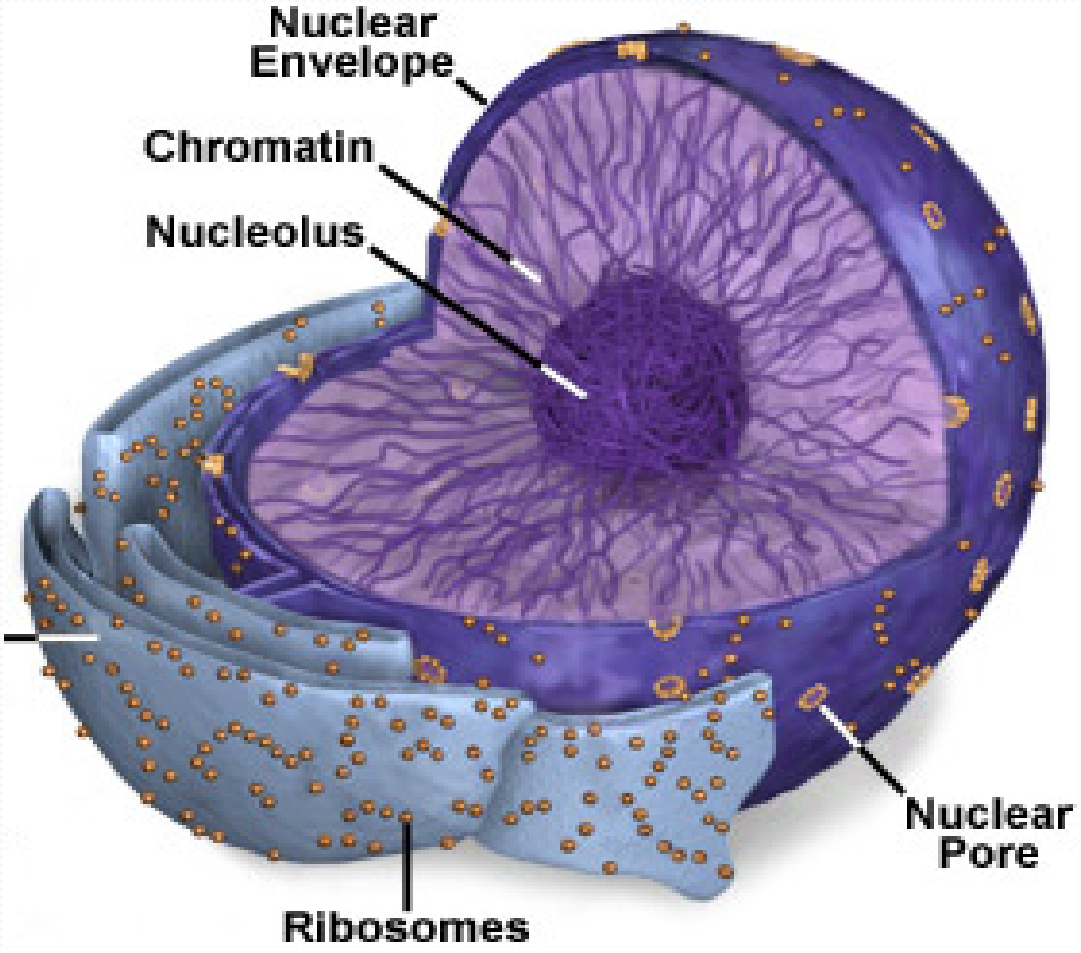
  ergastic bodies.

Stored food	Pigments
• Glycogen •Fat (lipids)	• Exogenous 1. carotene 2. carbon particles • Endogenous 1. haemoglobin 2. hemosiderin 3. bilirubin 4. melanin

NUCLEUS

- Control centre of the cell.
- Diameter usually varies between 5-10µm.
- Consists of:

a. Nuclear envelope
b. Nuclear chromatin
c. Nucleolus
d. Nuclear matrix

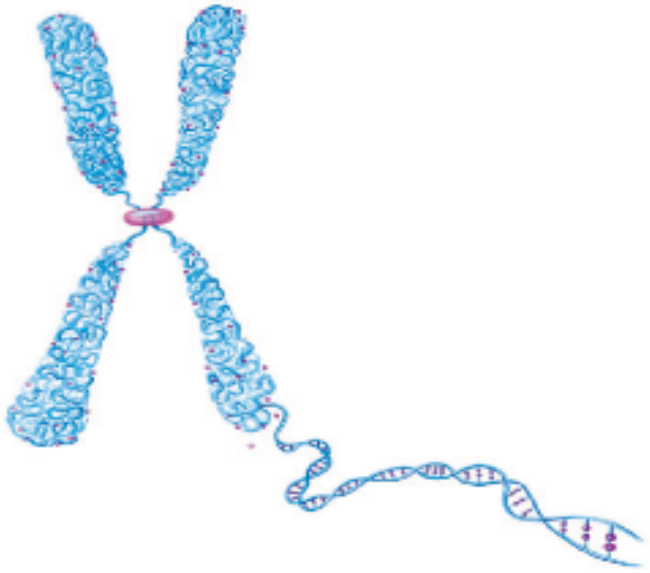


Nuclear envelope

- Bilayer membrane—outer layer continuous with rough endoplasmic reticulum.
- Penetrated by nuclear pores—to which protein molecules are attached.
- Area of pore—9 nanometers.

Nuclear chromatin

- Coiled thread like mass.
- Genetic material of cell.
- Consists principally of DNA and protein molecules.



- When a cell begins to divide, chromatin shortens and thickens into rod shaped structures called chromosomes.
- Each chromosome carries thousands of genes that determine structure and function of a cell.

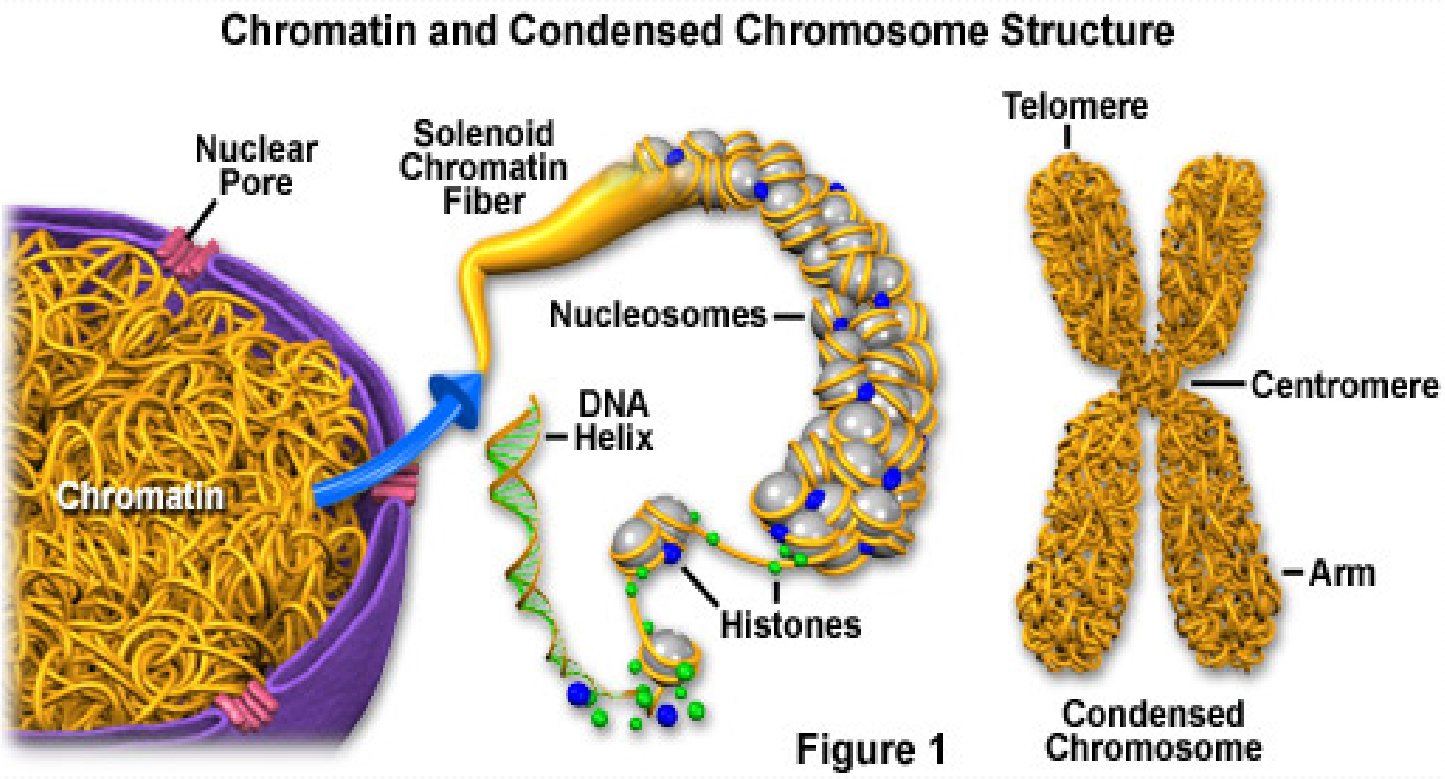
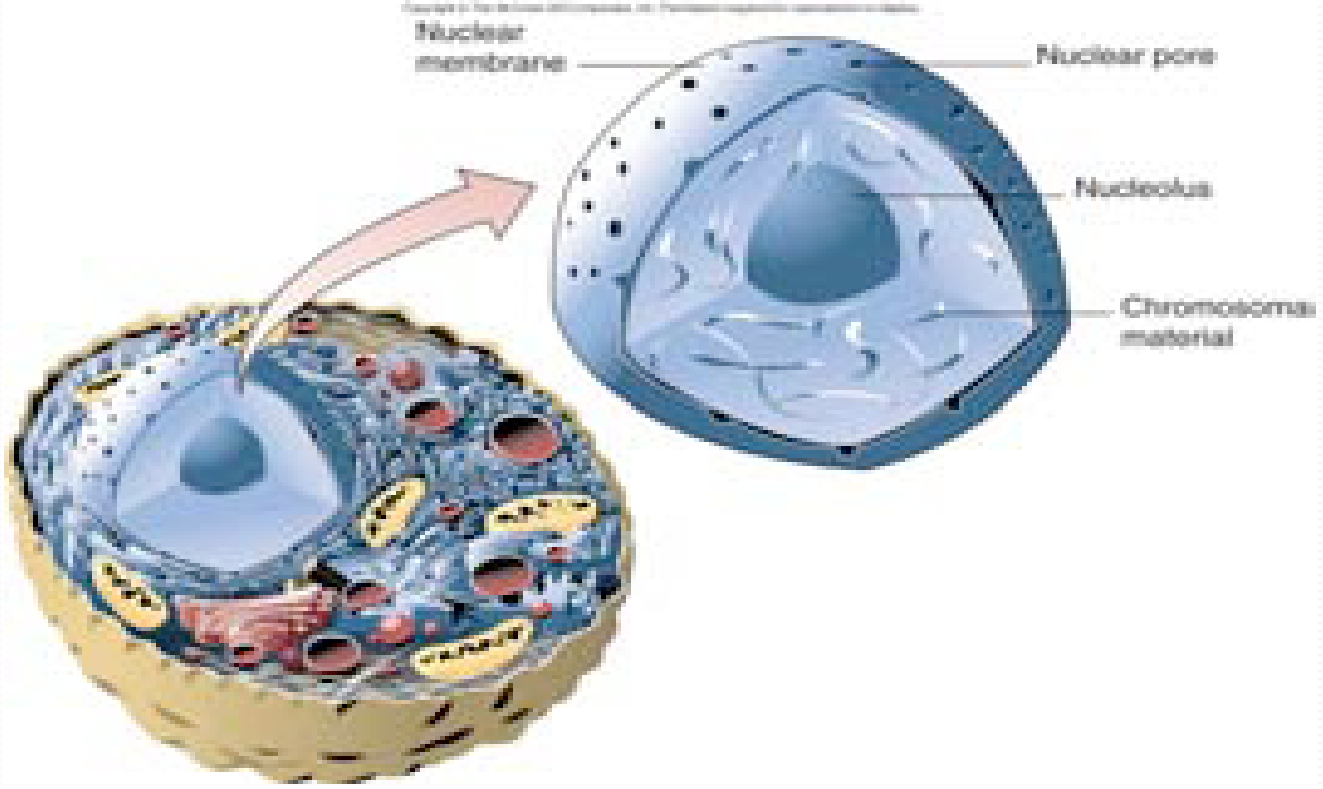


Figure 1

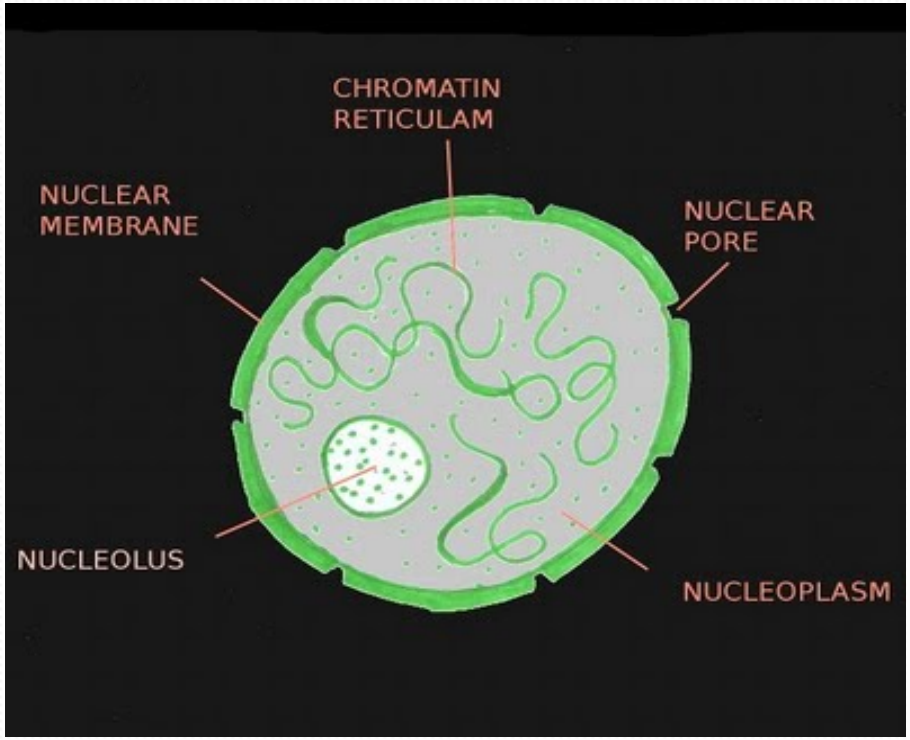
Nucleolus

- Spherical structure
- 1mm in diameter
- Rich in rRNA & protein
- Basophilic when stained with hematoxylin & eosin
- Enlarges when cell is actively synthesizing.



Nuclear matrix(nucleoplasm)

- Fills the space between the chromatin & the nucleoli in the nucleus.
- Composed mainly of proteins, metabolites & ions.
- When its nucleic acids & other soluble components are removed, a continuous fibrillar structure remains called nucleoskeleton.
- Nucleoskeleton contributes to the formation of a protein base to which DNA loops are bound.

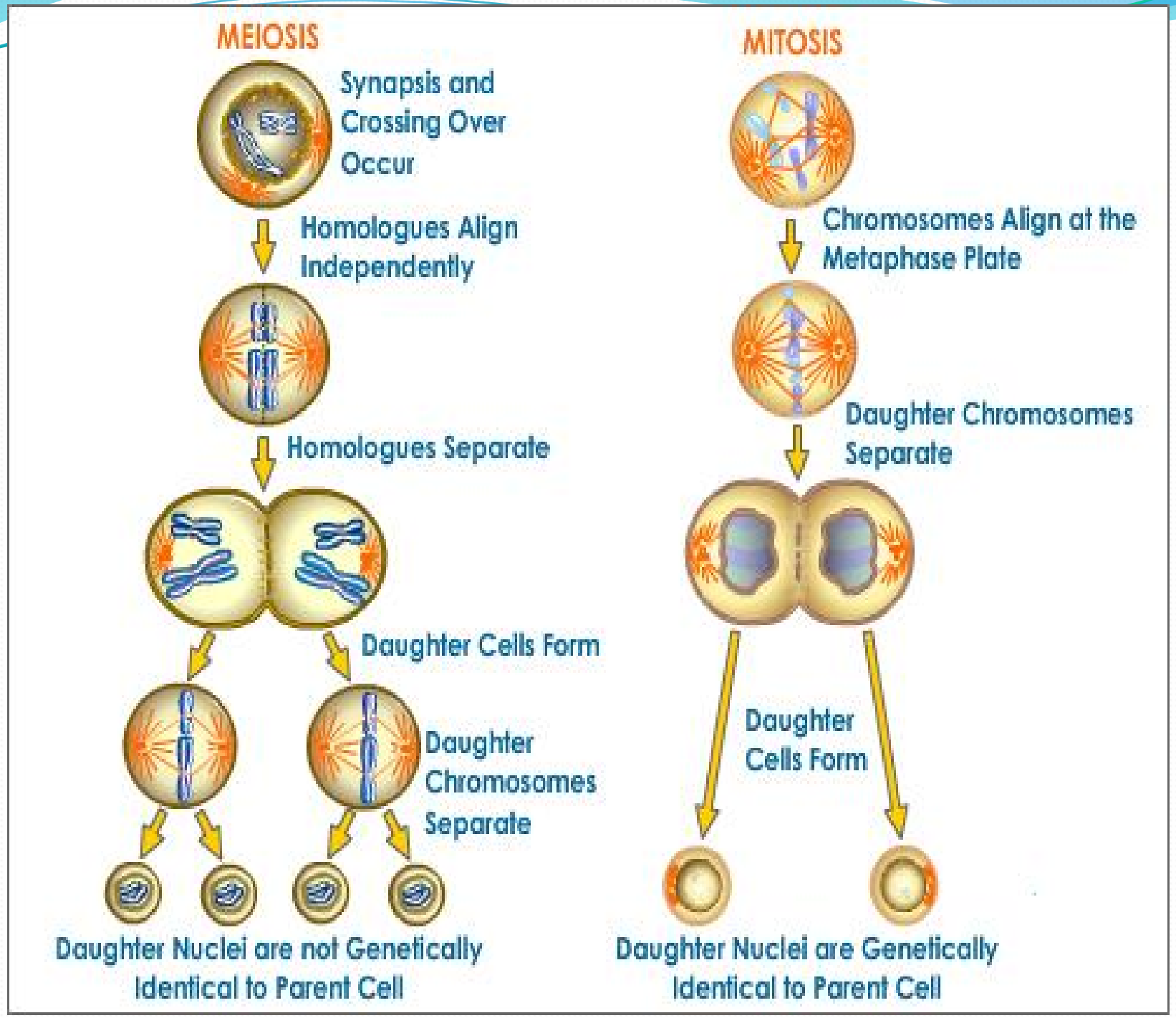


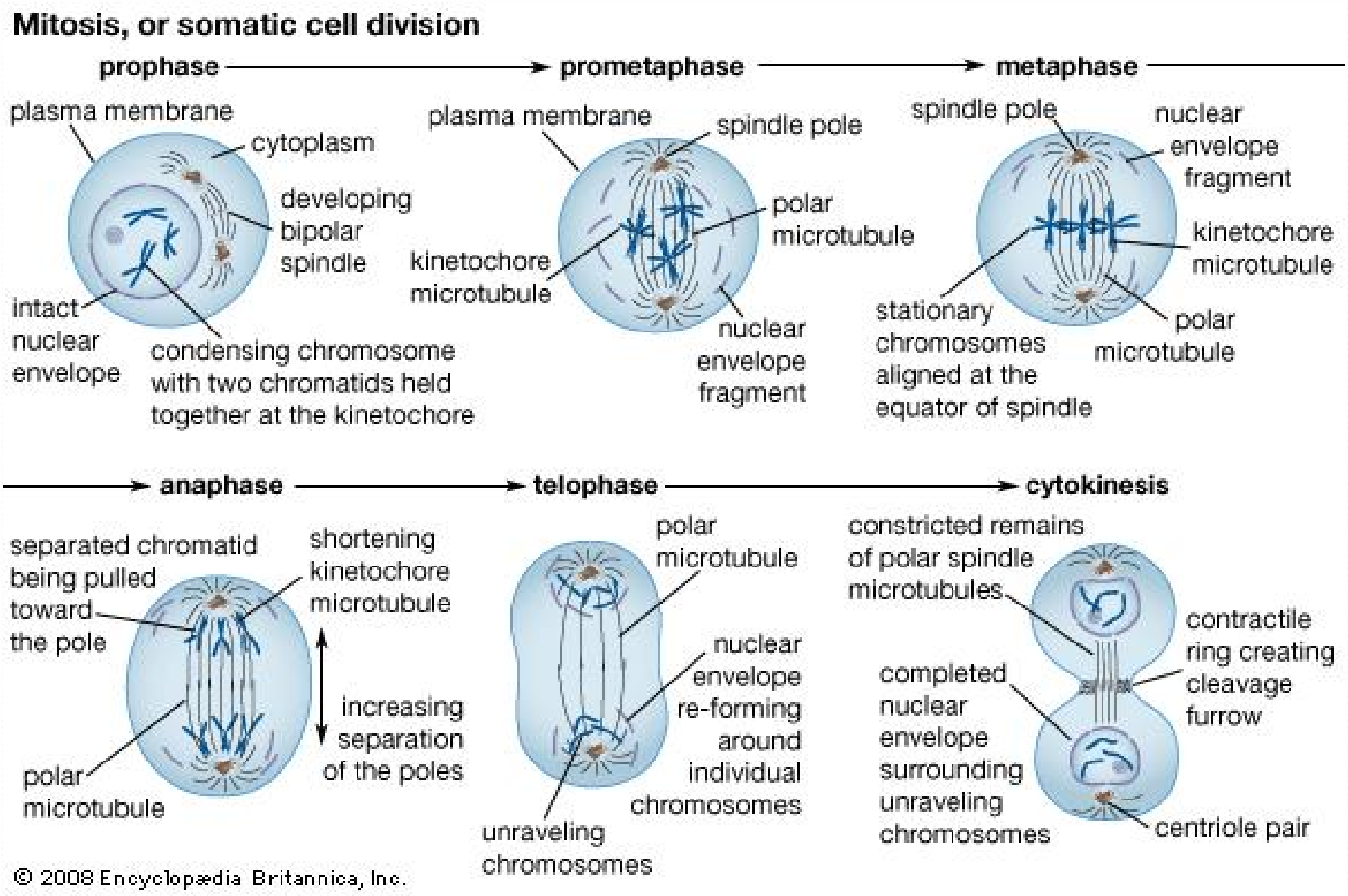
Cell division

- It is of two types:

  Mitosis

  Mieosis


MEIOSIS
Synapsis and Crossing Over Occur
Homologues Align Independently
Homologues Separate
Daughter Cells Form
Daughter Chromosomes Separate
Daughter Nuclei are not Genetically Identical to Parent Cell
MITOSIS
Chromosomes Align at the Metaphase Plate
Daughter Chromosomes Separate
Daughter Cells Form
Daughter Nuclei are Genetically Identical to Parent Cell


Mitosis, or somatic cell division
prophase
prometaphase
metaphase
plasma membrane
cytoplasm
developing bipolar spindle
intact nuclear envelope
condensing chromosome with two chromatids held together at the kinetochore
plasma membrane
spindle pole
polar microtubule
kinetochore microtubule
nuclear envelope fragment
spindle pole
nuclear envelope fragment
kinetochore microtubule
stationary chromosomes aligned at the equator of spindle
polar microtubule
anaphase
telophase
cytokinesis
separated chromatid being pulled toward the pole
shortening kinetochore microtubule
increasing separation of the poles
polar microtubule
polar microtubule
nuclear envelope re-forming around individual chromosomes
unraveling chromosomes
constricted remains of polar spindle microtubules
contractile ring creating cleavage furrow
completed nuclear envelope surrounding unraveling chromosomes
centriole pair
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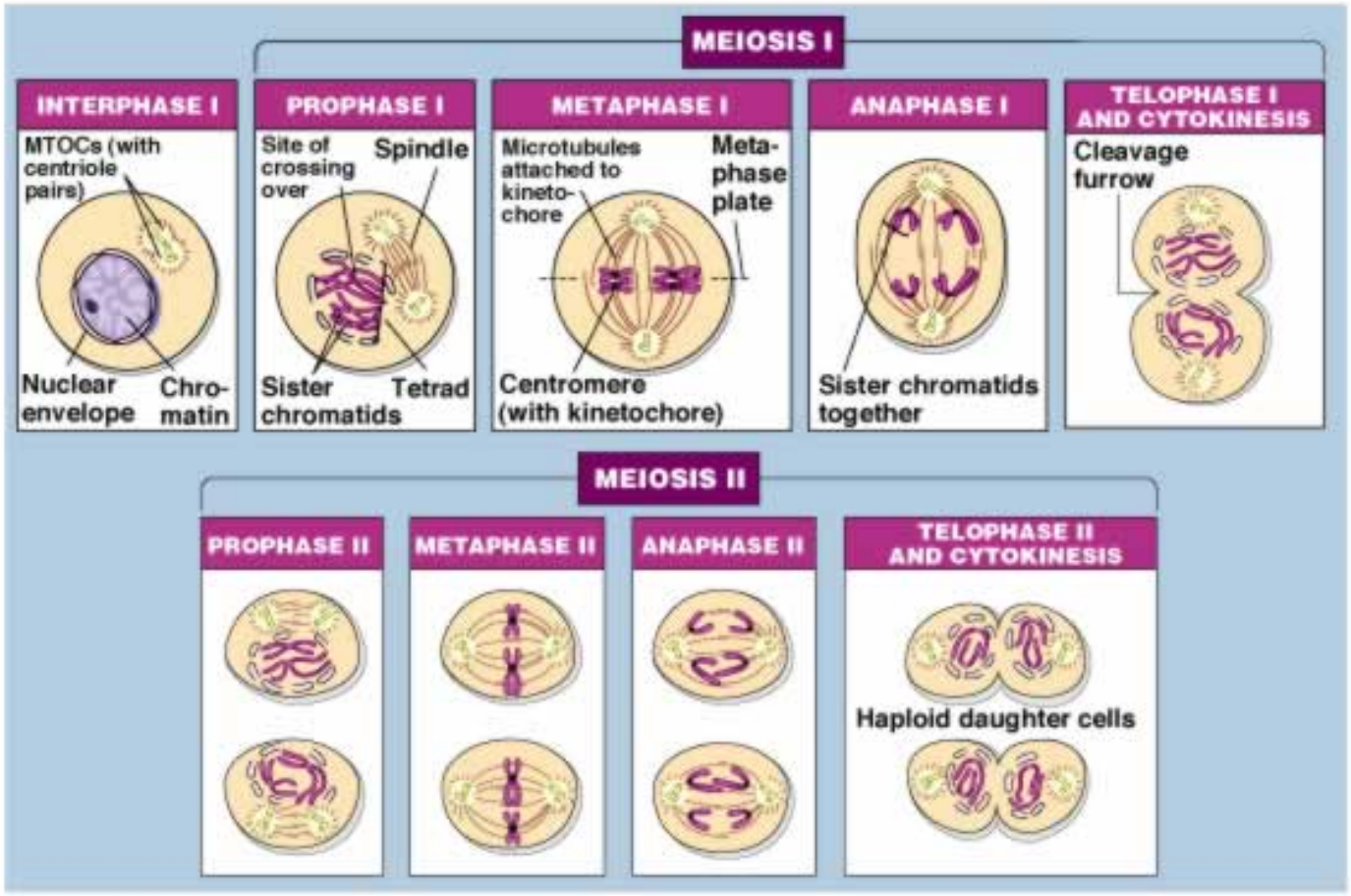
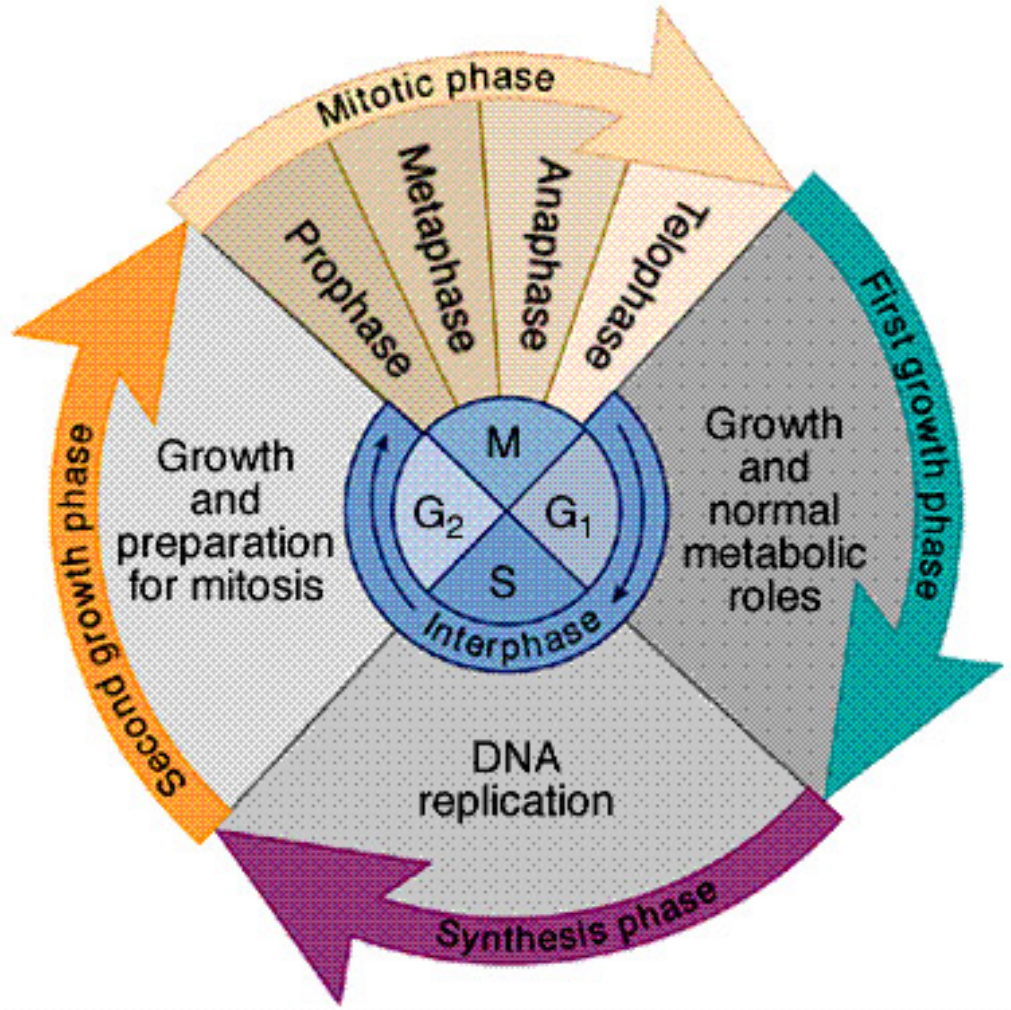
Meiosis I and Meiosis II



Cell cycle


Mitotic phase
Prophase
Metaphase
Anaphase
Telophase
First growth phase
Growth and normal metabolic roles
DNA replication
Synthesis phase
Second growth phase
Growth and preparation for mitosis
M
G2
G1
S
Interphase

Cell death

- Pathological processes involved in cell death are:-
  - Autolysis
  - Apoptosis
  - Necrosis

CELLULAR ELEMENTS OF PERIODONTIUM

GINGIVAL EPITHELIUM

- Keratinocytes
- Non keratinoctes
  - Langerhans cells
  - Merkel cells
  - Melanocytes

GINGIVAL CONNECTIVE TISSUE

- Fibroblast
- Mast cells
- Adipose cells
- Eosinophils
- Plasma cells
- Lymphocytes
- Neutrophils

(inflamatory cells are usually present in small amounts in clinically normal gingiva)

PERIODONTAL LIGAMENT

- Connective tissue cells
  - Fibroblasts
  - Cementoblasts
  - Osteoblasts
- Epithelial rests of Malassez
- Defense cells
  - Neutrophils
  - Lymphocytes
  - Macrophages
  - Mast cells
  - Eosinophils

CEMENTUM

- Cementoblasts
- Cementoclasts
- Cementocytes

ALVEOLAR PROCESS

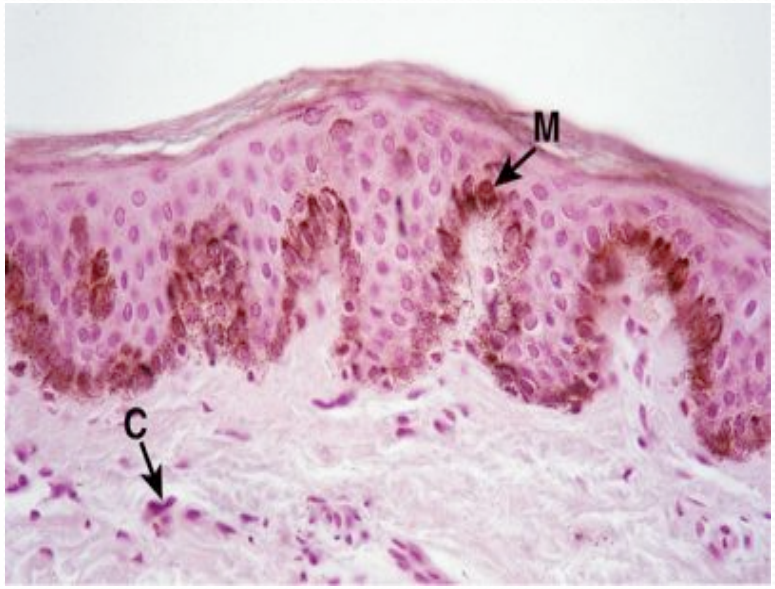
- Osteoblasts
- Osteoclasts
- Osteocytes

Keratinocytes

- Proliferation and diffrentiation of keratinocytes in gingival epithelium protects the deep structures, while allowing a selective interchange with oral environment.

Melanocytes

- Dendritic cells located in basal and spinous layer of gingival epithelium.
- They synthesize melanin in organelle called *premelanosomes or melanosomes.*
- These contain tyrosinase, which hydroxylates tyrosine to dihydroxyphenylalanine (DOPA), which in turn is progressively converted to melanin.
- Melanin granules are phagocytosed and contained within other cells of epithelium and connective tissue called *melanophages or melanophores* .

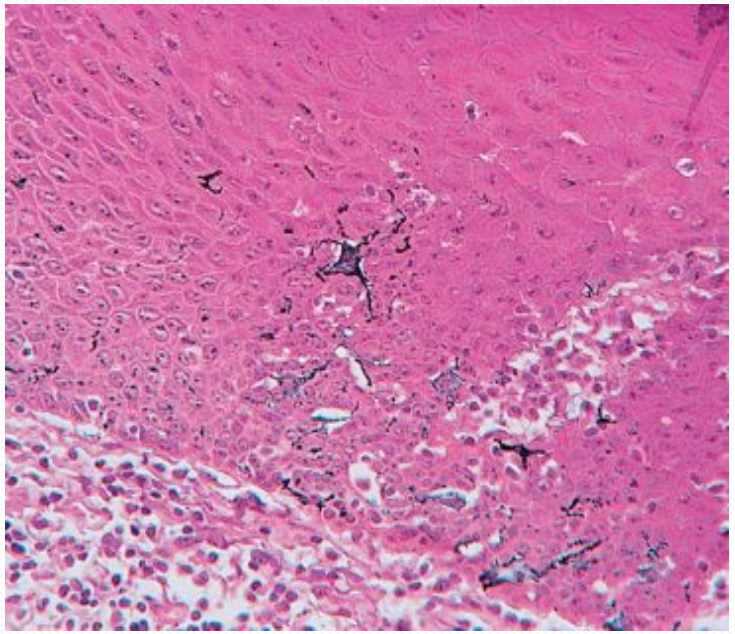


Pigmented gingiva of dog showing melanocytes (M) in the basal epithelial layer and melanophores (C) in the connective tissue

Langerhans cells

- Dendritic cells located among keratinocytes at all suprabasal levels.
- They belong to the mononuclear phagocytes system (reticulo-endothelial system) as modified monocytes derived from bone marrow.
- They contain elongated granules and are considered macrophages with possible antigenic properties.

JPERIODONTOl56:48, 1985



Human gingival epithelium, oral aspect. Immunoperoxidase technique showing Langerhans cells.

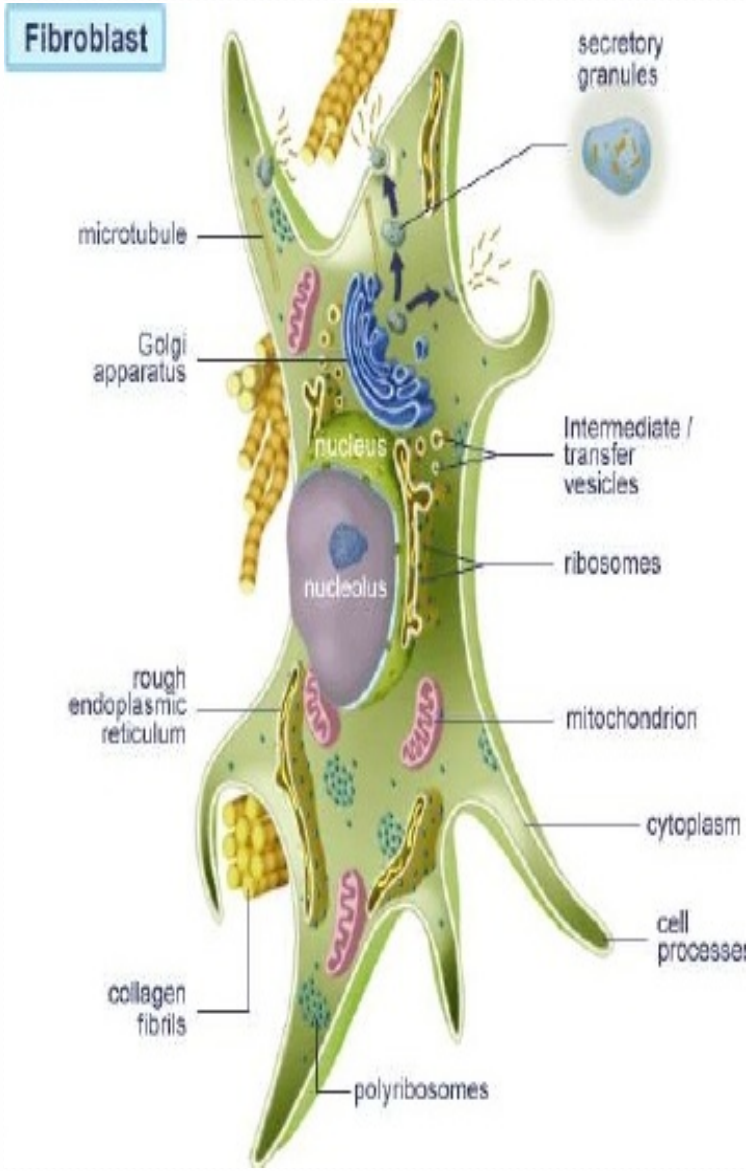
- They have an important role in immune reaction as antigen- presenting cells for lymphocytes.
- They contain g-specific granules (Birbeck's granules) and have marked adenosine triphosphatase activity.
- They are found in oral epithelium of normal gingiva and in smaller amounts in sulcular epithelium; they are probably absent from junctional epithelium of normal gingiva

Merkel cells

- They are located in deep layers of the epithelium, harbor nerve ending and are connected to adjacent cells by desmosomes.
- They have been identified as tactile receptors.

Fibroblasts

- The fibroblast is the predominant cell in the periodontal ligament.
- Fibroblasts origin in par from the ectomesenchyme of investing layer of dental paiplla and from dental follicle.
- These cells are different from cells in other connective tissue in number of respects for example rapid degradation of collagen by fibroblast phagocytosis is basis for fast turnover of collagen in periodontal ligament



- Periodontal ligament contains a variety of fibroblast cell populations with different functional characteristics. For xampe, fibroblasts on bone side of ligament shows abundant alkaline phosphatase activity than on tooth side.
- Developmental differences may also exist. It has been demonstrated that, the fibroblasts near cementum are derrived from ectomesenchymal cells of the investing layer of dental papilla, while fibroblasts near alveolar bone are derrived from perivascular mesenchyme.
- Fibroblasts are regularly distributed throughout the ligament, and are oriented with their long axis parallel to the direction of collagen fibrils.

- Fibroblasts are fusiform and arranged parallel to the tooth surface on examination of the ligament sectioned only in longitudnal plane. If the ligament is sectioned both transversely and longitudnally, cells take the formm of flattened irregular disk.
- The fibroblasts are large cells with extensive cytoiplasm and abundant organelles, associated with protein synthesis and secretions.
- The nuclus occupies a large volume og cells and contains one or more prominent nucleoli.
- During development and initial formation of periodontal ligament, the fibroblast appears very active with extensive network of rough endoplasmic reticulum, well developed golgi apparatus and abundant secretory granules containing type 1 collagen molecules.

- The cells also develops long and thin cytoplasmic extensions that form three dimensional veils that compartmentalize collagen fibrils into fibers
- These cells also have developed cytoskeleton and shows contracts of adherns and gap junction types.
- Golgi complex contains several Golgi stacks, comprised of cisternae and terminal saccules.
- The fibroblasts of periodontal ligament have cilia. These cilia are associated with control of the cell cycle or inhibition of centriolar activity.
- Fibroblasts produce growth factor and cytokines such as PDGF, BMP's, IL-1

FIBROBLAST-MATRIX ADHESION AND TRACTION

- Fibroblasts attach to substratum of extracellular matrix through surface receptors for collagen and fibronectin.

Assembly is initiated by binding soluble fibronectin molecules to cell surface integrin receptor (alfa5 beta 1 and alfa5 beta 3)

The cytoplasmic domain of integrin receptors attaches to the peripheral ctoplasmic proteins, talin.

Interacts with protein called vinculin

Conformational changes in vincullin causes it to bind to actin

Completing the molecular bridge between cells contractile apparatus and fibronectin in extracellular matrix

↓

The linkage extends from cytoplasmic contractile apparatus to extracellular collagen fibrin network.

↓

Exerting traction on the collagen fiberes

↓

This cell to matrix contact enables the extracellular matrix to exert an effect on cell shape and behaviour

DIFFERENCE BETWEEN PERIODONTAL LIGAMENT FIBROBLASTS AND GINGIVAL FIBROBLASTS

- Periodontal ligament fibroblasts are ectomesenchymal in origin whereas gingival fibroblasts are mesodermal in origin.
- Expression of alkaline phosphatase and cyclic AMP is more in periodontal ligament fibroblasts. Gingival fibroblasts are less proliferative.
- Periodontal ligament fibroblasts can generate a force for tooth erruption as they are motile and contractile.
- Fibroblasts in periodontal ligament are capable of degradation also.

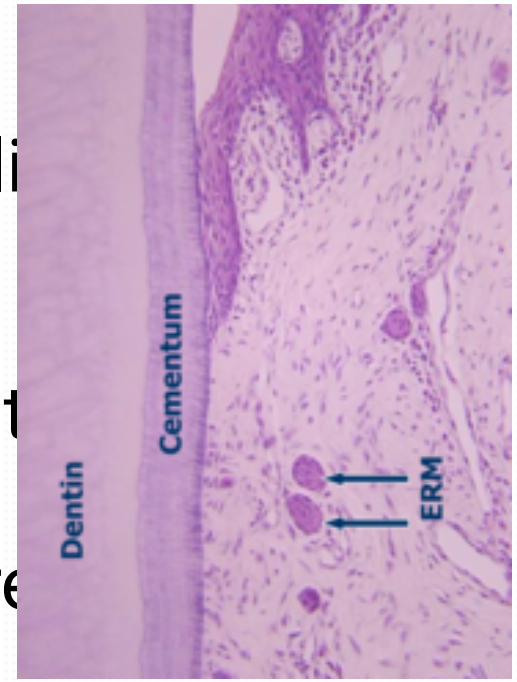
Functions

- Synthesize Collagen (Esterl 1961)
- Synthesize fibrils (Stallard 1963).
- Organize fibrous network & generate force for tooth eruption.
- Produce extracellular matrix of PDL (Sodek 1977).
- Have capacity to give rise to cementobalsts and osteoblasts.
- Maintain normal width of PDL.
- Synthesize and shape the proteins of ECM in which collagen fibrils form bundles and insert as Sharpey's fibers.
- Regulate collagen turnover by PHAGOCYTOSING old collagen fibers.

Epithelial rests of Malassez

.

- First described by Malassez in 1884.
- Found close to cementum.
- These are remnants of HERS (Hertwigs Epitheli root sheath).
- Epithelial rests persists as network, strand, islands, or tube like structure near and parallel t root surface.
- In cross section they appear cluster like and are abundant in furcation area.
- Function is not clear but could be involved in periodontal repair and regeneration.



Morphology

- The cell rests can be distinguished from fibroblasts in PDL by close packing of their cuboidal cells and their nucleus stains more deeply.
- The cytoplasm is scanty, and shows tonofibrils that inserts into desmosomes and into hemidesmosomes.
- Tight junctions are also seen between the cells and mitochondria is distributed throughout the cytoplasm.
- RER and golgi appratus are poorly developed, indicating lack of protein synthesis.

- The distribution of these cells varies according to the site and age.

- Upto the second decade, these cells are more commonly found in apical region, later they are mainly located cervically in the gingiva above the alveolar crest.
- These cell may proliferate to form cysts and tumours and may undergo calcification to become cementicles.

Mast cells

- Mast cell is relatively small, round or oval cell having diameter of about 12 to 15µm.
- Mast cells are often associated with blood vessels.

Morphology

- Characterized by numerous cytoplasmic granules, which frequently obscure the small, round nucleus.
- The granules stains with basic dyes but most readily demonstrated by virtue of their capacity to stain metachromatically with metachromatic dyes such as azure A.

- Electron microscopy of mast cells shows that the cytoplasm contains:
  - Free ribosomes
  - Short profiles of granular ER
  - Few round mitochondria
  - Prominent Golgi apparatus
  - Granules average about 0.5 to 1 μm in diameter and are membrane bound.

- Mast cell histamine play role in the inflammatory reaction, and mast cells have been shown to degranulate in response to Ag-Ab formation on their surface.
- Occasionally may be seen in healthy PDL.
- The release of histamine into extracellular environment cause proliferation of endothelial cell and mesenchymal cells
- Mast cells may play an important role in regulating endothelial and fibroblast cell population.

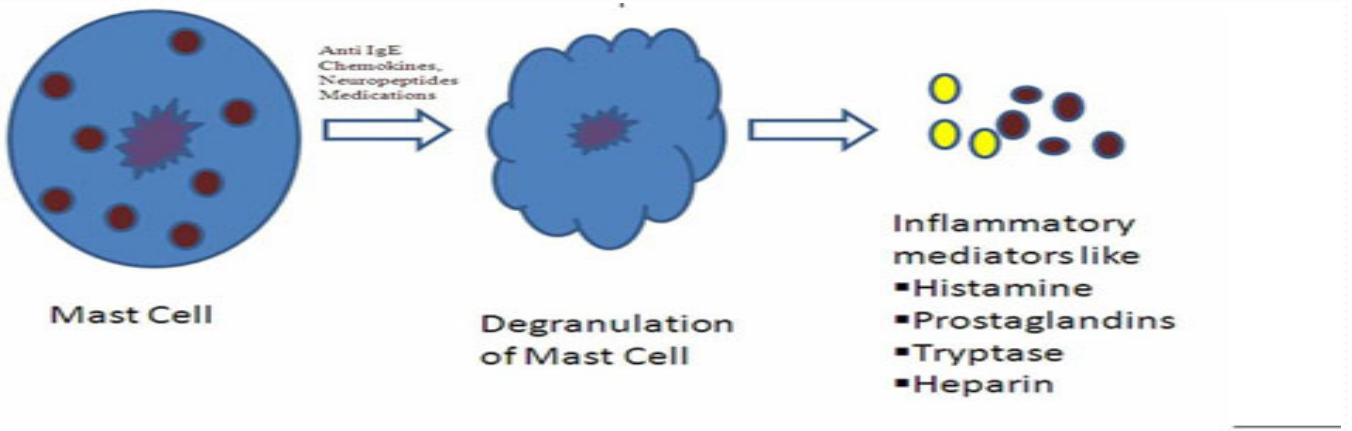


Figure.1 Mast cell degranulation leads to release of inflammatory mediators like histamine, heparin, tryptase and prostaglandins.

Macrophages

- Predominantly located adjacent to blood vessel.
- **Resting macrophages** can be distinguished from fibroblasts in the electronmicroscope by the presence of:
  - numerous microvilli
  - lysosome
  - membrane bound vesicles of various density
  - paucity of RER and golgi complex

- **Wandering types of** macrophage also has characteristic ultrastructure that differentiate from fibroblasts .
  - It has nucleus which may be horse shoe or kidney shaped and which exhibit a dense uneven layer of peripheral chromatin.
  - Nucleoli are rarely seen

Function

- In the PDL macrophage may have dual role:
  - Phagocytosing dead cells
  - Secreting growth factors that fregulate the proliferation of adjacent fibroblasts.
- Macrophages also sunthesize a range of molecules with important functions like,
  - Interferons
  - Prostaglandins
  - Factors that enhance the growth of fibroblast and endothelial cells.

Eosinophils

- Occasionally seen in PDL.
- They posses granules that consist of one or more crystalloid strucyure
- Cells are capable of phagocytosis.

Osteoblasts

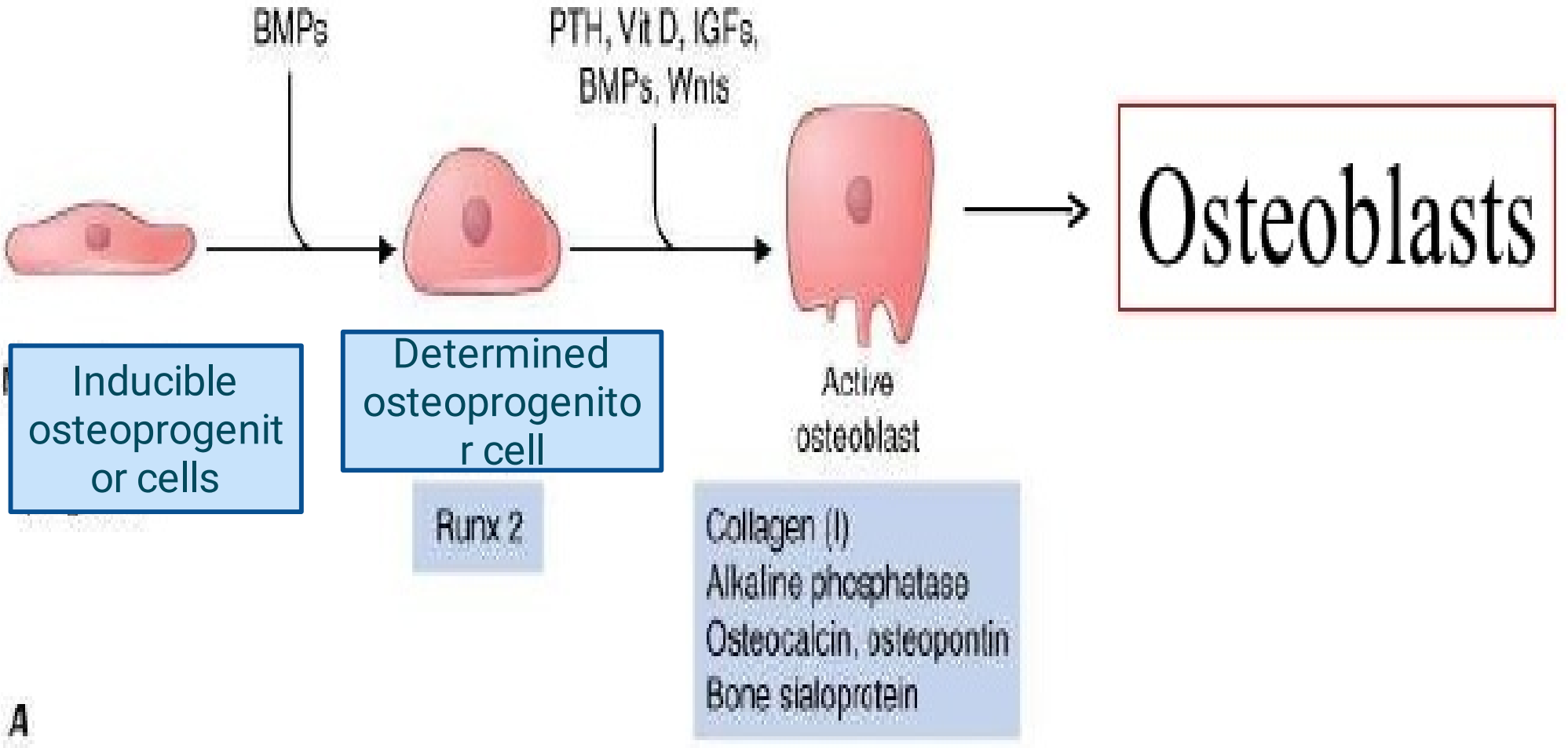
- The osteoblasts covers the periodontal surface of the alveolar bone. Alveolar bone constitutes a modified endosteum and not a periosteum. A periosteum comprises at least two distinct layers:
  1. **Inner -Cellular layer**
  2. **Outer –Fibrous layer**
- A cellular, but not an outer fibrous layer is present on periodontal surface of alveolar bone.

Morphology

- Osteoblasts are basophillic, plump cuboidal or slightly flattened cells.
- The cells are found on the forming surface of growing or remodelling bone.
- They form a protein mixture known as osteoid, which mineralizes to become bone.
- Osteoid is primarily composed of type 1 collagen.
- Osteoblasts exhibit abundant and well developed protein synthetic organelle.

- The intense cytoplasmic basophilia is due to an abundance of RER.
- Nucleus is situated in the part of the cell that is farthest away from the adjacent bone surface.
- The cells contact one another by adherns and gap junctions.
- Osteoblasts also contain prominent bundles of actin, myosin and cytoskeletal proteins which are associated with maintainence of cell shape, attachment and motility.

Maturation Pathway



Formation of Osteoblasts

- They are derrived from undiffrentiated pluripotent stem cells.
- Osteoprogenitor cells are divided into two types
  - Determined osteogenic precursor cells
  - Inducible osteogenic precursor cells
- The osteoprogenitor cells express transcriptional factor cbfa-1/Runx-2 and osterix which are essential for osteoblast diffrentiation.
- The activity of osteoblasts is regulated by hormones like PTH, vit D3, growth hormone and insulin.
- The other factors are BMPs, IGF-1 and 2, FGF, TGF-b and PDGF.

- They robustly produce alkaline phosphatase, an enzyme that has role in the mineralization of bone, as well as many matrix protein.
- Osteoblasts re the immature bone cells, and eventually become entrapped in the bone matrix to become osteoccytes, which are the mature bone cells.

Functions

- Formation of new bone via synthesis of various proteins and polysacharides.
- Regulation of bone remodelling and mineral metabolism.
- It plays significant role in the mineralisation of osteoid.
- They secretes type 1 collagen which is widely distributed and not unique to osteoblasts wheress, osteocalcin and cbfa-1 are specific to cells of osteoblast lineage.

- Osteoblasts also secretes small amount of type 5 collagen, osteonectin, osteopontin, RANKL, osteoprotegerin, proteoglycans, proteases,growth factors etc.
- They exhibit high level of alkaline phosphatase on outer surface of plasma membrane-used as a cytochemical marker to distinguish preosteoblasts from fibroblasts.
- Total alkaline phosphatase activiy has been reognised as a reliable indicator of osteoblasts functoion.

- Osteoblasts recognise the resorptive signal and transmit it to the osteoclast.
- RANKL is a membrane bound TNF related factors that is expressed by osteoblast/stromal cells. The presence of RANKL is vital in osteoclast diffrentiation.

OTEOCYTES

- Cells of mature bone.
- Lie in the lacunae of bone.
- Represents osteoblasts imprisoned in matrix during bone formation.
- Their functions include formation of bone, maintenance of matrix and homeostasis of calcium
- The number of osteoblasts that becomes osteocytes depends on the rapidity of bone formation.
- The average half life of human osteocytes is approx 25 years.
- During the preperation of ground substance the osteocytes are lost, but the spaces are filled with debris and appears black, when viewed under microscope.

- Within the bone matrix, the osteocyte reduces in size, creating a space around it called the osteocytic lacuna.
- The lacuna can appear ovoid or flattened.
- Narrow extensions of these launae form channels called canaliculi.
- The canaliculi do not extend through and beyond the reversal line surrounding an osteon, and so do not communicate with neighbouring systems.
- Osteocytic processes are present within these canaliculi.

- These processes contain bundles of microfilaments and smooth ER.
- At the distal end, these processes contact the processes of adjacent cells, i.e other osteocytes through gap junctions.
- They also maintain contact with osteoblasts and bone lining cell on the surface.
- The canaliculi penetrates the bone matrix and permit difusion of nutrients, gases and waste products between osteocytes and blood vessels.
- This interconnecting system maintains the bone integrity and bone vitality.

- Failure of the interconnecting system between osteocytes and osteoblasts leads to sclerosis and death of bone.
- Old osteocytes reteact their processes from the canaluculi, and when dead, their lacunae and cznaliculi may get plugged with debris.
- The death of osteocytes leads to rresorption of the matrix by osteoclasts.

Functions

- Maintains the integrity of the lacunae and canaliculi.
- Keep open the channels for diffusion of nutrients through bone.
- Play role in removal and deposition of matrix and of calcium when required.

Osteoclasts

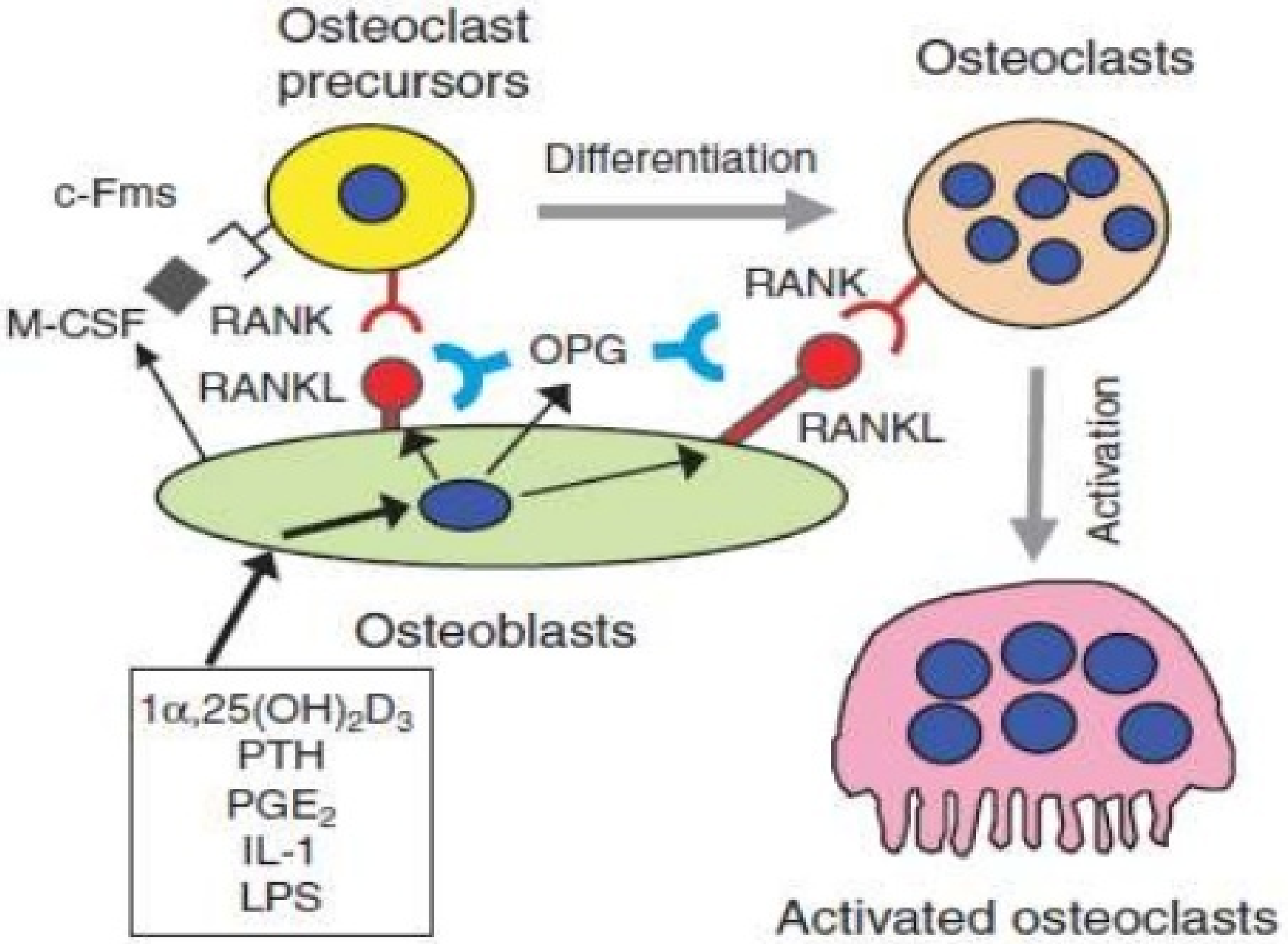
- Bone resorbing cells derived from hemopoetic cells of monocyte-macrophage lineage.
- The word osteoclast is derived from the Greek words for “one and broken”.

Morphology

- Osteoclasts lie inn resorption bay called Howship's lacunae.
- These are large cells approx 40-100μm in diameter with 15 to 20 closely packed nuclei.
- These cells are variable in shape due to their motility.
- The cytoplasm of the osteoclast shows acid phosphatase containing vesicles and vacuole.
- Mitochondria are extensive and distributed throughout the cytoplasm, except below the ruffled border.

- RER is relatively sparse for the size of the cell.
- Golgi complex is extensive and arranged in stacks.
- The cytoplasm also contains microtubules which transports vesicles between golgi stacks and ruffled membrane.
- Cathepsin containing vesicles and vacuoles are present close to the ruffled bordwer indicating resorptive activity of these cells.

OSTEOCLASTIC DIFFERENTIATION



Cementoblasts

- Cementoblasts are mesenchymal cells that form the cementum and are found lining the root surface, interposed between the periodontal fibers.

STRUCTURE

- Soon after Hertwig's sheath breaks up, undifferentiated mesenchymal cells from adjacent connective tissue differentiate into cementoblasts.
- Synthesize collagen & protein polysaccharides which make up the organic matrix of cementum.
- Have numerous mitochondria, a well-formed golgi apparatus, & large amounts of granular endoplasmic reticulum

- Active cells are round, plump with basophilic cytoplasm and all the organelles associated with protein synthesis.
- Inactive Cells or resting cells have little cytoplasm and closed nucleus.
- When acellular cementum is being formed, the cementoblasts rest behind the cementum matrix.
- When cellular cementum is being formed, the cementoblasts become trapped in lacunae with their own matrix and are then known as cementocytes

Cementocytes

- A typical cementocyte has numerous cell processes or canaliculi radiating from its cell body.
- Most of the processes are directed towards the periodontal surface of the cementum .
- Cytoplasm of cementocytes in deeper layers of cementum contains

(a) few organelles

(b)the endoplasmic reticulum appears dilated

(c) mitochondria are sparse .

Cementoclast

- They resemble osteoclast and are occasionally found in normal functioning periodontal ligament.
- Cementum is not remodeled in the fashion of alveolar bone and periodontal ligament but that it undergoes continual deposition during life.
- However, resorption of cementum can occur under certain circumstances.
- In these instances mononuclear cementoclasts or multinucleated giant cells, often located in howship's lacunae, are found on the surface of the cementum.
- The origin of cementoclast is similar to that of osteoclasts from ciruclating monocytes

Structure

- Cytoplasma exhibit numerous lysozomes and mitochondria.
- Ruffled border->part of plasma memberane lying adjacent to bone.
- Few ribosomes.
- Less rough endoplasmic retiuculum.

Conclusion

- Cell is basic unit of the organization containing plasma membrane cytoplasm and different organelles.
- Cell act as a store house of genetic material which is composed of chromosomes i.e. DNA and PROTEINS
- Genes present in nucleus determine the structure and function of proteins which enhance direct and control the various cellular processes and activities.
- Helps in co-relating the clinical findings with the disorders related to malfunctioning of specific organelles within the cell
- Cell biologists working in animal, plant and medical science will be able to develop new vaccines and more effective medicines.

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